Crucell

Crucell 2008
Combating Infectious Diseases

Annual Report and Form 20-F
www.crucell.com

Combating Infectious Diseases

Crucell's mission is to develop, produce and market vaccines and antibodies that prevent or treat infectious diseases.

Research & Development:
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Products:
p20

Technologies:
p30

For further information visit **www.crucell.com**

Cover photo
Crucell's coworker Marjolein van der Meer (Technician) submitted this photo of herself for an internal photo contest, wearing The Crucell Ambition T-shirt. The photo was taken during a visit to a friend who is doing volunteer work in Africa. The joyful energy of these children in a poor fishing village in Ghana is a powerful reminder of our shared ambition as Crucell employees: to improve global health by advancing the fight against infectious diseases.

Shareholders information
Crucell N.V. is a public limited liability company registered in the Netherlands. Crucell's shares are listed on NYSE Euronext (Amsterdam), and SWX Swiss Exchange (Zurich) stock exchanges and Crucell's American Depositary Shares (ADSs) are listed on NASDAQ (New York). The shares listed on NYSE Euronext, as well as the ADSs listed on NASDAQ, are traded under ticker symbol CRXL. The shares trade under ticker symbol CRX at SWX Swiss Exchange.

Our website can be found at www.crucell.com.

This publication comprises the full Annual Report that complies with all applicable Dutch regulations for statutory purposes and the Form 20-F for filing with the Securities and Exchange Commission (SEC) in the US. Cross-references to Form 20-F are set out on pages 188 to 189.

The Crucell 2008 Annual Report and Form 20-F (hereinafter referred to as the Annual Report) is prepared in English as approved by the General Meeting of Shareholders and expressed in Euro. All amounts set forth in this Annual Report, unless otherwise noted, are in thousands of Euro, except share and option data.

2008 Key Highlights

- Profitability for the year 2008
- Additional contracts Quinvaxem® and Hepavax-Gene® bring total to $0.5 billion for the period 2007-2009
- Hepavax-Gene® approved in China
- Flu antibody outperforms oseltamivir
- Rabies antibody combination and tuberculosis vaccine enter Phase II
- Important advances made in antibody production using PER.C6® technology
- Record yield of over 27 g/L of an antibody product achieved
- First PER.C6® licensee entered Phase III
- Key license agreements signed

€283.3 mln

Total revenues and other operating income in 2008
An increase of 33% compared to €213.1 mln in 2007.

45%

Gross margin in 2008
Significant improvement from 34% in 2007.

€14.6 mln

Net profit in 2008
Compared to a net loss of €42.9 mln in 2007.

Crucell at a Glance

Who we are

Crucell is a fully integrated biopharmaceutical company. We focus on developing, producing and marketing products that combat infectious diseases. We are the largest independent vaccine company in the world. The sustainability of our business is demonstrated by our solid balance sheet and strong cash position, as a consequence we do not need to raise capital in the foreseeable future. For a company of our size, we invest relatively heavily in research and development: our R&D expenditures in 2008 were €70 million.

Strategy

We develop products that address currently unmet medical needs, particularly in the field of infectious diseases. We have a fully integrated infrastructure for in-house development, production and marketing of vaccines, and we are leveraging our knowledge in the vaccines field to excel in the antibodies market. Our competitive edge comes from our proprietary technology platforms like PER.C6®, which is used to produce high-value biotech products in scalable and cost-efficient ways. This combination of markets we operate in, technological knowledge and quality marketed products, positions us to be a major player in the multi-billion dollar biopharmaceutical arena.

We are a fully integrated biopharmaceutical company, focusing on developing, producing and marketing products that combat infectious diseases.

Partners and licensees

In addition to our own research and development activities, we have strategic partnerships with several leading healthcare companies. Through these agreements, our technologies play a vital role in the development of a vast number of vaccines and antibody products. Some examples of partners and licensees we work with are mentioned below.

- CSL
- DSM Biologics
- Gedeon Richter
- GSK
- MedImmune
- Merck
- Novartis
- Sanofi pasteur
- Talecris
- Wyeth

Why infectious diseases?

Infectious diseases currently account for a significant number of human casualties throughout the world. The number of infectious outbreaks is increasing for many reasons: higher population density which raises exposure to infectious agents; an ageing population which is more susceptible to infection; and the volume of global travel which boosts the potential for spreading diseases across borders.

€171.0 mln

Cash and cash equivalents at year-end 2008
Strong cash position to invest in profitable growth.

33%

Growth in 2008
Revenues and other operating income growth.

We have strategic partnerships with leading international healthcare companies.

€0.22

Net profit per share in 2008
Compared to net loss per share of €0.66 in 2007.

Crucell: A Global Perspective

Global facilities

Technology	Research	Development	Manufacturing	Sales & Marketing
Netherlands HQ	Netherlands	Netherlands	Netherlands	Netherlands (Benelux)
Switzerland	USA*	Switzerland	Switzerland	Switzerland
USA*			Sweden	Sweden (Nordic)
			Spain	Spain
			Korea	Italy
				Korea
				China
				Indonesia
				Vietnam
				Argentina
				Canada
				USA

* PERCIVIA, a Joint Venture with DSM Biologics

We have a fully integrated infrastructure for in-house development, production and marketing of vaccines.

80+

We sell our vaccines in over 80 countries.

Products

Our vaccine business provides stable and predictable sales and cash flow. We sold more than 100 million vaccine doses in over 80 countries throughout the world, which makes us the largest independent vaccine player. Within vaccines we operate in three main markets: paediatric, travel and endemic, and respiratory.

Pipeline

We have a number of programs in various stages of development. Most of these are based on Crucell's innovative PER.C6® technology.

Technologies

We have five core technologies; of which PER.C6® technology is Crucell's most important proprietary technology. With over 60 commercial licenses issued on PER.C6® technology, Crucell has set new industry standards for the development and industrial-scale manufacturing of vaccines, recombinant proteins including monoclonal antibodies, and gene therapy products.

We license proprietary technologies to the biopharma market.

Products

Paediatric:
Quinvaxem® vaccine against five important childhood diseases.
Epaxal® Junior aluminum-free hepatitis A vaccine for children.
Hepavax-Gene® vaccine against hepatitis B.
MoRu-Viraten® vaccine against measles and rubella.

Travel and Endemic:
Epaxal® aluminum-free hepatitis A vaccine.
Vivotif® oral typhoid vaccine.
Dukoral® oral cholera vaccine.

Respiratory:
Inflexal® V virosomal adjuvanted influenza vaccine.

Details on:
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Research & Development

Vaccines in development:
- **Yellow fever**
- **Influenza seasonal**[1]
- **Tuberculosis**
- **Malaria**
- **Ebola and Marburg**
- **HIV**

Human antibodies in development:
- **Rabies antibody combination**
- **Influenza antibodies H1 & H5**

Details on:
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[1] Developed by sanofi pasteur using PER.C6®.

Technologies

PER.C6® human designer cell line for the development and large-scale manufacturing of biopharma products.
AdVac® used in combination with PER.C6®, to develop recombinant vaccines.
MAbstract® applied for discovery of novel drug targets and identification of human antibodies.
STAR® designed to enhance production yields of recombinant human antibodies and proteins on mammalian cell lines.
Virosome a vehicle enabling the use of virus antigens in the making of vaccines.

Details on:
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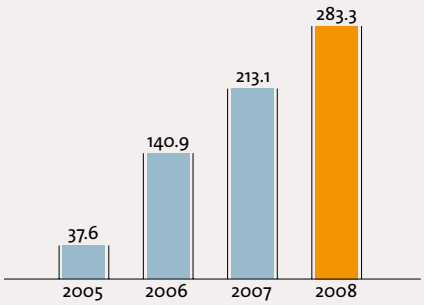
Performance Highlights

20%

2009 outlook for total revenues and other operating income.[1]

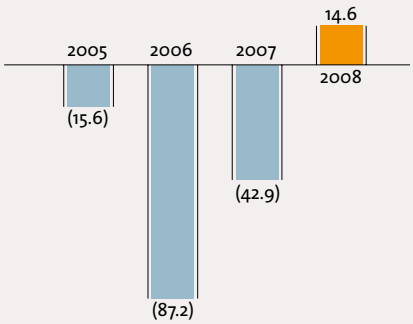
Financials

Total revenues and other operating income
(€ million)

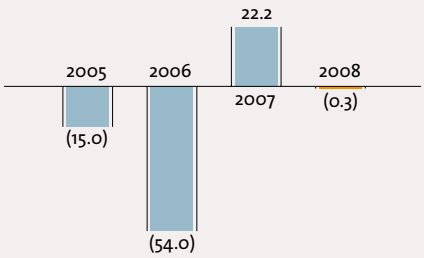


45% gross margin in 2008 and improving

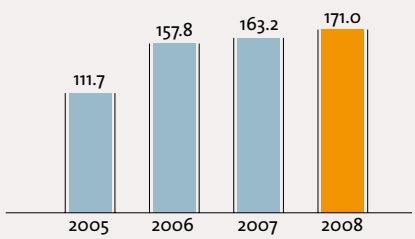
Profit (loss) for the period
(€ million)



Net cash flow from operating activities
(€ million)



Cash and cash equivalents at December 31
(€ million)



[1] Guidance currency = EUR/USD rate of 1.35.

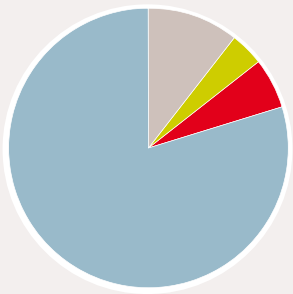
Profitable and strong cash position

€171.0 mln

2008 year-end cash position.

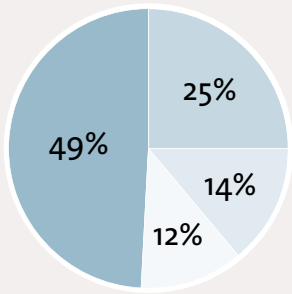
Revenues and other operating income

Revenues and other operating income
(€ million)



Product sales	226
License fees	30
Service fees	11
Other operating income, e.g. grants	16
Total	**283**

2008 Product sales
(€226 million)



- Paediatric
- Travel and Endemic
- Respiratory
- Other

Outlook for 2009

Total revenues and other operating income[1]	20% growth
Operating profit	Significantly improved
Cash flow	Solid

[1] Guidance currency = EUR/USD rate of 1.35.

Performance Highlights continued

Selected financial data

Our consolidated financial statements and company financial statements (hereinafter referred to as the 'financial statements'), and the notes thereto, as of and for the years ended December 31, 2008, 2007 and 2006 have been prepared in accordance with International Financial Reporting Standards ('IFRS') as endorsed by the European Union ('EU') and as issued by the International Accounting Standards Board ('IASB'). No differences resulted in our financial statements as a result of the preparation in accordance with IFRS as endorsed by the EU and IFRS as issued by IASB as applied to Crucell.

For the years prior to 2006, we prepared our financial statements, as included in form 20-F, in accordance with accounting principles generally accepted in the US ('US GAAP'), which differs in certain significant respects from, and is not comparable with, IFRS. On December 21, 2007 the SEC approved rule amendments under which Form 20-F as prepared by Foreign Private Issuers (FPIs) will no longer require reconciliation to US GAAP if the financial statements are prepared in accordance with IFRS as issued by the IASB. This rule is applicable for the 2008 financial year. As a result, we do not provide reconciliation to US GAAP.

In May 2006, we published our 2005 Annual Report as required under Dutch law. In the Annual Report we presented our financial statements as of and for the years ended December 31, 2005 and 2004 prepared in accordance with IFRS. The 2004 consolidated financial statements are the first comparative figures that have been prepared in accordance with IFRS.

When we adopted IFRS for the first time, pursuant to IFRS 1, we elected to use one exemption. Business combinations that were recognized before January 1, 2004 were not restated to IAS 22/IFRS 3 'Business Combinations'.

The following table shows the selected financial data under IFRS for the years ended December 31, 2004 through 2008.

The selected financial data should be read in conjunction with 'Operating and Financial Review and Prospects' and our financial statements and accompanying notes thereto, included elsewhere in this Annual Report.

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IFRS selected financial data

Year ended December 31, (In thousands of Euro, except share data)	2008	2007[1]	2006[1]	2005	2004
Consolidated income statement data:					
Revenues:					
Product sales	**226,055**	177,569	103,918	—	—
License revenues	**30,202**	12,211	16,955	20,848	12,429
Service fees	**10,900**	14,006	10,694	11,881	5,712
Total revenues	**267,157**	203,786	131,567	32,729	18,141
Total cost of goods sold	**(145,755)**	(134,884)	(90,489)	(7,156)	(5,644)
Gross margin[2]	**121,402**	**68,902**	**41,078**	**25,573**	**12,497**
	45.4%	*33.8%*	*31.2%*	*78.1%*	*68.9%*
Total other operating income	**16,152**	9,330	9,356	4,840	4,481
Operating expenses:					
Research and development	**(70,229)**	(63,995)	(67,606)	(34,048)	(23,676)
Selling, general and administrative	**(64,350)**	(61,752)	(46,732)	(13,689)	(16,819)
Restructuring	**—**	—	(3,120)	—	—
(Reversal of) impairment	**4,888**	(171)	(30,416)	—	—
Total other operating expenses	**(129,691)**	(125,918)	(147,874)	(47,737)	(40,495)
Operating profit/(loss)	**7,863**	(47,686)	(97,440)	(17,324)	(23,517)
Financial income	**6,935**	13,190	13,453	2,332	1,789
Financial expenses	**(9,597)**	(11,812)	(11,706)	(131)	(394)
Results non-consolidated companies	**1,442**	1,190	(1,956)	(455)	(704)
Disposal of subsidiaries	**(367)**	—	—	—	—
Profit/(loss) before tax	**6,276**	(45,118)	(97,649)	(15,578)	(22,826)
Income tax	**8,310**	2,208	10,451	—	—
Profit/(loss) for the year	**14,586**	(42,910)	(87,198)	(15,578)	(22,826)
Net profit/(loss) per share – undiluted	**0.22**	(0.66)	(1.52)	(0.39)	(0.63)
Weighted average shares outstanding – undiluted	**65.593**	65,103	57,064	39,852	36,383
Consolidated balance sheet data:					
Assets:					
Cash and cash equivalents	**170,969**	163,248	157,837	111,734	76,711
Total current assets	**322,318**	303,262	317,071	131,038	84,155
Total assets	**636,297**	629,838	653,961	169,737	101,015
Liabilities and shareholders' equity:					
Total shareholders' equity	**453,492**	441,103	497,886	137,609	80,659
Total non-current liabilities	**64,504**	73,993	65,823	9,380	5,583
Total current liabilities	**118,301**	114,742	90,252	22,748	14,773
Total liabilities and shareholders' equity	**636,297**	629,838	653,961	169,737	101,015
Number of employees	**1,126**	1,126	1,073	282	210

[1] 2007 and 2006 numbers have been adjusted retrospectively, following the adoption of IFRIC 14 as of January 1, 2008.
[2] Gross margin = total revenues less cost of goods sold.

Message from our CEO

In 2008, Crucell's vaccines were administered to a vast number of people worldwide, thereby preventing more than 3 million cases of infectious disease and over 700,000 deaths that would otherwise have occurred.

Dear fellow shareholder,
I am very proud that for the first time in the history of Crucell, we achieved profitability for the full year. Together with strong revenue growth and cash position, we were able to end 2008 on a historic high.

Crucell is a rapidly growing biopharmaceutical company with ambitious goals. We aim to create shareholder value by following a clear and convincing strategy for profitable growth. Our core business is stronger than ever and, with a clear strategy for sustainable growth and even more focus on research and development activities, we continue to increase the number of people we can protect from infectious diseases.

The progress we made in 2008 is a clear indication that we are executing on our strategy – The Crucell Ambition. Autonomous growth is the major theme underlying all our efforts; our sales in 2008 increased by 33% compared to 2007 and were driven by strong sales of our paediatric vaccines, travel and endemic vaccines as well as a doubling in license revenues and licensee milestone income. In 2008 Crucell sold more than 100 million vaccine doses in more than 80 countries throughout the world, which makes us the largest independent vaccine player in the world.

The significant growth of Quinvaxem® in 2008 is expected to continue in 2009. This product makes a significant contribution to children's vaccination programs in the developing world and is Crucell's best selling product. Quinvaxem® has enabled the company to become a major supplier to paediatric vaccination programs worldwide.

We intend to use the expansion into new markets and the sales and marketing potential of our marketed products as an important driver for future growth. This growth will further be supported by the progress of our clinical programs, in particular our rabies antibody combination, our tuberculosis and malaria programs, as well as a revolutionary discovery of monoclonal antibodies which have the potential of being used as a universal therapy against flu.

Our PER.C6® cell line production process has already proven that it is fully scalable, producing high yields in large bioreactors, and transfers seamlessly to large-scale GMP manufacturing. Furthermore, another key milestone was achieved with the PER.C6® technology in 2008 when our scientists reached a record production level of 27 g/L at harvest for an antibody product. This demonstrates the power and robustness of the PER.C6® technology and shows the impact it will have to the overall economics of manufacturing biopharmaceuticals. This was reflected in the increased number of licensees and income we realized in 2008.

As we grow further, capturing synergies and rationalization becomes ever more important. A rigorous review of Crucell's business processes

worldwide has been completed. Our operational excellence program 'Healthy Ambition' was rolled out in 2008. The program is targeting savings of €30 million by the end of 2009; initial net cost savings of €5 million were achieved in the second half of 2008. This program contributed to our positive results through improved yields in our production facilities, savings in overhead and several other 'quick wins' delivered in 2008.

Crucell understands its responsibilities with regard to the environment and strives to be as transparent as possible about its activities. This year we included a special section, in which we take the opportunity to share with you our ideas, ambitions and activities regarding Corporate Social Responsibility (CSR). Crucell is fully committed to being a good corporate citizen and conducting business in an honest and ethical way with the lowest possible environmental footprint. See page 34 of this 2008 Annual Report, for more information on our CSR activities.

For 2009, we expect another good year for Crucell. Our sense of shared purpose is stronger than ever, and we look forward to the ongoing growth of our product sales as well as further progress of our pipeline programs.

Our achievements so far are thanks to the tireless efforts and motivation of our employees, Crucell's most important asset, and to your willingness as a shareholder to invest in Crucell. We thank you for your continuous support.

Ronald H.P. Brus
President and Chief Executive Officer
Leiden, the Netherlands, April 21, 2009

Our ambition:
Protect lives from infectious diseases by bringing innovation to global health.

"We are proud to prevent a significant number of deaths as the largest independent vaccine player in the world."

Ronald H.P. Brus
President and
Chief Executive Officer

The Crucell Ambition

"The Crucell Ambition has focused and aligned the company. We are now all moving in the same direction."

"A logical step that is good for Crucell as a company and brings clarity to its employees."

1

THIS SIDE UP
THE CRUCELL AMBITION

The Crucell Ambition is a strategic program encompassing coordinated efforts in the four priority areas: Organization & People, Focus, Operational Excellence and Deliver on Promises. In 2008, The Crucell Ambition was rolled out throughout the whole organization and the Management Board has met with more than 60% of Crucell's employees from different parts of the organization. The priority areas, which were carefully defined after a thorough review of Crucell's operations, objectives and potential, are described as follows:

Quotes:
Taken from Crucell employees about The Crucell Ambition.

Images:
Examples of photos submitted by employees for an internal photo contest.

1 Winning photo
2 Runner up

"Working for Crucell makes every day, however long or challenging, fun!"

The Crucell Values

Integrity

Respect

Complementarity

Reliability

Innovation

Passion and Drive

Organization & People

Development of our organization and our people is the foundation for achieving our ambition as a company. Multiple measures are being implemented to develop this, such as talent management, linking our company values to performance measurement and sharing knowledge across disciplines.

Operational Excellence – Healthy Ambition

Crucell launched its 'Healthy Ambition' operational excellence program at the start of 2008 and is now implementing the validated plans drawn up in the first half of 2008. By streamlining and optimizing our business processes, the program is expected to generate run-rate cost savings of €30 million by the end of 2009, of which €5 million have already been achieved in the second half of 2008.

Focus – Focused Ambition

Crucell is clearly focused on its mission to protect human lives from infectious diseases by bringing innovation to global health. We are building on our strengths by prioritizing those programs that are in line with this ambition and that contribute to our strategic and financial objectives. Focused investments of both human capital as well as cash enables us to increase successful innovation.

Deliver on Promises

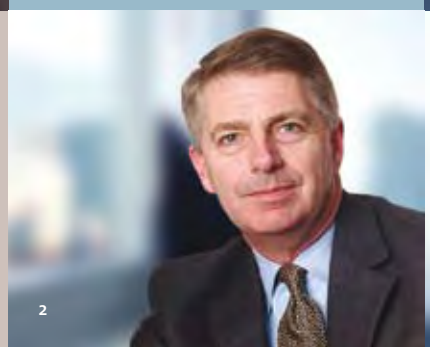
Crucell has set its sights high and is firmly committed to delivering on its ambitious promises. Evidence-based target setting and a company-wide emphasis on organization and people, focus and operational excellence will enable us to do so. Ultimately delivering on promises to all our stakeholders.

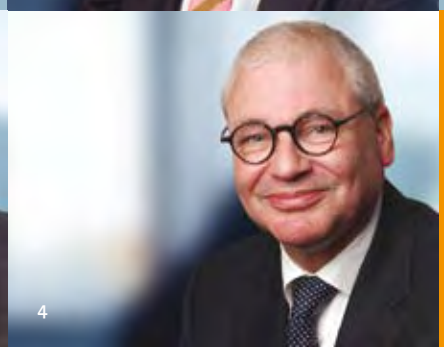
1 Ronald Brus
President and Chief Executive Officer

2 Leonard Kruimer
Chief Financial Officer

3 Cees de Jong
Chief Operating Officer

4 Jaap Goudsmit
Chief Scientific Officer





Management Committee

Crucell has a two-tiered board structure in which executive and supervisory responsibilities are clearly separated.

The Supervisory Board is comprised of independent, non-executive individuals who are charged with supervising and advising Crucell's Management Board.

The Management Board, which is a subset of the Management Committee, is responsible for the general affairs and business of the company and, as such, is responsible for achieving Crucell's goals, strategy and policy, as well as results.

Dr. Ronald Brus (1963)*
President and Chief Executive Officer

Dr. Ronald Brus is Crucell's President and Chief Executive Officer. He has been a member of Crucell's Management Committee since the company's incorporation and was formerly Chief Operating Officer (March 2003 to January 2004) and Chief Business Officer (October 2000 to February 2003). Prior to that, he was Executive Vice President Business Development after joining the company in 1997. From 1994 to 1996 he was product planning physician at Forest Laboratories in New York and from 1990 to 1994 he was Medical Director for Zambon B.V. He holds a medical degree from the University of Groningen, the Netherlands.

Dr. Brus is Chairman of the Management Board.

Leonard Kruimer (1958)*
Chief Financial Officer

Mr. Kruimer has been Chief Financial Officer, since he joined Crucell in 1998 and is a member of Crucell's Management Board and Management Committee. Prior to Crucell, he held interim executive positions at Pepsico and Royal Boskalis Westminster. From 1993 to 1995, he was Managing Director Continental Europe at TIP Europe, a unit of GE Capital. Prior he held senior executive positions at Kwik-Fit Europe and Continental Can Europe. He was a consultant with McKinsey & Co and started his career at PriceWaterhouse & Co in New York. He holds an MBA from the Harvard Graduate School of Business Administration and an undergraduate degree from the University of Massachusetts. He is a CPA in New York State.

Dr. Cees de Jong (1961)*
Chief Operating Officer

Dr. Cees de Jong joined Crucell as Chief Operating Officer in September 2007. He became a member of Crucell's Management Board in May 2008. Prior he worked at Quest International in Naarden, the Netherlands, as a member of the Board responsible for the Flavours Division. Prior to Quest, he worked as Managing Director of DSM Anti-infectives. In 1989 he started his career at Gist Brocades, holding a variety of roles in Business Development, Strategy and General Management before the company's acquisition by DSM in 1998. He holds a medical degree and earned

5 René Beukema
General Counsel and Corporate Secretary

6 Arthur Lahr
Chief Strategy Officer and EVP Business Development

7 Björn Sjöstrand
Chief Business Officer

an MBA at the Erasmus University Rotterdam, the Netherlands.

Dr. Jaap Goudsmit (1951)* Chief Scientific Officer

Dr. Jaap Goudsmit is Crucell's Chief Scientific Officer and is responsible for all R&D activities. He became a member of Crucell's Management Board in January 2004. He joined Crucell in 2001 as Senior Vice President Vaccine Research and became a member of Crucell's Management Committee in July 2002. Prior to that, he held various positions at the Academic Medical Center at the University of Amsterdam and was Chairman of the Research Institute for Infectious Diseases and the Institute for Science Education. Since 1989 he has been a professor at the University of Amsterdam and the Academic Medical Center. He holds a medical degree and a PhD from the University of Amsterdam, the Netherlands.

René Beukema (1964) General Counsel and Corporate Secretary

Mr. Beukema is Crucell's General Counsel and Corporate Secretary since the company's incorporation. He held the same position at IntroGene after joining the company in 1999. From 1994 to 1999, he was Senior Legal Counsel for GE Capital/TIP Europe. From 1991 to 1994, he was Legal Counsel for TNT Express Worldwide N.V. He has a Masters in Law from the University of Amsterdam, the Netherlands.

Arthur Lahr (1968) Chief Strategy Officer and Executive Vice President Business Development

Mr. Arthur Lahr is Crucell's Chief Strategy Officer and Executive Vice President Business Development. He joined Crucell in April 2001 as Executive Director Business Development and became a member of the Management Committee in January 2004, Executive Vice President in January 2006 and assumed responsibility for European marketing & sales and company strategy in 2006. From 1994 to 2001 he was a consultant with McKinsey & Co. in the Netherlands and New York. Prior to that, he worked at Unilever. He holds a Masters in Business Administration from INSEAD and a Masters in Science in Applied Physics from the University of Delft, the Netherlands.

Björn Sjöstrand (1968) Chief Business Officer

Mr. Björn Sjöstrand is Chief Business Officer and a member of Crucell's Management Committee. He was Chief Executive Officer at SBL Vaccines before it was acquired by Crucell in November 2006. He headed the Crucell-SBL integration committee and directed the travel franchise and the Nordic sales force for the Crucell Group. Prior he worked as Vice President Operations & IT at Active Biotech and was a member of the Senior Management Team. He completed a Bachelor of Science (BSc) degree in Economics and Business Administration at the University of Örebro, Sweden. He also studied Financial Investment theory and Commercial law at the same university.

❁ Full details of the Management Committee can be found on page 110.

* Member of the Management Board.

1 Jan Pieter Oosterveld
Chairman
2 Arnold Hoevenaars
3 Steve Davis
4 Seán Lance
5 Phillip Satow
6 Claes Wilhelmsson

Report of the Supervisory Board

Dear shareholder,
The Supervisory Board is pleased to submit to you the combined Annual Report and Form 20-F, including the financial statements of Crucell N.V. for the year ended December 31, 2008, as prepared by the Management Board. Attached to the financial statements is the auditor's report by Deloitte Accountants B.V., free from any qualification. We adopted the financial statements for the year 2008 and advise the General Meeting of Shareholders to approve these statements and to grant discharge to the Management Board, with respect to its management; and to the Supervisory Board, with respect to its supervision.

The Supervisory Board held seven meetings with the Management Board in 2008, of which three were in the form of conference calls. The meetings were arranged in such a way that on several occasions, the Supervisory Board could meet immediately after the departure of the Management Board, so called closed sessions. There were also a number of more informal contacts between Supervisory Board Members and the Management Board.

The Supervisory Board was closely involved in all developments affecting the company in terms of strategy, tactics and operations in the financial year 2008. The Board's meeting schedule not only reflects its commitment to the company's affairs, but also to the dynamic way in which the company is rapidly consolidating its position in the biotech industry. Thanks to the well-documented information provided by and to the frequent discussions with the Management Board, the Supervisory Board was able to acquire a comprehensive perspective on all aspects of the company's strategy. Where Supervisory Board approval of proposals was required, it was able to arrive at decisions based on solid facts and coherent arguments.

All Supervisory Board meetings and conference calls were well attended. Regular items on the agenda included the company's financial performance, based on quarterly reports, its budget and its business, including the research and development portfolio, intellectual property matters and operational updates. Importantly the Board also discussed the company's strategy and its near-; mid- and long-term risks, the current and future strategic objectives, planned acquisitions, our DSM collaboration and the reports from the Audit Committee and the Remuneration Committee. Other significant issues addressed were compliance with Section 404 of the American Sarbanes-Oxley Act of 2002 and related regulations (SOX 404), the ongoing corporate rationalization processes and the progress made in integrating acquired businesses.

The Supervisory Board also discussed its own performance, reviewing its function and its individual members; and the performance of the Management Board and its individual members. The friendly discussion which took place between Wyeth and Crucell to explore a potential combination of the two companies was also discussed with the Supervisory Board and its financial advisors.

Supervisory Board Committees

In order to make decisions, the Supervisory Board has established an Audit Committee, a Remuneration Committee, a Nomination Committee and a Scientific Committee. For detailed information on the composition and activities of these committees see page 107 of this 2008 Annual Report.

In 2008 the Audit Committee met ten times, of which six were held by conference calls. The company's external auditor, Deloitte, routinely attended these meetings, in particular where the


4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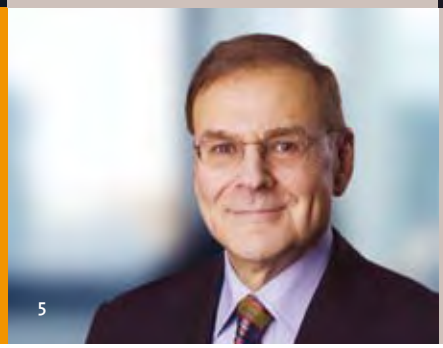
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Annual Report, the auditor's report and the quarterly results were discussed.

The Nomination Committee consists of the full Supervisory Board and, as such, met four times during the 2008 fiscal year to discuss the Supervisory Board's composition and functioning. The Scientific Advisory Committee held four meetings with R&D management to discuss issues around protein production and various infectious diseases. They also covered R&D budgets and organizational matters.

The Remuneration Committee met five times, of which one via conference call, to review collective 2008 milestones and set objectives for 2009; to approve and ratify option grants and to discuss the remuneration policy for second and third tiers of management. The Remuneration Committee and the Supervisory Board operate within the framework of the remuneration policy for the Management Board, which was amended and adopted by the Annual General Meeting of Shareholders in May 2008. The remuneration of the Management Board members is determined by the Supervisory Board, based on a proposal by the Remuneration Committee. It conforms to market practice and is aimed at attracting qualified and expert management with the skills required to run a publicly listed company active in the biotechnology industry.

The remuneration of members of the Supervisory Board complies with almost all aspects of the provisions of the Dutch Corporate Governance Code. The exceptions are where it conforms more closely to customary practice in the biotechnology industry worldwide. These exemptions are disclosed in the section 'Corporate Governance – Exceptions to Compliance with the Code'.

The compensation of all Supervisory Board members consists of a fixed fee in cash and an annual share grant. Instead of the share grant, a Supervisory Board member may instead choose to receive a cash amount equaling the value of the share grant minus a discount.

The remuneration of the Supervisory Board is further detailed in note 5.23 of our financial statements. The remuneration policy can be found on Crucell's website (www.crucell.com), which is not incorporated by reference herein.

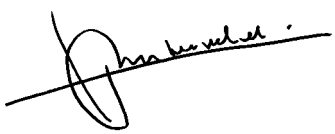
The Nomination Committee initiated a global search to fill the vacancy in the Supervisory Board. As a result, and after careful consideration, the Supervisory Board is pleased to report that Steve Davis was appointed to the Supervisory Board by Crucell's shareholders in May 2008. At the same time Dominic Koechlin resigned.

External auditors

Deloitte Accountants B.V. have been Crucell's external auditors since 2006. The performance of Deloitte will be evaluated by the Audit Committee, which will present its findings to the full Board.

The Supervisory Board would like to thank the Management Board, the Management Committee, senior management and all employees for their devotion, their motivation and their loyalty in a year in which we achieved profitability for the full year, we continued to show significant growth and took further strides toward realizing Crucell's ambitious aspirations.

Finally we would like to thank our shareholders for their continued support.



Jan P. Oosterveld
Chairman of the Supervisory Board
Leiden, the Netherlands, April 21, 2009

Our Products and Research & Development Pipeline

Epaxal® Junior

Inflexal® V

€283.3 mln

Total revenues and operating income
Continued strong autonomous product growth.

MoRu-Viraten®

Quinvaxem®

Epaxal®

100+ mln

Vaccine doses sold in 2008.

Dukoral®

Hepavax-Gene®

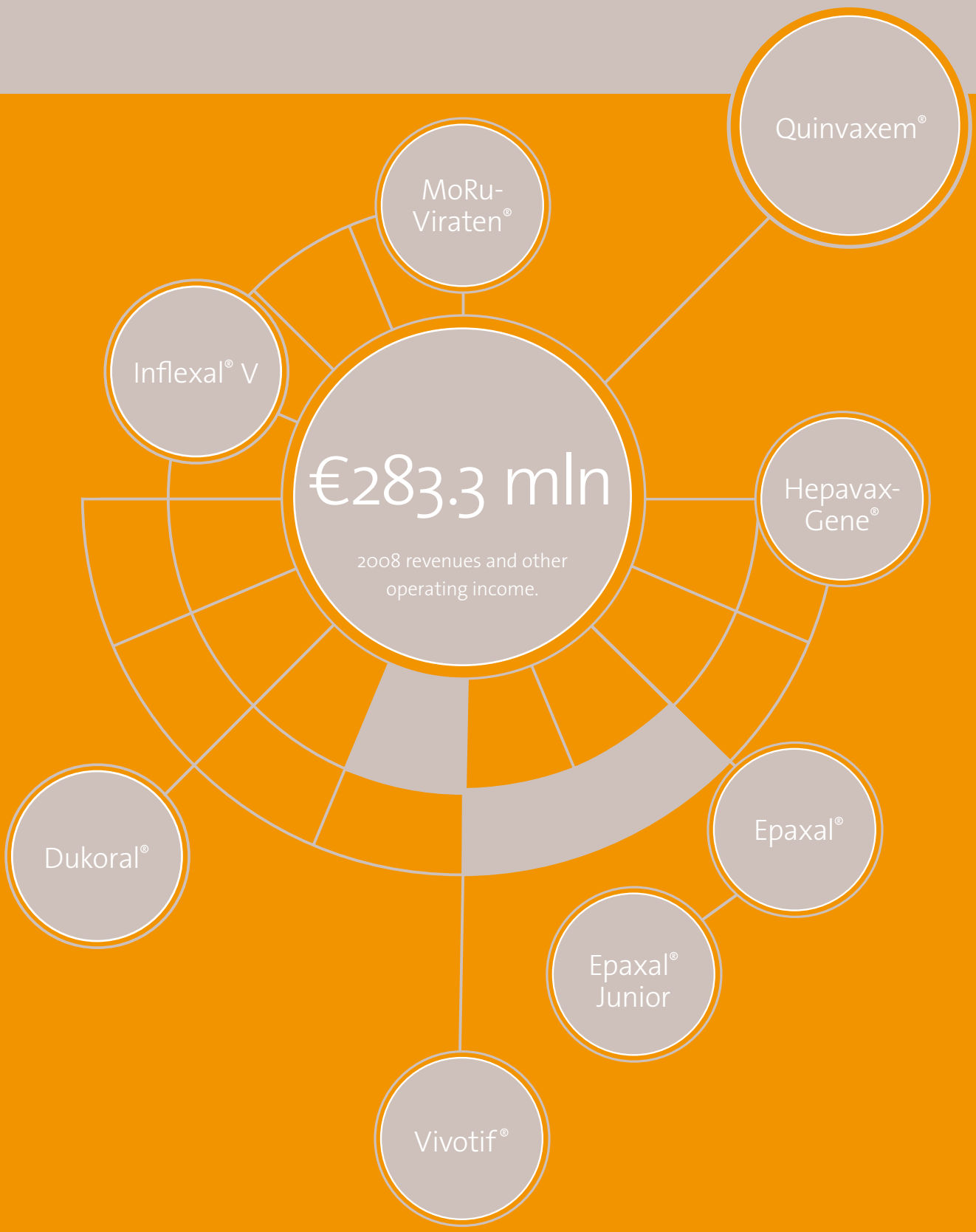
Vivotif®

Development stage	Research/ Pre-clinical	Phase I	Phase II	Phase III	Marketed	Comment
Marketed products:						
Quinvaxem®						Fully liquid vaccine for protection against five childhood diseases.
Hepavax-Gene®						Recombinant hepatitis B vaccine.
MoRu-Viraten®						Vaccine for protection against measles and rubella (all age groups).
Epaxal®						Aluminum-free hepatitis A vaccine.
Epaxal® Junior						Low dosage unique aluminum-free hepatitis A vaccine (0.25 ml).
Vivotif®						Oral typhoid vaccine.
Dukoral®						Internationally licensed oral vaccine against cholera (and ETEC).
Inflexal® V						Virosomal adjuvanted influenza vaccine (all age groups).
Vaccines in development:						
Flavimun®						Yellow fever vaccine.
Influenza seasonal						Pandemic (or seasonal) influenza vaccine.[1]
Tuberculosis						Recombinant AdVac®-based tuberculosis vaccine.[2]
Malaria						Recombinant AdVac®-based malaria vaccine.[3]
Ebola and Marburg						Recombinant AdVac®-based Ebola and Marburg vaccine.[3]
HIV						Recombinant HIV vaccine.[4]
Human antibodies in development:						
Rabies antibody combination			Fast track			Two human antibodies for post-exposure treatment of rabies.[5]
Influenza antibodies H1 and H5						Neutralizing antibody cross reactive against H1N1 and H5N1.
Other:						
Factor V L/C						Blood coagulation Factor V L/C.

[1] Developed by sanofi pasteur using PER.C6®. [2] Partnered with Aeras. [3] Partnered with NIAID/NIH. [4] Partnered with Harvard. [5] Partnered with sanofi pasteur.

Products

We focus on developing and marketing vaccines and antibodies against a range of infectious diseases. Vaccines play a vital role in protecting against these diseases and have contributed significantly to the improvement of global public health in the twentieth century. In this section you will find information about our marketed products.


Quinvaxem®
MoRu-Viraten®
Inflexal® V
€283.3 mln
2008 revenues and other operating income.
Hepavax-Gene®
Dukoral®
Epaxal®
Epaxal® Junior
Vivotif®

In 2008, Crucell's vaccines were administered to a vast number of people worldwide, thereby preventing more than 3 million cases of infectious disease and over 700,000 deaths that would otherwise have occurred.

Paediatric

Quinvaxem®

Epaxal® Junior

Hepavax-Gene®

MoRu-Viraten®

Products

Currently we are combating 12 major infectious diseases with our armamentarium of marketed vaccines. In 2008 we sold more than 100 million vaccine doses in more than 80 countries throughout the world, which makes us the largest independent vaccine player in the world. Our product portfolio consists of three distinct focus areas:

- Paediatric
- Travel and Endemic
- Respiratory

Our excellent products represent an untapped source of growth. We are focusing on four activities in order to unlock this growth potential:

Life-cycle management

Prolong sales through life-cycle management. For example, we are seeking to add another antigen to our pentavalent vaccine, Quinvaxem®, to create a novel vaccine and combine our travel vaccines.

Untapped markets

While we sell in more than 80 countries, most of our products are, for example, not sold in the US. For selected products we will go after untapped markets.

Growth by differentiation

We focus on products with higher margins. As noted above, we are already selling our products on a geographical basis. However, we also differentiate our products by creating variations of a vaccine that target a particular market, as we did with Epaxal® by introducing Epaxal® Junior aimed at the paediatric market.

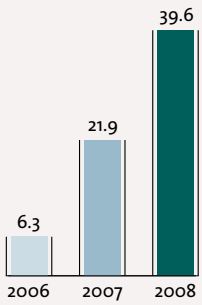
Sales and Marketing

In order to increase penetration, we are also focusing on sales and marketing. Our efforts relating to increasing the penetration of Dukoral® are an example of this type of activity.

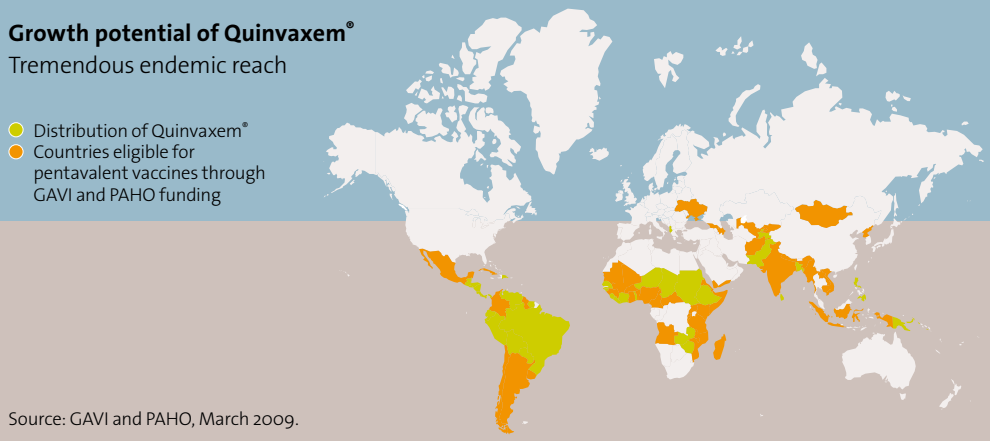
Quinvaxem®

Quinvaxem® is a fully liquid vaccine combining antigens for protection against five potentially deadly childhood diseases: diphtheria, tetanus, pertussis (whooping cough), hepatitis B, and Haemophilus influenzae type B. As the first internationally available fully liquid vaccine containing all five of these antigens, Quinvaxem® offers major healthcare advantages, particularly for low-income countries with infrastructure and hygiene problems. Supranational organizations awarded Crucell contracts worth $0.5 billion in the period 2007-2009 to supply Quinvaxem®, confirming the superior quality of our pentavalent vaccine, of which over half had been sold by the end of 2008. The remainder is expect to be sold in 2009. Quinvaxem® was launched in October 2006 and has a market share of over 50% already.

Quinvaxem® vaccines sold
(Doses in million units)



Growth potential of Quinvaxem®
Tremendous endemic reach



Source: GAVI and PAHO, March 2009.

Travel and Endemic

Respiratory

Epaxal®

Vivotif®

Dukoral®

Inflexal® V

Epaxal®

Epaxal® is the only aluminum-free hepatitis A vaccine on the market. The absence of aluminum reduces the pain caused on administration, offering significant advantages in terms of tolerability. This makes it particularly well suited to the paediatric market. Epaxal® induces protective antibody levels within 10 days of primary vaccination and provides seroprotection for at least 20 years following the second (booster) dose. It can be fitted into the regular immunization schedule for babies.

Hepavax-Gene®

Hepavax-Gene® is a recombinant hepatitis B vaccine. It is one of the WHO's pre-qualified vaccines for active immunization against hepatitis B virus. In December 2008 Crucell announced that Chinese authorities have approved Hepavax-Gene® for use in the private vaccine market in China.

MoRu-Viraten®

MoRu-Viraten® is a safe, well-tolerated and effective vaccine for protection against measles and rubella in children, adolescents and adults. MoRu-Viraten® is free of avian proteins and antibiotics, posing no risk to children with allergies to these substances. The vaccine has been marketed since 1986 and is on the WHO list of vaccines for purchase by UN agencies.

Vivotif®

Vivotif® is a live attenuated typhoid fever vaccine for oral administration. It is the only oral vaccine indicated for use against Salmonella typhi, the most prevalent of the typhoid fever-causing bacteria. The vaccine is indicated for adults and children over the age of five and has an excellent track record for safety, having been on the market for more than 20 years. It is currently licensed in over 30 countries, including in the USA. Recent results suggest that Vivotif® may be unique in also protecting against S. paratyphi, a similar but milder variant of typhoid.

Dukoral®

Dukoral® is a drinkable vaccine with a documented protective effect against diarrhea caused by cholera, as well as traveler's diarrhea. The vaccine stimulates a protective immune response in the gut and has a demonstrated protective efficacy against cholera of approximately 85%. Dukoral® was first licensed in 1992 and is now licensed in over 60 countries. It is presently the only internationally licensed oral cholera vaccine. To date, over 10 million doses of Dukoral® have been supplied with very few adverse events reported.

Inflexal® V

Inflexal® V is a virosomal adjuvanted vaccine against influenza, based upon the virosome technology developed and patented by the Crucell company, Berna Biotech. It is the only adjuvanted flu vaccine licensed for all age groups (up from six months). The vaccine's antigen composition follows yearly WHO recommendations.

Research & Development

Our research efforts today are focusing on developing vaccines and antibodies that address unmet medical needs and infectious diseases. Our research efforts are bolstered by our range of technologies, which play a critical role in our development programs. The following pages discuss key developments relating to our discovery programs, as well as providing key areas of focus.


Rabies
Yellow fever
Seasonal
Research & Development
Influenza
Pandemic
Ebola and Marburg
Tuberculosis
HIV
Malaria

Key pipeline developments:

- Successful Phase II results of studies in the US and Philippines of our rabies antibody combination, showing safety and tolerability. Third Phase II study in India in progress.
- Encouraging results from the Phase I Ad35 tuberculosis vaccine study, showing that CD8 immune responses are considerably higher than ever seen in a tuberculosis vaccine study. Program entered Phase II clinical testing.
- Alternative adenovirus serotypes like Ad26 and Ad35 using Crucell's AdVac®/PER.C6® technologies were used to express protein of SIV (HIV-like virus). Study showed strong T-cell immune response and provides protection against SIV. Malaria and TB vaccines in development using Ad26 and Ad35.
- Crucell's monoclonal antibodies (mAb) against influenza strongly outperforms the anti-influenza drug oseltamivir in pre-clinical tests.

Multiple products in a focused pipeline

As part of our product development program, we investigate many different product candidates.

Our discovery programs include a number of potential products that are in an early stage of development. The decision to pursue development of these products and add them to our product pipeline is dependent on stringent evaluation and selection.

AdVac® technology and AdVac®-based vaccines

AdVac® technology encompasses the use of adenoviral vectors such as Ad35 and Ad26 for vaccination against diseases caused by viruses, bacteria or parasites. These vectors are harmless adenoviruses that have been disabled so that they cannot replicate. A vector functions as an efficient 'gene taxi', delivering into the human body a fragment of DNA that carries the code for a protein from a specific pathogen. Once inside the body, the vectors express (produce) these proteins and present them to the person's immune system, which mounts its protective response. Using this versatile vaccine vector platform in combination with PER.C6® manufacturing technology, Crucell and partners are working to develop vaccines against diseases like tuberculosis, malaria, Ebola, Marburg and HIV.

Tuberculosis

Tuberculosis (TB) is a major cause of illness and mortality worldwide, with 9.2 million new cases and 1.7 million deaths due to TB in 2006. The current TB vaccine BCG, developed more than 85 years ago, is probably the world's most widely used but least effective of vaccines. It does reduce the risk of disseminated TB, a form of the disease that spreads from the lungs to other organs, which is especially lethal in children. However, it does not reliably prevent pulmonary TB, the most prevalent form of TB, in both children and adults. The problem is compounded by the emergence of extensively drug-resistant tuberculosis (XDR-TB), which is hampering treatment and control efforts (see map on page 27).

To address this urgent need, Crucell is collaborating with the Aeras Global TB Vaccine Foundation to jointly develop the novel TB vaccine candidate AERAS-402/Crucell Ad35. Data from all trials conducted to date support the immunogenicity and safety of AERAS-402/Crucell Ad35 at all dose levels evaluated. A phase II study of this vaccine candidate is being conducted in Cape Town, South Africa, by the University of Cape Town Lung Institute in conjunction with the South African Tuberculosis Vaccine Institute.

+16%

Growth of vaccine market
Operating in rapidly growing vaccine market.

Source: RNCOS, Global Vaccine Market Outlook, November 2007.

+14%

Growth of antibody market
Strategically positioned in growing antibody market.

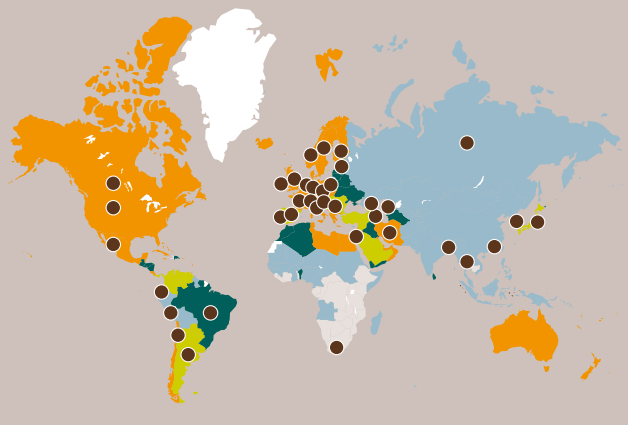
Source: Datamonitor, Monoclonal Antibodies Report, June 2007.

Tuberculosis

Estimated new tuberculosis cases (all forms) per 100.000 population

- 0 – 24
- 25 – 49
- 50 – 99
- 100 – 299
- 300 or more
- No estimate

- Countries with confirmed multi-resistant tuberculosis



Malaria

According to the WHO, malaria is one of the most prevalent infections in tropical and subtropical regions, causing severe illness in 300 to 500 million people and death in 1 to 3 million people. Children and pregnant women are the groups most severely affected. No licensed vaccine is available to fight this disease.

Crucell is collaborating with the US National Institute of Allergy and Infectious Diseases (NIAID) on malaria vaccine research and development. A candidate vaccine arising from this partnership is being tested in a Phase I trial at two US sites: Vanderbilt University in Nashville, Tennessee and Stanford University in Palo Alto, California.

Ebola and Marburg

Crucell is developing a multivalent filovirus vaccine against Ebola and Marburg in collaboration with the Vaccine Research Center of the National Institute of Allergy and Infectious Diseases (NIAID), part of the US National Institutes of Health (NIH). The candidate vaccine is based on Crucell's proprietary adenoviral vector technology and is produced using Crucell's PER.C6® technology. It is a recombinant DNA vaccine that expresses Ebola virus proteins in order to provide protection against infection with the Ebola virus.

HIV

Over the past 25 years, HIV infection resulting in AIDS has claimed the lives of nearly 25 million people, devastated entire communities, and enormously frustrated efforts to fight poverty, improve global health and promote economic development. In 2007, an estimated 2 million people died due to AIDS, 33 million people were living with HIV infection and 2.5 million people became infected with the virus. There is no licensed AIDS vaccine available.

With the support of a $19.2 million grant from the US National Institutes of Health, Crucell is collaborating with Harvard Medical School and its teaching hospital Beth Israel Deaconess Medical Center to develop an AdVac®-based vaccine against HIV. Adenovirus serotype 26 (Ad26) is being used as the vaccine vector, in order to avoid the problem of pre-existing immunity to the more commonly used adenovirus serotype 5 (Ad5).

Resistance of influenza (H1N1) against oseltamivir is almost universal

1. 98% United States
2. 13-82% South America (6 countries)
3. 97% European Union
4. 45% Russian Federation
5. 93% Japan
6. 91% Philippines
7. 100% South Africa
8. 94% Australia
9. 31% Southern hemisphere (16 countries)

Source: WHO, January 2009.

Crucell's monoclonal antibodies against influenza strongly outperform oseltamivir in pre-clinical trials.

Antibodies

Antibodies are proteins made naturally by cells of the body's immune system. They function as one of the body's principal defense mechanisms against pathogens, which are disease causing agents such as parasites, viruses or bacteria. Antibodies recognize and bind to invading pathogens, ultimately eliminating them, thus playing a crucial role in protecting humans against disease.

Influenza antibodies H1N1 and H5N1

There is a growing fear within the medical community concerning the potential reoccurrence of a pandemic influenza outbreak, similar to the 1918 'Spanish flu' pandemic. A pandemic can start when a new influenza virus subtype emerges that meets three conditions: it infects humans causing serious illness; it spreads easily; and there is sustained human-to-human transmission of the virus.

Crucell has discovered the first human monoclonal antibodies for the prevention and treatment of the 'bird flu' strain H5N1, as well as H1N1, which is similar to the strain responsible for the devastating pandemic in 1918. The antibodies provide immediate protection and neutralize a broad range of H5N1 and H1N1 strains in pre-clinical models. In December 2008, Crucell presented data showing that the mAb CR6261 was 100% successful in preventing infection with H5N1. When given after H5N1 infection, Crucell's mAb demonstrated the ability to prevent death and cure disease in all cases. The mAb also performed significantly better than the anti-influenza drug oseltamivir for the prevention and treatment of H1N1 infection, illustrating the potential use for seasonal applications as well. This is especially important as the resistance of influenza strains for oseltamivir is rapidly increasing.

Rabies causes over 50,000 deaths each year in endemic countries

Source: FX Meslin, WHO NECTM, KNobel and Tang et al EID, 2005; Zhang et al InFoRab 2005, APCRI data.

In Asia and Africa, where an estimated 40,000 to 70,000 people die from rabies each year, there is a significant unmet medical need for a safe, effective and affordable treatment.

Rabies Antibody Combination

Globally, around 10 million people a year are treated after exposure to rabies virus. Nevertheless, between 40,000 and 70,000 people die of rabies each year, mainly in Africa, China and India. This highlights the significant unmet medical need for a safe, effective and affordable rabies treatment. The approach currently used to prevent symptomatic disease and death in people exposed to rabies virus combines immunoglobulins (antibodies prepared from human or equine blood) with the vaccine. Concerns about the safety and availability of blood-derived rabies antibodies have prompted the search for alternatives.

Using MAbstract® and PER.C6® technology, Crucell scientists in collaboration with the Thomas Jefferson University in Philadelphia and the US Centers for Disease Control and Prevention in Atlanta have discovered a combination of human monoclonal antibodies (mAbs) for the post-exposure treatment of rabies. Clinical testing of this mAb combination made good progress during 2008, leading to the presentation in October of very promising efficacy and safety data from a Phase II trial in the USA. In order to test the mAb combination in different populations and settings, additional Phase II trials were started in May 2008 (among children in the Philippines) and February 2009 (among adults in India).

Since January 2008, the route towards global availability of this next-generation, life-saving rabies biological is being facilitated by Crucell's strategic partnership with sanofi pasteur, a world leader in rabies immunization. The US Food and Drug Administration (FDA) has granted Crucell's mAb combination Fast Track status, which paves the way for priority handling of the regulatory dossier.

Technologies

Our strong product portfolio is supported through a range of patented technologies. Our cutting-edge technology platforms enable the discovery, development and production of vaccines, therapeutic proteins and gene therapy products.


AdVac®
PER.C6®
5
core technologies
STAR®
MAbstract®
Virosome

What is PER.C6®?

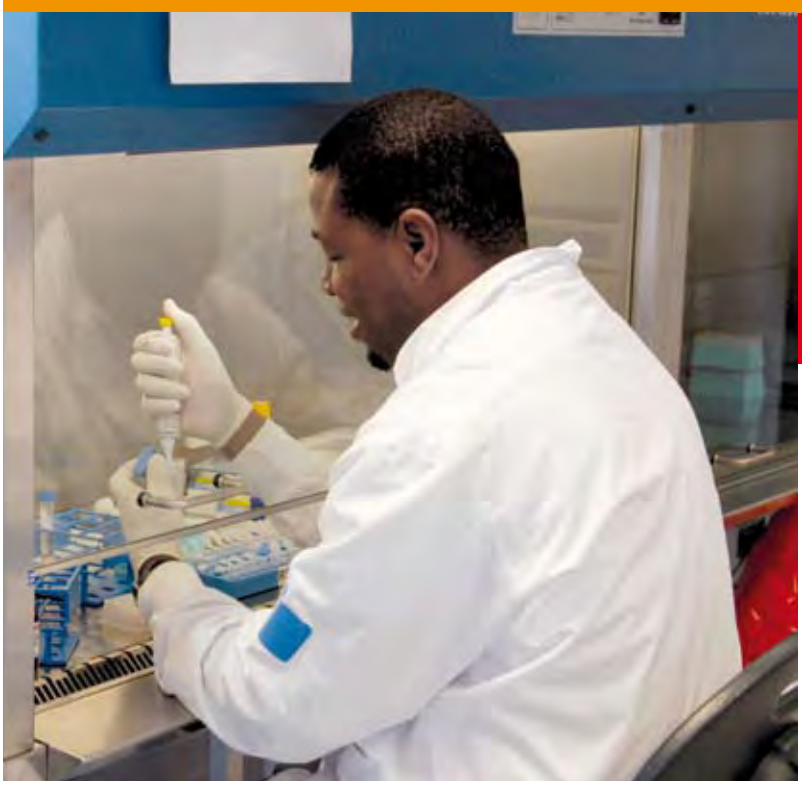
PER.C6® is a human designer cell line for the development and large-scale manufacturing of biopharma products. In areas where Crucell does not aim to develop its own products, we license the technology to the biopharmaceutical industry. Currently over 60 companies and organizations have selected our PER.C6® technology to develop their own products across a wide range of therapeutic areas.

PER.C6® adaptable

Manufacturing of biopharmaceuticals has to take account of rapidly changing factors, such as rising volume demands and more stringent safety requirements. These shifts are a major challenge to conventional manufacturing platforms that have not adapted or become sufficiently flexible to cope with such changes. Our PER.C6® production cell line, however, is designed to meet these demands.

Our other core technologies:

AdVac®	Technology, used in combination with PER.C6®, to develop recombinant vaccines.
MAbstract®	Applied for discovery of novel drug targets and identification of human antibodies.
STAR®	Designed to enhance production yields of recombinant human antibodies and proteins on mammalian cell lines.
Virosome	A vehicle enabling the use of virus antigens in the making of vaccines.



MAbstract®

27 g/L

Record-level titer achieved at harvest for an antibody product using PER.C6® technology.

PER.C6® well protected

Our PER.C6® technology is protected by numerous patents. In addition, in order to benefit from our proprietary technology, potential customers not only need our know-how, but also our PER.C6® cells, which are only available from us under agreement. These agreements put certain restrictions on further dissemination and use of the PER.C6® cells. This combination of protections – patented know-how and the need to have access to the actual PER.C6® cells results in the PER.C6® technology being the best protected human cell technology in the world.

PER.C6® for protein and antibody production

We have a collaboration with DSM Biologics for the application of PER.C6® for proteins and antibodies. Together with DSM we license PER.C6® for proteins and antibodies as well as invest in further innovation of PER.C6®.

Working alongside DSM Biologics on the PER.C6® manufacturing platform, we believe that there is tremendous potential to reduce the production costs of monoclonal antibodies, whilst increasing yield resulting in more affordable treatments for patients.

In June 2008, we jointly announced that we had achieved a record-level titer of 27 grams per liter at harvest for an antibody product using PER.C6® at our PERCIVIA joint venture development center in Massachusetts, the USA.

75+

Proprietary technologies licensed by over 75 companies and organizations.

AdVac®

Virosome

PER.C6®

STAR®

Key achievement for PER.C6® technology:
Scale up of high-titer Fed-Batch Process to 250 liters.

Corporate Social Responsibility

Our commitment to CSR

"Crucell aims to bring significant benefits to people's lives, rather than simply make a profit."

Ronald Brus (President and Chief Executive Officer)

What Corporate Social Responsibility means to us

Crucell's commitment to CSR

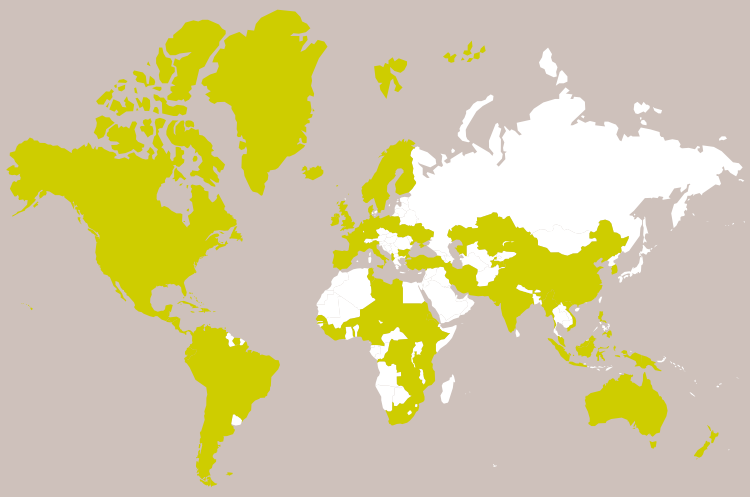
Crucell's core business is protecting people from illness and death caused by infectious diseases. This in itself is a social responsibility, which we take very seriously. However, our commitments to the principles of Corporate Social Responsibility (CSR) go beyond this. We recognize that Crucell has a responsibility towards its customers, partners, employees, shareholders, local communities and society at large. In order to fulfil this obligation, everyone in our organization has to be conscious of what we stand for and the way we want to conduct our business.

In 2008 we took an important step forward in this regard by defining a core set of values for the organization. The Crucell Values are the foundation on which all our activities and relationships are based. They express what unites us and serve as a guide for our performance as a responsible company geared for sustainable success.

We see the definition of our Crucell Values as the beginning of a more comprehensive approach to CSR throughout the company. We want to raise awareness, internally and externally, of the standards we have set for doing business in a responsible way. Improvements in both our CSR performance and reporting are priorities.

In this section of our Annual Report, we take the opportunity to share with you our ideas, ambitions and activities regarding CSR, as well as to introduce the parties who are supporting us in CSR development.

○ Distribution of Crucell products



"Improving our CSR performance and reporting are priorities for Crucell in the coming years."

What we do

Crucell has a clearly defined vision: to bring innovation to global health by discovering, developing, manufacturing, and marketing products that protect people from illness and death caused by infectious diseases. Crucell is the largest independent vaccine company in the world. The sustainability of our business is demonstrated by our solid balance sheet and strong cash position, which means that we do not need to raise capital in the foreseeable future. As a result, the unfolding economic crisis so far has had limited effects on our financial outlook.

Crucell's definition of profit is twofold. We aim for financial profitability, but also to bring the greatest possible benefit to human health worldwide. The approach we have chosen to achieve this is essentially different from that of our biotechnology peers or traditional pharmaceutical companies. Whereas many others focus on treating illness, Crucell focuses on its prevention. And whereas most of the money currently spent on pharmaceutical research is directed towards finding solutions for lifestyle-related illnesses of the developed world, Crucell has developed a truly global healthcare strategy. Our existing and pipeline products are designed to meet the long underestimated – and still significantly unmet – need for vaccines and antibodies in developing countries and emerging economies, as well as the industrialized world. For a company of our size, we invest relatively heavily in research and development: our R&D expenditures in 2008 were €70 million.

Infectious diseases are responsible for almost one-fifth of the total number of deaths that occur each year, according to the latest World Health Organization (WHO) statistics (source: World Health Statistics 2008). Overall, they rank second after cardiovascular disease as the leading cause of death worldwide. The vast majority of people who die from infectious diseases live in the world's poorest and most densely populated countries, although increased global travel and climate change are expanding the reach of infectious pathogens. The full impact of infectious diseases has to be measured not only by the millions of fatal cases, but also in terms of the much larger burden of illness and suffering, lost productivity and even ruined holidays. Children and the elderly are

A CSR dilemma: The perfect is the enemy of the good (Voltaire, 1772)

Our aim to bring the greatest possible benefit to human health and healthcare presents a dilemma. It is conceivable that while developing a new medical product we might discover that particular changes in the production process or product characteristics could enhance its healthcare benefits. Implementing such changes would inevitably delay the time to market, potentially by as much as 5 years. Should we aim for perfection, knowing that people will suffer and die during the period of delay? This dilemma was expressed succinctly by the French philosopher Voltaire: 'The perfect is the enemy of the good'. In this situation, Crucell has to weigh up conflicting benefits. Our choice would be to take the well tested candidate product already in development and to market it as soon as is safely possible in order to start saving lives. In the meantime we will continue in-house research and development aimed at a next generation product.

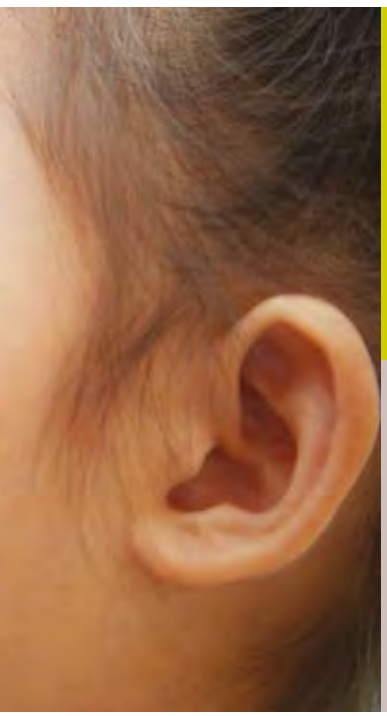
especially vulnerable to infectious diseases, with the latter forming a growing group due to the aging population. According to the WHO, about 25 million deaths that occur each year in children under five are caused by diseases that can be prevented with vaccines.

Crucell's focus on the prevention of infectious diseases offers long-term benefit to individuals and society, compared to treatment-based approaches. Our vaccines – and the antibodies now progressing through our R&D pipeline – have a vital role to play in protecting lives, preventing suffering and supporting the economic well-being of societies. Vaccination is one of the most cost-effective healthcare interventions and has many indirect benefits for society, as demonstrated by childhood immunization programs. As well as protecting the children themselves from illness, death and possibly permanent disability, these programs prevent the spread of disease in the community.

Crucell is currently combating twelve major infectious diseases with its armamentarium of marketed vaccines (see pages 22-23). In 2008 Crucell sold more than 100 million vaccine doses in more than 80 countries throughout the world, which makes us the largest independent vaccine player in the world. We focus strongly, though not exclusively, on unmet medical needs in the developing world, where infectious diseases exert their heaviest toll.

In 2008, Crucell's vaccines were administered to a vast number of people worldwide, thereby preventing more than 3 million cases of infectious diseases and over 700,000 deaths that would otherwise have occurred. These figures are based on the expected number of cases, and fatalities among those cases, in a given population assuming a vaccine waste rate* of 2%.

Our production processes are described in more detail on page 52. The complex chain of steps to reach a final Crucell product has its impact on both society and the environment in which we operate. We understand that our impact on the planet is relatively modest, but we take our environmental footprint seriously, especially in relation to the end result of our core business: protecting people from illness and death caused by infectious diseases. In this chapter however we want to be transparent about our efforts to manage our responsibilities.



Trust is the basis for successful business relationships. Crucell is committed to building trust both internally and externally by delivering on what we promise.

* A waste rate is the percentage of doses that have gone to waste either because they were out of the 'cold chain' (i.e. they experienced temperatures that rendered the vaccine not useable) or because the vial was broken or because the shelf life has expired.

Crucell on its mission to combat infectious diseases

Crucell took part in two mass vaccination campaigns against cholera in 2008, with its oral vaccine Dukoral®. The campaigns were organized in Myanmar and Zanzibar, two parts of the world where cholera epidemics are all too common.

Together with the International Vaccine Institute, Crucell distributed 137,000 doses of Dukoral® in Myanmar to help prevent an outbreak of cholera following the cyclone that devastated the country. Another 100,000 doses of Dukoral® were distributed in cooperation with the WHO in Zanzibar, Tanzania, as part of a clinical research program investigating the value of routine vaccination for establishing widespread protection of a population (herd immunity).

Cholera remains a significant threat to human health, particularly in developing countries where access to safe drinking water and adequate sanitation cannot be guaranteed. By making an essential tool available to international public health organizations, Crucell is delivering on its mission to combat infectious diseases.

137,000

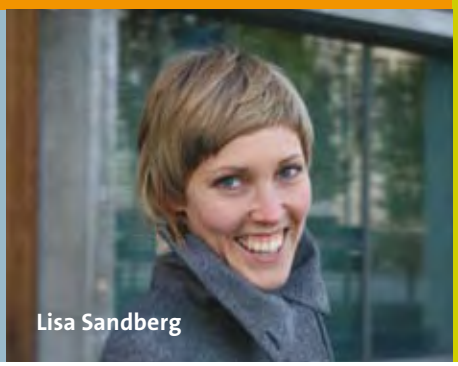
Doses used in Indonesia during the outbreak of cholera in 2004.

Previous mass vaccination campaigns with Dukoral®:

- Uganda 1997 (63,220 doses distributed)
- Mayotte 2000 (93,000 people vaccinated)
- Mozambique 2003-2004 (41,000 people vaccinated)
- Sudan (Darfur) 2004 (50,000 people vaccinated)
- Indonesia 2004 (137,000 doses used)

"Although we cannot know how many people at risk received the two doses of Dukoral® needed for protection, it is clear that this mass vaccination initiative saved many thousands of people from serious illness and death."

Lisa Sandberg, Global Product Manager for Dukoral®



Lisa Sandberg

An example:
One world, one vaccine

To avert the threat of such a cholera outbreak in Myanmar, Crucell teamed up with the International Vaccine Institute (IVI), an international organization based in Korea, to send 137,000 doses of Dukoral® to the cyclone survivors. This is enough to vaccinate at least 65,000 people. Crucell donated 50% of the doses and sold the other 50% to IVI at a price below production cost. The South Korean government supplied IVI with the necessary funds. Crucell shipped the vaccines in special 'emergency' packs, each containing 170 vials, rather than the usual two-dose package. This made transport and administration more efficient and helped to speed up the vaccination process.

Who we work with

Crucell cannot operate in isolation. In our daily work to bring benefits to people's lives, we interact with a large number of stakeholders worldwide. These include legislators, investors, strategic business partners, licensees, suppliers, and customers. Establishing and maintaining good relationships through continuous dialogue with all of these parties is integral to our CSR. The dialogue has had a specific impact on our approach to CSR. A good example is our partnership with customers as described on the following pages.

Legislators

The business in which Crucell operates is highly regulated, and Crucell complies with the wide range of legislation that applies to our activities. Besides adhering to regulations, we cooperate with representatives of various legislative bodies.

Investors

Crucell maintains an active and transparent approach to relations with shareholders and investors, informing them regularly about the company's strategy and developments. Quarterly results releases, presentations and press releases on important business developments are disseminated on a regular basis and reinforced with briefings by phone and in person. Crucell has a dedicated Investor Relations team whose mission it is to ensure the investor community clearly understands the company's prospects and performance. This reflects a serious ambition to widen our investor base as well as to deepen existing investors' understanding of Crucell while always listening to investors' needs and ideas. Our investors make our work possible and share in our success. They share our vision and support our core business of protecting people all over the globe from infectious diseases. A continuous dialogue with investors is therefore at the forefront of our activities. As described on page 177 of this Annual Report, we actively talked to large numbers of (potential and existing) shareholders and investors all over the world in 2008.

An example: Warm response to cold chain training

The cold chain is a temperature-controlled distribution process ensuring the quality and extended shelf life of foods and medicines. As part of the clinical good manufacturing practice (cGMP) environment, which regulates all drugs and biologicals, the cold chain has to conform to validated practices enforced by the regulatory authorities. Maintaining the cold chain is especially important – and challenging – when vaccines are being transported to remote clinics in countries with hot climates and poor infrastructure.

During 2008, Crucell's office in Latin America organized a successful series of workshops designed to enhance knowledge of the cold chain process among our institutional customers in the region. The workshops focused on theoretical and practical concepts for the cold chain handling of vaccines and other medicines in accordance with regulatory requirements.

Crucell conducted the workshops in three different cities of the Andean region: Bogotá in Colombia, Lima in Peru and Quito in Ecuador. Each attracted approximately 80 people who are directly or indirectly involved with the distribution of vaccines in their respective countries. These included national managers of the Expanded Program of Immunization (EPI), local representatives of the Pan American Health Organization (PAHO), and medical doctors and nurses.

Business partners

Partnering with other companies is of strategic importance to Crucell and essential for fulfilling our mission. Whether the partnership takes the form of a strategic alliance for product development, a technology licensing agreement, or a marketing and sales alliance, Crucell works closely with its partners to ensure success for both organizations. For more information on the strategic agreements Crucell has established with several leading companies go to www.crucell.com/partners.

Licensees

A wide range of pharmaceutical and biotech companies license Crucell's proprietary technologies, which enable the discovery, development and production of vaccines, antibodies, therapeutic proteins, and gene therapy products. One of the key Crucell technologies that attracts licensees is the PER.C6® manufacturing platform based on human cell lines.

Suppliers

Crucell must be able to rely on suppliers to provide raw materials and equipment of consistently high quality, without delay or interruption. We therefore keep close track of our suppliers, perform quality control tests on the goods they deliver and conduct inspections of their facilities as deemed appropriate. Legislation from regulatory authorities such as the US' Food and Drug Administration (FDA) lays down the minimum requirements for this monitoring of suppliers and supplies.

Customers

Crucell's customers are important to us in two ways. By buying our products, they fund the continuation of our activities, including R&D aimed at bringing further healthcare innovations to market. They also represent the vital link to the consumer, ensuring that our products reach the people who need them.

"The cold chain workshops were very well received by our customers and generate tangible loyalty to Crucell and our vaccines, and above all, better vaccine management practices among our customers."

Carlo Precali, Regional Director Crucell Latin America

Carlo Precali

A partnership with customers illustrated:

Crucell's work is supported by grants from both governmental and non-governmental organizations. Furthermore, Crucell works alongside other parties in order to reach common healthcare goals. One example of this type of cooperation is the GAVI Alliance, a global public-private partnership that brings together the talents of different constituencies and individuals to help the poorest parts of the world develop their own sustainable immunization programs. Within the alliance, Crucell invests time by working closely with other vaccine-producing companies, national governments, research and technical health institutes, supranational organizations (including the WHO, Unicef and The World Bank), the Gates Foundation and civil society organizations, in order to accelerate the introduction of new and underused vaccines.

This is considered crucial for meeting one of the United Nations (UN) Millennium Development Goals of reducing the mortality rate among children under five by two-third before 2015.

In September 2000 the UN set out concrete plans for action to meet the needs of the world's poorest, which resulted in eight Millennium Development Goals, to be achieved by 2015. More information about the Millennium Development Goals can be found on the UN website www.un.org/millenniumgoals.

Crucell is a leading supplier of innovative vaccines to countries supported by the GAVI Alliance, and currently represents the industrialized countries' vaccine industry on the Program and Policy Committee of the GAVI Alliance. This committee serves as the principal advisory body to the GAVI Board regarding program and policy development.

GAVI ALLIANCE

How we do business

Crucell is committed to adhering to high standards of ethics and transparency in dealing with our stakeholders. We regard this as a social responsibility and believe that it contributes to business success. In 2008 we made an important advance in this regard by defining a core set of values for the organization: Integrity, Respect, Complementarity, Reliability, Innovation, and Passion and Drive. These values represent the foundation on which all our activities and relationships are based, internally and externally. We are determined to ensure that these values are inherent to all our work and behavior.

People

The Crucell Values have been incorporated in the Code of Conduct, Crucell's commitment to integrity. The Code of Conduct is easily accessible via our website: www.crucell.com. In 2009 the Code of Conduct will be brought to the attention of all employees by means of 'town hall' meetings in which Crucell senior managers – together with local management – will explain and emphasize the importance of the policy. The Code applies to all Crucell representatives and is expressed in a form that all employees should be able to understand. It outlines Crucell's approach to good business conduct, focusing on the behavior of employees. Central to the code is the stipulation that Crucell's representatives must not take unfair advantage of anyone by any means and must not accept favors of any form from others. The Code of Conduct includes a whistle-blower policy, encouraging the reporting of any behavior or action that may be in breach of this code.

Our approach to animal testing follows the three Rs: Reduce, Refine and – ultimately – Replace.

Crucell's PER.C6® technology: A revolution in biopharmaceutical production

Many of today's vaccines are produced on animal substrates such as chicken eggs and mouse brains. Inherent problems with these manufacturing processes include limited scalability, lengthy processing times, and relatively low success rates due to the potential safety risks associated with animal-derived products.

Crucell's PER.C6® technology provides a state-of-the-art alternative. PER.C6® human cell lines are ideally suited for the development and industrial-scale manufacturing of a wide range of biopharmaceutical products, including vaccines, antibodies and gene therapies. PER.C6® cell lines are derived from a single cell taken from a human retina and immortalized using recombinant DNA technology. Because PER.C6® cells grow in suspension to very high densities, they provide an excellent platform for the production of many different types of vaccines (inactivated whole-virus, live-attenuated, live-vector, split and subunit vaccines). PER.C6® technology also allows efficient production of recombinant proteins, such as live adenovirus vector-based vaccines. For more information about Crucell's PER.C6® technology, see page 32 of this 2008 Annual Report.

PER.C6®

Animal testing

Before any candidate medical product can be given to humans, it must be rigorously tested in pre-clinical (non-human) models. At present, the stringent legal, ethical and scientific standards governing pharmaceutical research and development require pre-clinical tests in both cells (*in vitro* models) and animals (*in vivo* models). We are legally obliged to fulfil these requirements, and also feel a moral obligation to do our utmost to ensure the safety of people who receive our (candidate) products.

For these reasons, Crucell does perform animal testing to the minimum extent necessary. Safety studies in animals, which are required by law, are conducted in accordance with the highest international standards, which are designed to prevent or minimize any suffering of the animals tested.

Simultaneously, Crucell continuously applies the 3R principles – Reduce, Refine and (ultimately) Replace – to pre-clinical studies involving animals. Crucell has been working over many years to replace in vivo tests with in vitro assays, and these efforts have already resulted in the significant reduction of animal testing.

Crucell will continue to apply the 3R principles and work closely with the regulatory authorities to further minimize the experimental use of animals in the course of bringing new vaccines and antibodies to the people who need them.

How we see our responsibility

Having pictured the way in which Crucell sees itself and how it operates at large, we now would like to elaborate on what we do in the field of CSR in three areas: people, planet, and profit. Crucell's impact on the planet is relatively modest, but we do take our environmental footprint seriously.

Social aspects of our business

Crucell's work revolves around people. We value our role as employer and aim to conduct our activities in a manner that both improves the capabilities and performance of our people, and results in safe products of the best possible quality.

Crucell works in an environment that requires highly skilled employees.

We value both gender and ethnic diversity and accordingly act as an equal opportunity employer.
The characteristics of our workforce are as follows:

	China	Italy	Korea	Netherlands	Spain	Sweden	Switzerland	USA	Total
2008									
Number of male employees	9	12	167	139	30	45	225	11	638
Number of female employees	26	10	44	114	39	88	159	8	488
Total number of employees	**35**	**22**	**211**	**253**	**69**	**133**	**384**	**19**	**1,126**
Average age of employees	31	44	35	36	46	45	42	43	40
Number of women in management	3	3	4	23	2	10	10	3	58
Number of nationalities	2	1	3	19	2	4	10	5	n/a
2007									
Total number of employees	**30**	**38**	**162**	**325**	**66**	**129**	**357**	**19**	**1,126**

Our people

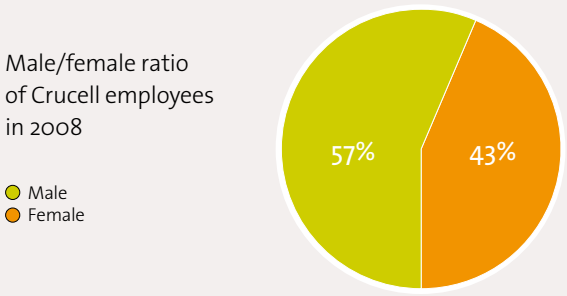
Crucell has grown rapidly over the past few years. The Netherlands-based company acquired Swiss Berna Biotech early in 2006, and later in the year further strengthened its presence in the vaccine industry by acquiring US-based Berna Products and Sweden's SBL Vaccines.

Employing talented people with the right mind-set is something to be proud of, but no reason to be complacent. During our period of rapid growth, we set up special programs focusing on talent management, succession planning and remuneration, in order to retain and further develop the best people in each area of our business. Part of the development of our employees is to raise their awareness of the impact of our products and the need for them across the globe.

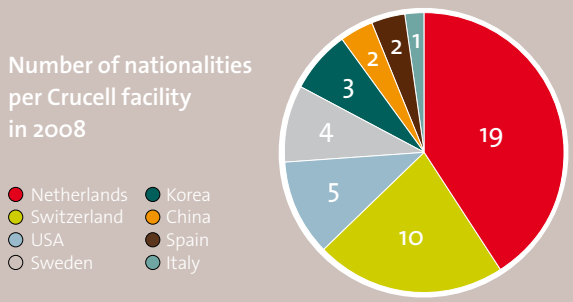
As described earlier, Crucell's operations are governed by the six Crucell Values that have been defined by a cross-section of employees from different functions and sites, together with Crucell's Management Board. These Values are a crucial component of our leadership development programs, which were introduced in 2008. Crucell managers worldwide have participated in these programs, which reflect and reinforce our company values. The Crucell Values have also been incorporated into our employees' performance review and coupled to remuneration decisions, thereby creating a solid incentive for our people to behave in accordance with the standards that have been defined. Crucell hopes that this approach will also have a positive effect on the way our employees behave in daily life and society at large.

Besides promoting adherence to the Crucell values, we want to create true corporate ownership among Crucell employees. For this reason, when The Crucell Ambition program was launched in 2008, employees representing different parts of the company were brought together in teams to help define the best way forward in a number of strategic business areas. Since the introduction of The Crucell Ambition strategic program, monthly questionnaires have been sent to groups of randomly selected employees worldwide, asking them for feedback on the progress made with implementation of our global strategy, and further improvements needed in the organization. For more information on The Crucell Ambition program, see page 12 of this Annual Report.

Male/female ratio of Crucell employees in 2008



Number of nationalities per Crucell facility in 2008



Innovative safety approach

As an additional safety measure, Crucell recently introduced a Personal Protection System (PPS) for employees at the facilities in Leiden. The system works with portable transmitters that raise an alarm in the event of an accident or unsafe situation. The warning signal can be sent actively by the person carrying the transmitter, but also transmits automatically if an inbuilt sensor detects that the person has fallen or not moved for a pre-defined period of time. Use of the PPS is mandatory for anyone working alone and/or outside regular office hours at the Leiden site. The system has been implemented as a pilot project in the Dutch facilities and results are being monitored to guide decisions about possible expansion to other sites.

Another example of employee ownership in Crucell is the system of stock options employees can receive in remuneration for services rendered to the company. In this way, Crucell employees can receive a tangible share of the business for investing their talents and efforts in the success of the company. Approximately 6.4 million of outstanding options are held by Crucell employees of which 1.7 million by the Executive Board.

Safety

Ensuring the safety of Crucell's employees is of the utmost importance. Because the biotechnology business potentially involves exposure to hazardous substances, all employees working in laboratories are trained in bio-safety procedures and regulations. Primarily, this training focuses on standard operating procedures (SOPs and work instructions), which generally include specific safety precautions. When necessary, Crucell facilitates employee participation in additional training by external organizations.

The total number of reported incidents that occurred in 2008 is limited to 34 cases at Crucell sites where product manufacturing and/or development takes place. More than 90% of our employees work in these facilities. The accidents vary in severity, but are mostly relatively minor and generic in nature, such as a sprained ankle caused by slipping in a wet hallway. Continuous improvement of accident prevention and of the accident reporting system is a priority, and Crucell aims to report accurate and levelled numbers for the whole organization in the years to come.

In an important new safety initiative, Crucell started the roll-out of global systems for risk and crisis management in 2008. By raising employee's awareness of possible risks and establishing a systematic consolidation and escalation approach to their management, the program provides a basis for prioritization of preventive activities and resource allocation within Crucell, and aims to enable any potential crises that might occur to be resolved with optimal speed and efficiency. A well-defined structure with clearly defined responsibilities ensures that everyone in the organization knows how to respond in a potentially unsafe situation so that harms are avoided or minimized.

Our Consumers

Crucell's core business is protecting people from illness and death caused by infectious diseases. We have described our product range in the section 'What we do'. In addition to our marketed products, we have a broad pipeline of candidate products at various stages of research and development. Details can be found on page 26 of this 2008 Annual Report.

Crucell products are characterized by their outstanding quality and safety. Medical products – such as vaccines and antibodies – that are used in healthy people to prevent illness have to meet even higher regulatory standards of quality and safety than apply to medicines for treating the sick. Crucell does not simply comply with these stringent regulatory requirements; we surpass them. The products we sell are thoroughly monitored, reviewed and evaluated to the highest standards both during development and following commercialization. Regular inspections of our facilities, procedures and products by external authorities, as required in our highly regulated business, provide our consumers with a further guarantee of safety and quality.

More fundamentally, Crucell's focus on product safety, quality and convenience determines the innovative design and unique properties of our products. For example, our hepatitis A vaccine Epaxal® is based on virosome technology, a revolutionary adjuvant system that combines high efficacy with unprecedented safety. As a result, Epaxal® is the only hepatitis A vaccine on the market that is free of aluminum, a vaccine adjuvant (efficacy enhancer) that is commonly used but raises some safety concerns.

Beyond legislation for safety

Crucell's new manufacturing facility in Leiden, the Valerio Building, is currently being used to produce clinical materials for vaccines. These activities must be conducted in accordance with a range of legislative safety procedures in order to prevent the release of any clinical material into the environment. Besides complying with these legal requirements, Crucell has gone further by installing a sophisticated air exhaust system. Air is channelled through a high-tech afterburner, where it is heated to 450 degrees Celsius to destroy any airborne clinical material. It is then transferred to a cooling station to bring the air temperature back to an environmentally friendly level before it is released from the building.

As new facilities are built, environmentally friendly solutions are being incorporated into the design of the building.

Valerio Building

Environmental impact

Crucell understands its responsibilities with regard to the environment and strives to be as transparent as possible about its activities.

At Crucell, we are committed to ensuring that our environment, health and safety principles are integrated throughout our business units and facilities worldwide. In 2008 the decision was made to strengthen this commitment through the development of a management system that measures performance. Using a comprehensive plan-do-check-act model, our future EHS Management System is consistent with international standards such as OHSAS 18001 and ISO 14001.

At this stage, our system for reporting environmental indicators is still in its infancy and does for example not enable CO_2 calculations. Crucell is working on developing this reporting system so that we will be able to publish more comprehensive and more comparable data in the future.

Crucell is aware of the environmental footprint of packaging, and is researching the potential for improvements in this area, such as biodegradable products/packaging. We will continue to explore our options in this regard.

In the area of greening our information services, we have already made significant progress by moving towards 'virtual' servers, replacing paper-based data storage with digital archives and working wherever possible with environmentally friendly suppliers. For example, our intranet supplier was chosen partly because it offers a sustainable Co_2-neutral hosting service.

Further opportunities for reducing Crucell's impact on the environment include improving insulation and making better logistical use of our existing facilities. As new facilities are built, environmentally friendly solutions are being incorporated into the design of the building, utilities and equipment from the blueprint stage. A case in point is the design of the Valerio building, our state-of-the-art manufacturing facility in Leiden, the Netherlands.

Crucell's environmental efforts go beyond legal compliance.

An example: Combining vaccines for a diversity of benefits

Crucell's development of the pentavalent vaccine Quinvaxem® is a good example of how we are working to increase vaccination coverage and save lives in countries where healthcare resources are less than optimal. Quinvaxem® is a fully liquid vaccine combining antigens for protection against five potentially deadly childhood diseases: diphtheria, tetanus, pertussis (whooping cough), hepatitis B, and Haemophilus influenzae type B. As the first internationally available fully liquid vaccine containing all five of these antigens, Quinvaxem® offers major healthcare advantages, particularly for low-income countries with infrastructure and hygiene problems. The fully liquid, single-vial formulation of Quinvaxem® reduces waste and decreases the risk of contamination compared to products requiring reconstitution, as well as being more convenient. And because five antigens are delivered in a single shot, fewer injections and visits to a clinic are necessary.

This greatly increases the chance that children will receive protection against important diseases. Supranational organizations have awarded Crucell contracts worth $0.5 billion to supply Quinvaxem®, confirming the superior quality of our pentavalent vaccine, of which over half had been sold by the end of 2008. The remainder is expect to be sold in 2009. Quinvaxem® was launched end 2006 and has a market share of over 50% already. Currently Crucell is working on developing a hexavalent vaccine.

Energy & water consumption

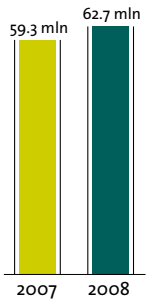
The first graph reflects the total energy consumption in kWh at Crucell facilities involved in product manufacturing and development, which represent over 90% of our global employees base. A 5.8% increase of energy consumption compared to 2007 can be noted. This increase can be explained by a general increase in activity worldwide, but especially by the start-up of operations at our new Valerio building in the Netherlands. In the future we expect energy efficiency gains as a result of this new building.

Energy use includes electricity, natural gas, oil, and other fuels as gasoline and diesel, all of which are converted to kWh. Compared to an average household (using 3400 kWh and 1650 m^3 of natural gas), Crucell's total energy consumption for 2008 resembles that of some 3502 households (in 2007: 3309 households).

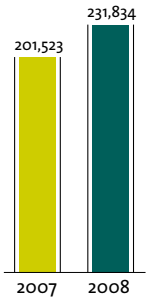
The second graph depicts the total water consumption in cubic meters (m^3) at Crucell facilities involved in product manufacturing and development, which represent over 90% of our global employees base. A 15% increase of water use compared to 2007 can be noted. This comes down to some 221 m^3 of water use per employee annually in 2008 (in 2007: 194 m^3).

Crucell has taken measures to reduce work-related travel, implementing a travel policy and actively encouraging employees to make use of a virtual conferencing system. Crucell's new travel policy defines the principles our employees should adhere to in order to travel in a safe and cost-effective manner as they conduct company business. It is the company objective to simultaneously reduce travel costs while supporting business development.

Total energy consumption
(in kWh)



Total water consumption
(in m^3)



Crucell is fully committed to being a good corporate citizen and conducting business in an honest and ethical way with the lowest possible environmental footprint.

Economic aspects of our business

Crucell's core business is protecting people from illness and death caused by infectious diseases. We aim for financial profitability, but also to bring the greatest possible benefit to human health worldwide. These two goals are inextricably linked. Our solid balance sheet and strong cash position demonstrate the sustainability of our company and of the healthcare benefits we deliver.

Crucell is making progress with regard to reporting its CSR activities and this section of the 2008 Annual Report marks the beginning of a more comprehensive, transparent approach to CSR. Our efforts to develop a more comprehensive management system will certainly contribute to the achievement of this ambition. This year we have not chosen to perform a third party verification of our CSR chapter and data. We see this as a possible future option that could strengthen our CSR performance.

Crucell is a rapidly growing pharmaceutical company with ambitious goals and a clear strategy for sustainable growth. By optimizing our business performance we are continuously increasing the number of people we can protect from illness and death caused by infectious diseases. Crucell is fully committed to being a good corporate citizen and conducting business in an honest and ethical way with the lowest possible environmental footprint.

Crucell welcomes any feedback with regard to activities and disclosure around CSR on: csr@crucell.com.

Forward-looking statements

This Annual Report contains forward-looking statements. All statements regarding our future financial condition, results of operations an business strategy, plans and objectives are forward-looking. Statements containing the words 'believes', 'intends', 'expects', and words of similar meaning are also forward-looking. In particular, the following are forward-looking in nature: statements with regard to strategy and management objectives; technology and product development efforts; our ability to realize commercially valuable discoveries; our intellectual property portfolio; our ability to develop potential products and technologies suitable for commercialization; the effects of changes or prospective changes in regulation; and trends in results, operations and overall market trends.

These forward-looking statements involve risks, uncertainties and other factors, some of which are beyond our control, that may cause our results, performance or achievements or conditions in the markets in which we operate to differ from those expressed or implied in these forward-looking statements. We describe certain of these risks and uncertainties in the section 'Risk factors'. We caution not to place undue reliance on these forward-looking statements, which reflect our Management's view only as of the date of this document.

Trademarks

New trademarks for our products are registered on a worldwide basis. Distribution and agency agreements normally include a clause specifying that, at the termination of the agreement, trademark and product registration rights return to us. We are the owner of over 150 registered trademarks. The most important of these are: CRUCELL®, BERNA®, SBL®, the Berna, SBL and Crucell logos, ChromaGenics®, EPAXAL®, Epaxal® Junior, INFLEXAL®, VIVOTIF®, FLAVIMUN®, DUKORAL®, HEPAVAX-GENE®, MoRu-Viraten®, PER.C6®, PER.C6® logo, AdVac®, MAbstract® and STAR®. In addition we hold rights to use certain trademarks that are owned by our partners, such as Quinvaxem® from Novartis (formerly Chiron). All other trademarks, service marks, trade names and registered marks used in this report are trademarks, trade names or registered marks of their respective owners. Crucell N.V. and its subsidiaries own a number of additional trademarks, including registered trademarks that are not referenced in this report.

Contents

All amounts set forth in this Annual Report, unless otherwise noted, are in thousands of Euro, except share and option data.

Report of the Management Board

Overview of the year

The year 2008 was truly unique for Crucell as we achieved net profit for the first time in the history of the Company. In addition we exceeded our revenue targets, considerably improved our gross margin and were cash flow positive. It is Crucell's ambition to deliver on promises and we clearly exceeded the targets set at the beginning of the year. Our 2008 financial highlights include:

- Growth of 33% in revenues and other operating income in 2008;
- Net profit of € 14,586 in 2008 compared to a net loss of € 42,910 in 2007;
- Gross margin for the year improved to 45% in 2008 compared to 34% in 2007; and
- Positive cash flow of € 7,721 increasing the 2008 year-end cash position to €170,969.

Our mission is to develop, produce and market vaccines and antibodies that prevent or treat infectious diseases. We have a fully-integrated infrastructure for in-house development, production and marketing of vaccines, and we are now leveraging our knowledge in this area to enter the antibodies market for infectious diseases. Our business strategy is based on the following business drivers:

- Leveraging presence of our marketed vaccines in public and private markets;
- Building a product pipeline with sustainable competitive advantage; and
- Building upon ongoing technology licensing programs.

The weakness of the global economy in 2008 is a challenge for many companies worldwide. The ongoing financial crisis became prominent in September 2008 with the failure or near-failure of several United States and European based financial institutions. The resulting deterioration in financial and market conditions spread around the globe. In recent months, the financial crisis has adversely affected businesses in many industries and geographical areas all over the world at an unexpected pace.

Despite the weak global economic climate we achieved all targets we set ourselves for the financial year 2008. Our success depends in part on our solid customer-base, which is relatively unaffected by deterioration in the global economy, since many of our customers are governmental agencies or supranational organizations. We do not expect our business will be significantly affected by the weak global economy in 2009.

Leveraging presence of our marketed vaccines
For the full year 2008, product sales were € 226,055, representing sales of paediatric vaccines (49%), travel and endemic vaccines (25%), respiratory vaccines (14%) and other products (12%). Our product sales grew by € 48,486 or 27.3%. The increase is primarily attributable to increased sales of our paediatric vaccines, specifically Quinvaxem, of € 33,668 and travel and endemic vaccines of € 8,290.

Quinvaxem is our fully liquid pentavalent vaccine against five important childhood diseases that is approved by the WHO. In 2008 we more than doubled the production and we were able to continue the success of Quinvaxem as sales grew from 21.3 million units in 2007 to 39.6 million units in 2008. In anticipation of the expected further growth of Quinvaxem in 2009, we continued to build up stock of Quinvaxem in the fourth quarter of 2008.

In 2008, the Chinese authorities approved Hepavax-Gene, our recombinant Hepatitis B vaccine, which is a significant advancement in the expansion of Crucell's business in the highly strategic Chinese vaccine market. This will accelerate the growth of our Chinese operations.

Operations
In February 2008, our Chief Operating Officer, Cees de Jong, was nominated to join the Management Board. This nomination was approved by our shareholders at the Company's annual general meeting on May 30, 2008. Cees joined Crucell in September 2007 and he was already part of Crucell's Management Committee, prior to his nomination to the Management Board.

In 2008, we also attracted several new senior managers to further improve the quality of our operations. During 2008 we strengthened the manufacturing organization and we were able to improve our performance significantly as yields of important production processes increased and scrap rates decreased. Expenses on operations were more or less stable compared to 2007 despite a significant increase in production volumes.

All our facilities were audited multiple times during the year by customers and/or regulatory authorities. All audits were successful, confirming our compliance with relevant rules and regulations. In Bern, Switzerland, we successfully refurbished our MoRu-Viraten (MR) filling line and obtained approval from Swissmedic to recommence production. In Madrid, Spain, we installed a new filling line for syringes, bringing the total capacity of our dedicated fill/finish center in Spain to approximately 100 million syringes per annum. The Spanish authorities audited and approved the new line in December 2008.

In October 2008, we announced that an agreement was reached to relocate our Korean production facility, that manufactures Quinvaxem and Hepavax-Gene, from the Shingal site in Yongin City to the Incheon, Free Economic Zone. We agreed on the time-line and conditions of this relocation with all parties involved, facilitating a smooth transition to the new production facility. The new facility will enable the further growth and efficient production of Quinvaxem and Hepavax-Gene. All litigation surrounding our production facility has been settled.

In August 2008, we announced the intention to move Dukoral and rCTB bulk production, formulation and fill/ finish activities from Sweden to other sites within the Crucell organization. The Group is currently conducting a feasibility study to determine the scope and timing of a potential move. The research activities conducted at our Swedish site were discontinued in 2008 and are now concentrated in Leiden, the Netherlands.

We entered into an exclusive vaccine development agreement with Wyeth Pharmaceuticals in which we will be responsible for the development and manufacturing of certain components of a vaccine for use by Wyeth in clinical studies. Wyeth will be responsible for the clinical development of the vaccine. The development activities will take place in Crucell's dedicated vaccine manufacturing facilities in Bern, Switzerland, which had been fully impaired in 2006, enabling a partial reversal of that impairment in 2008.

Product pipeline with sustainable competitive advantage

Our rabies candidate product achieved positive preliminary results in the phase II study that was carried out in the US. No adverse events were reported and the study confirmed the neutralizing activity of the monoclonal antibody product against the rabies virus. A second phase II clinical study evaluating the monoclonal antibody cocktail in combination with a vaccine in healthy children and adolescents was conducted in the Philippines from May to October 2008. Final data from this study is expected to become available in the first half of 2009. An additional phase II study in healthy adults evaluating Crucell's monoclonal antibody in combination with another rabies vaccine is scheduled to start in India in the second quarter of 2009.

For our Ebola and Marburg vaccine research we secured a contract with the US National Institute of Allergy and Infectious Diseases (NIAID), which is part of the National Institutes of Health (NIH) aimed at advancing the development of Ebola and Marburg vaccines, the ultimate goal being a multivalent filovirus vaccine. The contract provides us with funding of up to US Dollar ($) 30 million, with additional options that may be triggered at the discretion of the NIH worth a further $ 40 million. The phase I study of an adenovirus 5 (Ad5)-based Ebola vaccine, being developed in partnership with the Vaccine Research Center (VRC) of the NIAID/NIH, showed safety and immunogenicity. Based on these results, a second phase I study of an Ebola and/or Marburg vaccine is anticipated. The study will use alternative adenovirus vectors, which are able to bypass pre-existing immunity against Ad5.

Our research on a tuberculosis vaccine in collaboration with Aeras is ongoing. In October 2008, Crucell and the Aeras Global TB Vaccine Foundation announced the start of a phase I clinical trial in Kenya. The main parameters of the study are to test the safety of the vaccine candidate in healthy adults. We also started the enrollment of the first phase II study of the vaccine candidate, which will be conducted in South Africa by the University of

Cape Town Lung Institute in conjunction with the South African Tuberculosis Vaccine Institute.

Our malaria research in collaboration with the NIAID/ NIH is progressing as we are carrying out a phase I trial in the US. The study is being carried out at two sites: Vanderbilt University in Nashville, Tennessee, US, and Stanford University in Palo Alto, California, US. The first three groups have been enrolled and ongoing safety monitoring has revealed no significant safety concerns to date, but formal analysis awaits. Enrollment for the fourth and final group of volunteers is ongoing.

In our influenza research, Crucell's scientists discovered a set of human monoclonal antibodies that provides immediate protection and neutralizes the broadest range of H5N1. When tested in pre-clinical models for prevention or treatment of a potentially lethal H5N1 infection, these antibodies were shown to prevent death and cure the disease.

In another pre-clinical study, Crucell's mAb CR6261 was compared with the anti-influenza drug oseltamivir in terms of their value for flu prevention and treatment. In December 2008, we announced that our monoclonal antibody strongly outperformed oseltamivir in the tests that were conducted. The flu strains tested included the 'bird flu' strain H5N1, which, experts fear, has the potential to cause a pandemic, and H1N1, which is similar to the flu strain responsible for the devastating pandemic in 1918. Importantly, the study showed that CR6261 provides immediate protection against the influenza virus, suggesting that it will be able to prevent the spread of disease. In contrast, oseltamivir was less efficacious and in some cases not effective at all.

Registration submission of Flavimun, our yellow fever vaccine in Switzerland was completed in the first quarter of 2009. Registration submission in Germany is expected in 2009.

Unique technologies for licensing business
In 2008, our license revenues grew by € 17,991 or 147.3%. The increase is mainly due to revenues generated by our collaboration with sanofi pasteur.

In 2008, Crucell signed licensing agreements with Abraxis Bioscience, Inc., Affitech AS, Arana Therapeutics Ltd, Bioceros, Biochrom, Cangene Corp., Celltrion, Inc., Gedeon Richter, GlaxoSmithKline, CSL Ltd., Lonza, Medarex Inc., MorphoSys AG, Profibrix B.V., Synthon B.V., Talecris Biotherapeutics and Toyobo Gene Analysis Co. Ltd.

We signed two exclusive, commercial license agreements with Talecris Biotherapeutics for two undisclosed and specific proteins and the exclusive rights to produce those proteins using the PER.C6 cell line. In total, we received upfront payments of $ 4 million upon the execution of the agreement and will be eligible for milestone payments of approximately $ 50 million more.

There were also positive developments for our intellectual property. We were successful in opposing European patents of our competitors as we managed to obtain complete revocations of European patents owned or controlled by GenVec, Genentech, Baxter, Novartis Vaccines & Diagnostics, Wellcome Foundation (GlaxoSmithKline (GSK)), and others. In addition, we obtained a favorable decision from the South-Korean Supreme Court in the longstanding invalidity law suit in South Korea against GSK's multivalent Hepatitis B virus vaccine patent. These developments further paved the way for Crucell's pipeline development activities and marketed products. Conversely, we were successful in defending our own PER.C6 and AdVac patents against attacks by its competitors. Except for one PER.C6 patent that has been maintained in amended form and is now pending before the board of appeal, all PER.C6 patents have survived opposition before the European Patent Office essentially intact.

The following technological progress was achieved during 2008:

- We achieved important advances in antibody production using our PER.C6 technology platform together with our partner DSM Biologics. By employing the PER.C6 human cell line and proprietary XD™ technology, we achieved a record yield of over 27 grams per liter of IgG antibodies. In addition the high-titer fed-batch process was scaled up to 250 liters by DSM Biologics scientists at their GMP facility in Groningen, The Netherlands;

- Our PER.C6 technology licensee Ark Therapeutics has entered a phase III study with its product Trinam. Ark Therapeutics is the first of our licensees to enter into a phase III study with a product produced on Crucell's PER.C6 human cell line; and
- We announced that the novel recombinant adenovirus serotype 26 (rAd26) vector, which is jointly developed by Crucell and the Beth Israel Deaconess Medical Center (BIDMC) in the US, will be used in a phase I clinical study to test a new HIV vaccine. The rAd26 vector is specifically designed to avoid pre-existing immunity to the more commonly used adenovirus serotype 5 (Ad5), which has recently shown limitations as an HIV vaccine vector. This clinical trial is the first 'in man' study of this newly developed vector, which could provide a solution to problems seen in previous HIV vaccine trials. The rAd26 vaccine is the first HIV vaccine candidate to emerge from the Integrated Preclinical/Clinical AIDS Vaccine Development (IPCAVD) program.

In November 2008, the leading scientific journal 'Nature' published a study that demonstrated the value of our alternative adenovirus serotype technologies. Using Crucell's AdVac vaccine technology and PER.C6 manufacturing technology, scientists engineered the rare adenovirus serotypes Ad26 and Ad35 to express a protein of SIV, the primate equivalent of HIV. We have developed rare serotype adenoviral vectors, such as rAd26 and rAd35, to provide more potent prime-boost vaccine regimens. The study, which investigated the immunogenicity and protective efficacy of different vaccination regimes using rAd26, rAd35 or rAd5 as a primer, followed by a boost with rAd5, showed that in particular the rAd26/rAd5 combination elicits a strong T-cell immune response and provides protection against the HIV-like virus in primate subjects. We have several vaccines in development using alternative rAd26 and rAd35 vectors, including vaccines against malaria and tuberculosis.

For further details on licenses and licensees please see 'Information on the Company – Overview of Licensees and Partners' in this Annual Report.

Subsequent events
On January 7, 2009, we announced that we were in friendly discussions with Wyeth regarding a potential combination of the two companies. On January 26, 2009, we announced that Wyeth withdrew from these discussions.

Outlook 2009

The key to our strategy is continued growth. The outlook for 2009 is promising as we expect revenue and other operating income to grow, operating profits to increase significantly and to achieve a solid cash flow despite significant investments. Our Healthy Ambition program has a clear focus on achieving operational excellence and is on track to realize cost savings of € 30 million by the end of 2009. We do not expect our business to be adversely affected in 2009 by the weak global economy resulting from the continuing international financial crisis.

In 2009, we will focus on continued growth.

- We expect our combined full-year 2009 total revenue and other operating income to grow by 20% in constant currencies that are set at a guidance rate of Euro/US Dollar of 1.35;
- Operating profit for 2009 is expected to improve significantly compared to 2008;
- Furthermore, the Company expects solid cash flow despite significant investments in the new facility being built in Korea. These investments are expected to total approximately € 50 million, with the majority of the spending in 2009;
- We do not expect our business to be significantly affected by the weak global economy in 2009; and
- We will pursue key partnerships, focus on progress in clinical development and continue with broadly licensing our technologies.

In the course of 2009, we expect to make further decisions that may impact our income statement. Consequently we cannot comment on expected 2009 results in more detail than described above.

Our Healthy Ambition program has a clear focus on achieving operational excellence. The program works towards exploiting synergies, reducing costs and funding growth. Important elements of the program include: product portfolio optimization, process and infrastructure optimization, network rationalization and further integration and streamlining of various functions. Healthy Ambition is targeting savings of € 30 million by the end of 2009. For 2009, the focus will be on reducing complexity and further streamlining the organization.

We expect continued investments in our manufacturing facilities to ensure that they remain state-of-the-art and continue to meet the highest applicable regulatory standards. In October 2008, we announced that we will relocate our Korean production facility. The investments in the new facility are expected to total approximately € 50 million, with the majority of spending occurring in 2009. We entered into a mortgage loan facility in Korea for an amount of KRW 50 billion to partly finance the investments in the new Korean facility in 2009.

Our continued growth strategy also includes continued investments in R&D to ensure solid progress in clinical development. Both vaccine and antibody research is being focused on combating infectious diseases, with an emphasis on the existing categories of paediatric, travel and endemic, and respiratory illnesses. In addition, we will continue to invest in discovery programs and progress these into the clinical trial phase. Lifecycle investments are required to ensure that we continue to meet the highest regulatory standards and to further improve the lifecycle of our products.

We expect the deal flow from our PER.C6 licensing business to continue. We believe that the number of licenses and the revenue flow from the PERCIVIA joint venture will continue to be significant.

We expect revenues throughout 2009 to be phased similarly to those in 2008. Our cash flow position is expected to deteriorate significantly in the first half of 2009, which is normal due to the seasonality of our business. We build-up inventory in the first half of the year and sell our respiratory and travel vaccine products principally in the second half of the year.

Information on the Company

History and development of Crucell

We are a public limited liability company under Dutch company law, incorporated in Leiden, the Netherlands with the legal and commercial name Crucell N.V., ('Crucell' or the 'Company') registered under number 28087740. We were incorporated on October 9, 2000, as the holding company for Crucell Holland B.V., formerly called IntroGene B.V., following the combination of IntroGene B.V. and U-BiSys B.V. Our principal executive office is located at Archimedesweg 4-6, 2333 CN Leiden, the Netherlands. Our telephone number is +31 (0)71 519 9100. Our registered agent in the US is CT Corporation, 111 Eighth Avenue, New York, New York 10011. Crucell and its subsidiaries together constitute the Crucell Group, or the 'Group'. The Company has subsidiaries in the Netherlands, Switzerland, Spain, Italy, Sweden, Korea and the US.

In February 2006, we acquired a controlling interest in the Swiss biotech company Berna Biotech AG in a share exchange. In September 2006, we acquired the remaining 1.6% minority interest. Berna Biotech AG was founded in 1898. Prior to the acquisition, Berna was a fully integrated biotechnology company that marketed numerous vaccines on a global scale.

In October 2006, the Company purchased, via its subsidiary Crucell Vaccines Inc., the assets and liabilities of the Florida-based Berna Products Corp. from Acambis plc. Berna Products Corp. was originally established in 1990 by Berna Biotech AG to market Vivotif, Berna's oral typhoid fever vaccine, in the US and Canada and was acquired by Acambis plc in 2003.

In November 2006, we acquired the shares of Stockholm-based SBL Vaccin Holding AB (SBL) from 3i and SEB. SBL was a fully integrated independent Swedish biotechnology company. SBL's main product was Dukoral. In addition, SBL had a sales and distribution organization for vaccines in Scandinavia.

In November 2006, we and our technology partner DSM Biologics opened the PERCIVIA PER.C6 Development Center in Cambridge, Massachusetts, US. The joint venture was conceived and designed to further develop the PER.C6 cell line and provide turnkey solutions for the production of monoclonal antibodies and recombinant proteins.

On January 7, 2009, we announced that we were in friendly discussions with Wyeth regarding a potential combination of the two companies. On January 26, 2009, we announced that Wyeth withdrew from these discussions.

Business drivers

Our business strategy is based on the following business drivers:

Products

Leveraging presence of our marketed vaccines in public and private markets.
We produce and sell established paediatric, respiratory and travel vaccines. We intend to enhance our position in these markets by highlighting the unique features of these products and by providing outstanding customer service in terms of delivery, reliability and quality and by leveraging our worldwide presence in both public and private markets.

Our core portfolio consists of the following products:

- Quinvaxem, a fully-liquid vaccine for protection against five important childhood diseases;
- Hepavax-Gene, a recombinant vaccine against hepatitis B;
- MoRu-Viraten, a vaccine against measles and rubella (all age groups);
- Epaxal and Epaxal Junior, the only aluminum-free and biodegradable vaccine against hepatitis A;
- Vivotif, the only oral vaccine again typhoid fever;
- Dukoral, the only oral vaccine against diarrhea caused by cholear and ETEC (Enterotoxigenic E. Coli); and
- Inflexal V, the only virosomal adjuvanted influenza vaccine for all age groups.

Research and Development (R&D) product pipeline with competitive advantage

We believe that each of our selected products targets unmet medical needs, improves current medications or is otherwise believed to be marketable due to predictive study models and/or perceived favorable regulatory conditions. These products are predominantly based on our PER.C6 technology. In addition, we have various discovery programs to find new vaccine and antibody products.

Besides our portfolio of well known vaccines, we have a pipeline of new potential vaccines and antibodies. Product pipeline programs include

vaccines against yellow fever, influenza, tuberculosis, Ebola and Marburg, malaria, HIV, rabies and H5N1 antibodies. Our R&D activities are concentrated in our headquarters in the Netherlands, but we also have R&D facilities in Switzerland and Korea. Product development is concentrated at our Swiss operations in Bern.

Technologies – ongoing technology licensing program

We have a broad base of excellent technologies with applicability to vaccines, antibodies, other recombinant proteins and gene therapy. Our licensing program provides a source of revenue as well as the potential for future, additional revenue in the form of royalties from products developed by our licensees. In areas where we are not developing our own products, we offer our technologies to the biopharmaceutical industry for the development and production of diverse biopharmaceutical products.

We have developed various proprietary technologies such as PER.C6, AdVac, MAbstract, STAR, our virosomal technology, rCTB as well as our Hansenula polymorpha expression system. We believe our proprietary PER.C6 technology is well suited for the development and large-scale manufacturing of a wide range of biopharmaceuticals including vaccines, monoclonal antibodies, therapeutic proteins and gene therapy products. AdVac is used to develop novel adenoviral-based products. MAbstract can b used to develop human antibodies. Our STAR technology is useful for increasing production output of recombinant antibodies and therapeutic proteins on mammalian cell lines and there are indications that the technology is complementary to our PER.C6 technology.

Products

Overview

Our products are marketed by our own sales force as well as by our distribution partners. Our sales are subject to seasonal variations with the majority of our sales coming in the second half of the financial year. This is specifically the case for our influenza vaccines as vaccination programs mainly take place in the second half of the year. In addition, our travel vaccines are also subject to seasonal travel patterns. See 'Partners, agreements, investments and other collaborations – Marketing and sales partners' in this section for more details on our partners.

Vaccine markets
Our core product portfolio currently consists of seven marketed vaccines in three areas of the vaccine market: paediatric vaccines, travel and endemic vaccines and respiratory vaccines.

Paediatric vaccines
Our core paediatric vaccines are Quinvaxem, Hepavax-Gene and MoRu-Viraten.

Quinvaxem
Quinvaxem combines antigens for protection against five important childhood diseases: diphtheria, tetanus, pertussis (whooping cough), hepatitis B and Haemophilus influenzae type b, one of the leading causes of bacterial meningitis in children. It is the first internationally available fully-liquid vaccine containing all five of the above antigens, offering a major advantage in terms of convenience of use. Quinvaxem was co-developed with Novartis, which provides four of the five components in bulk. The fifth component is our vaccine Hepavax-Gene.

We produce Quinvaxem together with our hepatitis B vaccine Hepavax-Gene in Korea. In October 2008, we announced that we will relocate the Korean production facility from Yongin City to the Incheon, Free Economic Zone. The new facility will enable the further growth and more efficient production of Quinvaxem and Hepavax-Gene.

As Quinvaxem has been pre-qualified by the World Health Organization (WHO), it is available for purchase by supranational organizations. Supranational organizations are major customers for combination vaccines, which are used in large vaccination programs around the world. In September 2008, we were awarded with new contracts totaling over $ 140 million for our Quinvaxem and Hepavax-Gene paediatric vaccines by supranational organizations. The contracts provide for the supply of these vaccines for the period 2008 – 2009, bringing the total value of the contracts for the period 2007 – 2009 to $ 500 million.

Hepavax-Gene
Hepavax-Gene is a recombinant hepatitis B (HBV) vaccine made using Crucell's proprietary Hansenula polymorpha expression system. It is one of the WHO's pre-qualified vaccines for active immunization against HBV. A key competitive advantage for Hepavax-Gene is our stable and efficient production system.

In 2008, the Chinese authorities released Hepavax-Gene for registration and quality control in China. Market researcher Decision Resources estimates that the Chinese HBV drug market will more than double between 2007 and 2012 (from $340 million in 2007 to $800 million in 2012).

About hepatitis B
HBV is a viral infection of the liver that causes various complications if left untreated and may even ultimately cause death. Transmission of HBV occurs as a result of the exchange of blood, the exchange of fluids during sexual intercourse or the exchange of bodily fluids between an infected mother and a newborn baby at birth.

MoRu-Viraten
MoRu-Viraten is a safe, well-tolerated and effective vaccine for protection against measles and rubella in children, adolescents and adults. The immunogenicity and safety of MoRu-Viraten have been confirmed in clinical trials and extensive post-marketing surveillance. MoRu-Viraten is free of avian proteins and antibiotics, posing no risk to children with allergies to these substances. The vaccine has been marketed since 1986 and is on the WHO list of vaccines for purchase by UN agencies.

About measles and rubella
Measles is a highly contagious disease caused by the measles virus. It is spread by droplets or direct contact with nasal or throat secretions of infected persons and less commonly through the air or indirect contact. Measles continues to remain a serious public health concern worldwide with 30-40 million cases occurring annually. It may be ultimately responsible for more child deaths than any other single agent and is a major cause of preventable blindness in the world. Rubella is a moderately contagious disease caused by the rubella virus. Transmission of the virus is via airborne droplets. It has been estimated that over 100,000 cases of congenital rubella syndrome (CRS) occur in developing countries each year.

Travel and endemic vaccines

Our core travel vaccines are Epaxal, Vivotif and Dukoral.

Travel vaccines include all vaccine products that protect against diseases that are not native to the region travelers are from, but are present in the regions to which they travel. Generally, the target population groups for these vaccine products are individuals travelling to endemic and epidemic regions. Our vaccines for hepatitis A, typhoid and cholera are classified as travel vaccines.

Our travel vaccines are also increasingly used in expanded immunization programs. Vaccines used in countries with medium to high endemicity could also be characterized as routine or paediatric vaccination. Furthermore, even in some European countries where endemicity is low, childhood vaccination against Hepatitis A virus (HAV) is recommended. This vaccine represents a large potential upside for vaccine manufacturers as they can be targeted at multiple markets.

Epaxal
Epaxal is the only aluminum-free and biodegradable HAV vaccine on the market, offering significant advantages in terms of tolerability. It was the first product to be based on the virosome technology developed and patented by the Crucell company, Berna Biotech AG. It induces protective antibody levels within 10 days of primary vaccination, and provides seroprotection for at least 20 years following the second (booster) dose. In most countries, the vaccine is licensed for adults and children over the age of one. It is currently licensed in more than 40 countries under the brands Epaxal, HAVpur and VIROHEP-A.

About hepatitis A
Hepatitis A (HAV) is a highly contagious infection that causes temporary acute inflammation of the liver. It can range in severity from a mild illness lasting a few weeks to a severe illness lasting several months. HAV infection produces a self-limited disease that does not result in chronic infection or chronic liver disease. HAV is generally contracted orally and commonly spreads through improper handling of food, contact with household members, sharing toys at day-care centers or eating raw shellfish taken from polluted waters.

Vivotif
Vivotif is a live attenuated typhoid fever vaccine for oral administration. The vaccine is indicated for adults and children over the age of five and has an excellent track record for safety, having been on the market for more than 20 years. Protective efficacy is proven in several large-scale field trials including more than 500,000 subjects. It is currently licensed in over 30 countries, including the United States. Data suggests that Vivotif may be unique in also protecting against paratyphoid A and B fever

which is caused by Salmonella strains similar to Salmonella Typhi.

About typhoid fever
Typhoid fever is a debilitating and life-threatening illness caused by the bacteria Salmonella Typhi. Symptoms of the disease include fever, stomach pain, weight loss, loss of appetite, delirium, severe diarrhea (in children), constipation (in adults), cerebral dysfunction and intestinal perforation. The disease is transmitted by faecal contamination of food or water, or by person to person contact.

Typhoid fever is endemic in many parts of Africa, Asia and Latin America. 21 million people are estimated to develop typhoid fever each year. 1-4% of persons with typhoid fever die. At least 5 million people are believed to develop paratyphoid fever annually.

Dukoral
Dukoral is an oral vaccine that protects against cholera and the enterotoxigenic Escherichia coli (ETEC) and is registered in more than 60 countries. The vaccine has demonstrated a protective efficacy against cholera of approximately 85% and 60% against ETEC. Dukoral acts by inducing antibodies against both the bacterial components and cholera toxin (CTB). The vaccine is suitable for travelers and is indicated for use in adults and children over two years of age. Pregnant and lactating women may use it. Other than Dukoral there is no cholera and ETEC combination vaccine available in the world.

About Cholera
Cholera is an acute, diarrheal illness caused by infection of the intestine with the bacterium vibrio cholerae. Over 90% of all cholera cases are mild to moderate and present themselves as ordinary traveller's diarrhea. Approximately 10% of infected persons have a severe case, characterized by profuse watery diarrhea, leg cramps and vomiting, resulting in rapid loss of body fluids leading to shock and dehydration. Without treatment, death can occur within hours. According to the US Center for Disease Control and Prevention, cholera has been very rare in industrialized nations for the last 100 years; however, the disease is still common in other parts of the world and the cholear bacteria can be found in many travel destinations, for example in most part of Asia, Africa and South America. It spreads via contaminated food and water.

Respiratory vaccines

Our core respiratory vaccine is Inflexal V.

Inflexal V
Inflexal V is a virosomal adjuvanted Influenza vaccine (subunit), based upon the virosome technology developed and patented by the Crucell company, Berna Biotech AG. It is the only adjuvanted flu vaccine licensed for all age groups (from 6 months and up). The vaccine's antigen composition follows yearly WHO recommendations. Inflexal V was originally introduced in 1997, is registered in 38 countries and has extensive market experience, with more than 41 million doses confirming its safety profile. The tolerability of Inflexal V is excellent due to its biocompatibility and purity.

About influenza
Influenza, commonly known as 'flu', affects large sections of the world's population each year. The disease is characterized by annual winter outbreaks, which often reach epidemic proportions due to the fact that the virus can mutate quickly, often producing new strains against which human beings do not have immunity. Typical symptoms of flu are usually relatively mild but can become life threatening in vulnerable patient groups, such as the elderly and immunodeficient individuals. In a growing number of countries, small children have been added to the list of preferred protection groups. Transmission of the flu virus occurs through airborne particles and upon infection, the incubation period ranges from one to three days.

Each year approximately 5%-15% of the world's population contracts influenza and an estimated 250,000 to 500,000 people die annually from influenza-associated complications according to the World Health Organization. As well as these annual epidemics, a major genetic shift in the influenza virus can occasionally lead to a deadly new virus strain to which the human population does not have immunity, resulting in a global pandemic. Concerns currently exist that a new avian influenza strain (H5N1) endemic among birds in Asia, and showing high pathogenicity for humans, could present a genuine pandemic threat.

Several factors contribute to the rapid growth of the influenza vaccine market. We expect that the threat of a pandemic of avian flu, the ageing of the population in numerous developed countries,

national government-sponsored vaccination programs in many countries, higher awareness of the value of a flu vaccination among the public at large, as well as specific production contracts for vaccines that combat strains of pandemic flu and ongoing activities to increase the preparedness for a flu pandemic will lead to further growth in the seasonal flu markets.

Research and Development pipeline

Overview

Our product development programs comprise vaccines against yellow fever, influenza, tuberculosis, Ebola and Marburg, malaria, HIV, human monoclonal antibodies against rabies and human monoclonal antibodies against a broad range of influenza.

Overview of our pipeline based on proprietary technologies

Our PER.C6 technology, complemented by our AdVac and MAbstract technologies, drives the development of our product pipeline. We continue to develop our technologies while selecting product leads for further development based on careful product selection criteria that support our long-term business objectives. We have in the past and may again in the future, enter into collaborative and/or strategic alliance arrangements with third parties to co-develop and market products.

Our primary focus is the development of a range of novel vaccine and antibody products in the area of infectious diseases. We currently have a number of core potential products we are developing using our core technologies:

- An influenza vaccine, in collaboration with sanofi pasteur is being developed using our PER.C6 technology;
- Our Ebola and Marburg, malaria and TB vaccine candidates are recombinant vaccines based on PER.C6 technology that also employ AdVac technologies; and
- Our candidate rabies and influenza antibodies are generated and produced using our PER.C6 and MAbstract technologies.

Of the potential products we have under development, only our yellow fever vaccine does not use our core technologies.

Overview of our late-stage pipeline

Yellow fever vaccine
Crucell has developed the yellow fever vaccine, Flavimun, based on a well-established vaccine formerly produced by the Robert Koch institute in Germany. We acquired the rights and know-how for this vaccine against yellow fever from the Robert Koch Institute, which has produced the vaccine since 1963. Over 2.5 million doses of the vaccine have been distributed. The vaccine is safe, highly immunogenic and well tolerated. Protection starts ten days after a single dose and persists for ten years. The product was submitted for registration with the Swiss authorities in the first quarter of 2009. Registration submission in Germany is expected in 2009.

Overview of our early-stage pipeline

The following is a short description of our main potential products in the early-stage pipeline as well as the diseases those products target.

Influenza
Influenza vaccines were classically produced on embryonated chicken eggs. Currently, cell culture systems are being developed for more efficient influenza vaccine production based on Madin Darby Canine Kidney (MDCK) cells and VERO cells. In contrast to MDCK and VERO cells, PER.C6 cells grow well in suspension and are thus easily scalable, permitting the production of cost-efficient vaccines in large quantities. PER.C6 cells possess the different receptors required for the production of vaccines against both human and avian strains of influenza that may present a pandemic threat.

Sanofi pasteur
In December 2003, we entered into a strategic agreement with sanofi pasteur to further develop and commercialize novel influenza vaccines using our PER.C6 technology. Since the inception of the collaboration, production processes have been under development, with the production of a Good Manufacturing Practice (GMP) master cell bank already completed. Currently, we are working to develop a pandemic flu vaccine as well as an interpandemic, or seasonal, flu vaccine under this contract. A phase II testing of the cell culture-based seasonal influenza vaccine was initiated in the US and started in the fourth quarter of 2007. In the third quarter 2008, we received a milestone payment for the progress of the phase II trials involving healthy adult volunteers in the US.

The trials focus on the safety profile and immunogenicity of the cell-based vaccine.

Tuberculosis
Crucell is developing a recombinant tuberculosis (TB) vaccine based on our AdVac and PER.C6 technology. The development of this vaccine is being carried out in collaboration with the Aeras Global TB Vaccine Foundation (AERAS). The Crucell-Aeras TB vaccine program is focusing on an AdVac based vaccine that can boost the immune response against TB, initially induced by Bacille Calmette-Guérin (BCG) vaccine, using our PER.C6 and AdVac technologies.

A first phase I clinical trial, launched in October 2006 in Kansas, US, indicated that the vaccine candidate, AERAS-402/Crucell Ad35, is safe in healthy adults in the US. The preliminary results of a second study, launched in May 2007, showed that both critical arms of the cellular immune system, CD4 and CD8 immune T-cells, were induced and that in those participants who responded, CD8 immune responses were considerably higher than had ever previously been seen in a TB vaccine study. A third phase I study in St. Louis, Missouri, US was launched in December 2007 and focuses on the immunogenicity and safety of two AERAS-402/Crucell Ad35 boost doses administered at three to six month intervals after BCG priming in healthy adults.

An ongoing study in St. Louis, MO, US is evaluating a longer prime-boost interval. The study has been fully enrolled and has discovered no safety issues. Immunological data is expected to be available in the first half of 2009.

In October 2008, Crucell and AERAS announced the start of a phase I clinical trial in Kenya. The main parameters of the study will be to test the safety of the vaccine candidate in healthy adults, all of whom have been previously vaccinated with the BCG vaccine and a subset of whom have evidence of having been exposed to TB. This study is fully enrolled and now in its follow-up segment, with no safety issues identified. The companies also started the enrollment of the first phase II study of the vaccine candidate. The study is being conducted in Cape Town, South Africa by the University of Cape Town Lung Institute in conjunction with the South African Tuberculosis Vaccine Institute. No evidence of an unacceptable safety issue has been found in its dose escalation design.

About tuberculosis
TB is a major cause of illness and death worldwide, especially in Asia and Africa, with over 9 million new cases diagnosed in 2006. According to the World Health Organization (WHO), an estimated 1.7 million people died from TB in 2006. One third of the world's population has been infected with the TB bacillus and current treatment takes 6-9 months. The current TB vaccine BCG, developed over 85 years ago, reduces the risk of severe forms of TB in early childhood but is not very effective in preventing pulmonary TB in adolescents and in adults, the populations with the highest TB rates. As the disease is changing and evolving, new vaccines are even more crucial to control any pandemic. TB is the leading cause of death for people living with HIV/AIDS, particularly in Africa. Multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) are hampering treatment and control efforts. A need for an alternative vaccination approach has emerged in the last two decades.

Ebola and Marburg
Crucell is developing an Ebola vaccine in collaboration with the Vaccine Research Center (VRC) of the NIAID.

In May 2002, we entered into a Collaborative Research and Development Agreement (CRADA) with the VRC to jointly develop, test and manufacture an adenovirus-based Ebola vaccine. Under the terms of the agreement, we have an option for exclusive worldwide commercialization rights to the Ebola vaccine resulting from this collaboration. In August 2002, the CRADA was extended to cover vaccines against Marburg and lassa infections.

In experiments conducted by the VRC together with the US Army Medical Research Institute of Infectious Diseases (US.AMRIID) during the first half of 2004, our vaccine candidate confirmed single-dose protection in pre-clinical testing against Ebola. What set the results of this trial apart from the earlier successful trial, which established a proof-of-concept, was that the vaccine in this instance was produced on PER.C6 technology.

In March 2005, we extended the CRADA with the US NIH and continue to develop this vaccine and will use the Ebola vaccine results in the development of Marburg and lassa vaccines. In addition, we obtained an exclusive license to certain NIH patents to develop and commercialize recombinant vaccines against Ebola.

In October 2008, we secured a NIAID/ NIH contract aimed at advancing the development of Ebola and Marburg vaccines, ultimately leading to a multivalent filovirus vaccine. The contract provides funding of up to $ 30 million, with additional options that may be triggered at the discretion of the NIAID for an additional $40 million. The phase I study of an Ad5 based Ebola vaccine, being developed in partnership with VRC, showed safety and immunogenicity at the doses evaluated. Based on these results a second phase I study of an Ebola and/or Marburg vaccine is anticipated.

About Ebola and Marburg
The Ebola and Marburg viruses are capable of causing hemorrhagic fever, a severe, often-fatal disease in humans characterized by high fever and massive internal bleeding, causing death in 50% to 80% of all cases. Ebola and Marburg outbreaks occur regularly in tropical Africa, affecting both human and great ape populations. Since the Ebola virus was first recognized, approximately 2,200 cases, including over 1,500 deaths, have been reported. To date, over 440 cases of Marburg have been reported with approximately 360 fatalities. Ebola and Marburg usually appear in sporadic outbreaks, and spread within a health-care setting. Because of the high disease-related mortality rates and lack of any vaccine or therapy, the Ebola and Marburg viruses are on the US Centers for Disease Control and Prevention Category 'A' list of bio terror agents, together with smallpox and anthrax.

Malaria
We are developing a recombinant malaria vaccine based on our AdVac technology and produced on our PER.C6 production technology. The vaccine is made by inserting the gene for the circumsporozoite protein (CSP) from a malaria parasite into an adenoviral vector, which acts as a 'vehicle' for vaccination delivery.

The efficacy of our malaria vaccine candidate was tested in pre-clinical models. The study showed that a single administration of a prototype AdVac vaccine, provided protection against the specific parasite. Since March 2004, we have collaborated with the NIAID for the support of the development of our candidate malaria vaccine. In September 2006, we extended our collaboration with the NIAID by signing a clinical trial agreement.

In partnership with the NIAID, Crucell's malaria vaccine entered a phase I trial in the US in January 2007. The study is being carried out on two sites, Vanderbilt University in Tennessee and Stanford University in California. The first three groups have been enrolled and ongoing safety monitoring has revealed no significant safety concerns to date, but formal analysis awaits unblinding of the data. Further updates on this program are expected in the second quarter of 2009.

About malaria
Malaria is a life-threatening infectious disease caused by the plasmodium parasite and transmitted from person-to-person through the bite of a female Anopheles mosquito. It is currently one of the most lethal communicable diseases. The disease currently represents one of the most prevalent infections in tropical and subtropical areas causing severe illness in 300 to 500 million individuals worldwide according to the World Health Organization and causing 1 to 3 million deaths every year. Most of these deaths occur among children and pregnant women in the developing world, especially in sub-Saharan Africa. Unfortunately, mortality associated with severe or complicated malaria still exceeds 10-30%. The widespread occurrence and elevated incidence of malaria are a consequence of discontinued malaria control programs and increasing numbers of drug-resistant parasites and insecticide-resistant parasite vectors. Other factors include environmental and climatic changes, civil disturbances and increased mobility of populations. Although the overwhelming majority of morbidity and mortality associated with malaria occur in the developing world, this disease also affects travelers.

HIV
In August 2005, Crucell, along with Harvard Medical School, was awarded a $ 19.2 million grant by the US NIH to develop new adenovirus vector-based vaccines against HIV/AIDS. The Investigational New Drug Application (IND) for phase I of the trial with Harvard Medical School (supported by the NIH) was approved by the FDA in January 2008. In April 2008, the Company announced the start of a Phase I clinical study of the novel recombinant HIV vaccine that Crucell is jointly developing with the Beth Israel Deaconess Medical Center, using adenovirus serotype 26 (rAd26) as vector. The rAd26 vector is specifically designed to avoid the pre-existing immunity to the more commonly used adenovirus serotype 5 (Ad5). The phase I clinical study is being conducted at the Brigham and Women's Hospital in Boston, MA, US and is focused on assessing the safety and immunogenicity of the vaccine. Enrollment is currently ongoing.

About HIV
Human immunodeficiency virus or HIV is a retrovirus that causes acquired immune deficiency syndrome (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening infections. HIV infection occurs on a global scale. A joint United Nations Program on HIV/ AIDS and the WHO estimate that AIDS has killed more than 25 million people since it was first recognized on December 1, 1981, making it one of the most destructive pandemics in human history.

There currently is no treatment for HIV or AIDS. The only known methods of prevention are based on avoiding exposure to the virus or, failing that, an antiretroviral treatment directly after a highly significant exposure, called post-exposure prophylaxis (PEP). Protective sex is another form of prevention of the deadly disease. Antiretroviral drugs (ARVs) which significantly delay the progression of HIV to AIDS and allow people living with HIV to live relatively normal, healthy lives, have been available in wealthier parts of the world since around 1996.

Antibodies

Rabies monoclonal antibody combination
We are developing a human monoclonal antibody combination for the post-exposure treatment of rabies. The use of Crucell's MAbstract technology resulted in a combination of two human anti-rabies antibodies. The monoclonal antibodies are produced on Crucell's PER.C6 technology.

Post-exposure treatment for rabies, when given timely, is 100% effective and involves the use of a vaccine plus antibodies. Neither vaccine nor antibodies are effective independent of one another. Current supply and quality of rabies vaccine is sufficient, but anti-rabies antibodies (Human Rabies Immune Globulin (HRIG) and Equine Rabies Immune Globulin (ERIG)) are widely recognized as being insufficient in quality and supply, and pose safety concerns because they originate from human or equine serum. Market opportunities for rabies treatments are projected to grow significantly as the customer base grows in affected countries such as India and China.

We have developed the human monoclonal antibody combination in collaboration with the Thomas Jefferson University (TJU) based in Pennsylvania, US and the Center for Disease Control (CDC) in Georgia, US using MAbstract and PER.C6 technology. Our rabies monoclonal antibody combination demonstrated protection at least equivalent to HRIG in pre-clinical trials.

In December 2007, we signed an exclusive collaboration and commercialization agreement with sanofi pasteur for our rabies monoclonal antibody combination to be used in association with rabies vaccine for post-exposure prophylaxis against this disease. We will continue to perform the development activities and will be responsible for the manufacturing of the final product and will retain exclusive distribution rights in Europe, the rights to sell to supranational organizations such as UNICEF and co-exclusive distribution rights in China.

The program has been granted a Fast Track designation by the US Food and Drug Administration (FDA).

Phase I clinical trials demonstrated that the antibody product is well tolerated, provides the expected immediate passive neutralizing activity and that it can be safely administered in combination with a rabies vaccine without interfering with the vaccine's ability to induce an active immunity.

Phase II clinical trials began in the US in March 2008. In October 2008, the positive preliminary results of the US study were presented. No serious adverse events were reported and the study confirmed the neutralizing activity of the antibody product against the rabies virus. In May 2008, a second phase II clinical study began in the Philippines and was completed before year-end 2008. Final data from this study are expected to become available in the first half of 2009.

An additional phase II study in healthy adults evaluating Crucell's monoclonal antibody in combination with a rabies vaccine started in February 2009.

About rabies
Rabies is a viral disease of mammals most often transmitted through the bite of an infected animal. The virus infects the central nervous system, causing encephalopathy and ultimately death if medical treatment is not sought before symptoms become more severe. Rabies is prevalent in all the continental regions of Europe, Asia, America and Africa. Globally, approximately 10 million people a year are treated after exposure to rabies. Some

40,000 to 70,000 people are thought to die of the disease each year, mainly in China and India, according to various medical publications.

Human monoclonal antibodies against a broad range of influenza
Crucell's scientists discovered a set of human monoclonal antibodies that provides immediate protection and neutralizes the broadest range of H5N1 strains. When tested in pre-clinical models for prevention or treatment of a potentially lethal H5N1 infection, this antibody was shown to prevent death and cure the disease.

In another pre-clinical study, Crucell's mAb CR6261 was compared with the anti-influenza drug oseltamivir in terms of its value for flu prevention and treatment. In December 2008, Crucell announced that its monoclonal antibody had strongly outperformed the most current anti-influenza drug in these tests.

The flu strains tested included the 'bird flu' strain H5N1, which, experts fear, has the potential to cause a pandemic, and H1N1, which is similar to the strain responsible for the devastating pandemic in 1918. Importantly, the study showed that CR6261 provides immediate protection against the influenza virus, suggesting that it will be able to prevent disease spread. In contrast, oseltamivir was less efficacious and in some cases not effective at all.

Technologies

Licensing our technologies to the market
We generate a portion of our revenues and other operating income from licensing our proprietary technologies to pharmaceutical and biotechnology companies, from grants and government subsidies obtained to support the development of our technologies and potential products and from service fees earned under development contracts with our partners. We intend to increase our revenues in the future from initial license fees, license maintenance fees and milestone and royalty payments from products that our licensees develop using our technologies.

Our business development strategy historically involved contacting prospective licensees and partners and assessing their interest in our technologies and products. If the prospective licensee or partner indicates interest we negotiate a license and/or collaboration agreement pursuant to which we deliver the applicable technology to, or collaborate with, the licensee or partner. For some of the contracts we provide services, for which we are paid at different rates.

Core proprietary technologies
Our product portfolio is supported through five core proprietary technology platforms.

PER.C6 technology

Overview
Our PER.C6 technology provides a manufacturing system that can be used to produce a variety of biopharmaceutical products. Crucell's PER.C6 cell line is derived from a single, human retina-derived cell, which was purposely immortalized using recombinant DNA technology. As a result, PER.C6 cells can replicate indefinitely, allowing them to be cultured in single cell suspension under serum-free conditions in quantities appropriate for large-scale manufacturing.

The technology has been successfully adapted to grow without the need for serum components or materials that allow cell attachment (micro carriers) and demonstrates excellent cell densities in bioreactors. These features are important because they allow us to produce safe biopharmaceutical products in sufficient quantities.

In September 2008, DSM Biologics and Crucell announced that the high-titer-fed batch process developed at the PERCIVIA PER.C6 Development Center, their joint venture in Massachusetts, US (PERCIVIA) was scaled up to 250 liters by DSM Biologics scientists at their GMP facility in Groningen, the Netherlands. They successfully achieved 8 grams per liter for an IgG antibody expressed by PER.C6 cells using chemically defined cell culture medium in a single-use bioreactor. In June 2008, the Company reported record-breaking protein yields of 27 grams per liter using DSM's innovative XD™ technology.

There are four areas in which our PER.C6 technology is currently being applied:

Vaccine production
PER.C6 technology can be used as a production system for developing and manufacturing both classical and recombinant vaccines.

- For classical vaccine production, PER.C6 cells are infected with the virus against which the vaccine is meant to protect. The virus is subsequently

multiplied on PER.C6 cells to high virus titer, yielding a potent starting material that can be processed and purified to produce a final formulation of a whole-killed, split or sub-unit vaccine; and

- For recombinant vaccine production, the PER.C6 technology produces delivery agents called adenoviral vectors. These vectors have been made replication incompetent and thus are only capable of delivering into the human body a portion of DNA encoding for a protein from the pathogen against which the vaccine is meant to protect. The DNA inserted into the vector can be derived from a virus, a parasite or even bacteria, providing a versatile vaccine vector platform.

Protein production

PER.C6 technology can be used as a production system for developing and manufacturing both antibodies and other proteins. DNA encoding for a particular protein of interest is inserted into PER.C6 cells. These modified PER.C6 cells will secrete the desired antibody or other protein. We are further developing the application of PER.C6 for protein production at PERCIVIA.

Gene therapy

The primary function of PER.C6 technology in the field of gene therapy is the production of adenoviral vectors a gene delivery mechanism based on a common cold virus that carries therapeutic genes and facilitates the delivery of the gene into the cells. Since the PER.C6 technology is the only available cell line that does not allow any formation of classical replication competent adenoviruses during the production of replication deficient vectors, the cell line may be applied across the entire adenovirus gene therapy field.

Functional genomics

Our PER.C6 technology can be used to produce libraries of adenoviruses into which individual human genes are inserted to study gene function. The adenovirus libraries carry many genes with unknown functions, which can be used to determine the role of individual genes in a disease process. We believe that our PER.C6 technology, therefore, represents a key analytical tool in the discovery of new genes and their role in biological pathways and human disease.

Key features and advantages

We believe that our PER.C6 technology has the following key advantages over alternative manufacturing systems:

- PER.C6 technology potentially offers a system for high yield, large-scale biopharmaceutical product production. PER.C6 technology can be cultured at high densities and engineered to produce large quantities of biopharmaceuticals and may reduce production expense.
- PER.C6 cells can be cultured in a serum-free medium, without micro-carriers, using a variety of scaling systems, including bioreactors. This simplifies the expansion from laboratory- to industrial-scale production, which may lead to the production of cost-efficient biopharmaceuticals in large quantities. The use of a serum-free medium also offers the potential to significantly improve the purification of biopharmaceuticals produced using the PER.C6 technology and may facilitate regulatory approval.
- We have filed a Cell Substrate Biologics Master File (BMF) with the US Food and Drug Administration (FDA) describing the PER.C6 technology, including its establishment, development and potential use in production processes. The FDA will only evaluate the PER.C6 technology in the context of Investigational New Drug (IND) applications. We believe that the information in the BMF will facilitate the FDA's approval of any biopharmaceutical product that we or our licensees produce using the PER.C6 technology.
- The PER.C6 technology can now claim to have achieved a broad endorsement within the industry. For an overview of our most important licensees and partners subsidiaries please see the 'Appendix Overview licensees and partners'.
- We believe that antibody and other protein products based on the human based PER.C6 technology may demonstrate enhanced biological properties, rendering them potentially more efficacious. In addition, PER.C6 technology efficiently supports the growth of certain human viruses for vaccine development.

AdVac technology

Overview

Crucell has been a key player in the development of adenoviral-based vaccines for more than five years, resulting in the availability of proprietary AdVac vectors. Crucell has generated a wide variety of research and GMP clinical batches based on AdVac technology for diverse infectious diseases.

AdVac technology is based on vectors constructed from adeno viruses that do not regularly occur in the human population, such as Ad35. The technology supports the practice of inserting DNA coding of pathogen-derived proteins into a vector. AdVac technology may also be used to develop gene therapy products. AdVac vectors are used in combination with our PER.C6 technology. Currently AdVac technology is used by Crucell and its licensees to develop vaccines against hemorrhagic fevers (Ebola, lassa, Marburg), malaria, TB, HIV/AIDS and hepatitis C (HCV). While no adenovirus-based recombinant vaccines are currently licensed for human use, AdVac-based vaccines for malaria, HIV/AIDS, HCV, hemorrhagic fevers, and TB have been successfully constructed and are currently in clinical trials.

Crucell has generated a series of adenoviruses including Ad35 and derivatives thereof as well as manufacturing platforms for these vectors. The AdVac vectors can be produced to carry genetic information derived from viruses, parasites and bacteria, and thereby have the potential to allow immunization against life-threatening diseases.

Crucell has laboratories to develop purification methods closely resembling an end-stage manufacturing process. With this facility we can manufacture Ad35 vaccine vectors for comprehensive pre-clinical programs. These products can be manufactured using PER.C6 technology under serum-free conditions.

Key features and advantages

We believe our AdVac technology has the following key advantages over other commonly used vector systems:

- Vectors used with AdVac technology share the advantages of the commonly used adenoviral vectors such as: scalable production, high yields and the ability to mediate a strong T-cell immune response;
- The AdVac technology can circumvent pre-existing immunity offering accurate dose control of the vaccines; and
- AdVac vectors can be engineered to contain small genetic fragments of different viruses, parasites and bacteria. This makes possible the development of a wide variety of novel vaccines against a broad range of dangerous human pathogens.

MAbstract technology

Overview

Our MAbstract technology can be applied to the discovery of novel drug targets and the identification of human antibodies against those drug targets. MAbstract technology employs a bacteria-infecting virus called a bacteriophage, or phage, which expresses part of a human antibody on its surface. The technology employs a library of phages that carry many different human antibodies. To identify and subsequently isolate relevant antibodies, the library is put in contact with pathogens, or cells suspected of carrying the drug target, or if the target is already known in advance, the library may be put in contact with the target directly. Subsequently, phage antibodies binding to the diseased cells or the known target are separated from phage antibodies that do not bind at all, or bind to healthy cells added to eliminate irrelevant phage antibodies present in the library. Since irrelevant phage antibodies for the target in question are often present in great abundance, the elimination step aids in enriching the phage-antibody population for potentially relevant, selectively binding phage antibodies.

Once such phage antibodies have been isolated, they can either be used to subsequently identify the target or a specific binding place on the target (referred to as epitope), or be used to subsequently isolate the DNA coding for the binding part of the antibody. This part may genetically be combined with other parts of the antibody that have no binding function but have accessory functions in the human immune system. Thus, different formats of antibodies with different modes of action or functions can be made, but with the same specificity for the target.

We use our MAbstract technology to identify antibodies reactive with whole pathogens, antibodies against protein elements from pathogens or antibodies directed against targets already known to be associated with disease. In addition MAbstract can be used to identify targets or epitopes on disease-causing agents that were previously unknown and may make suitable candidates for antibody-based diagnosis, prevention or therapy of the associated disease.

Key features and advantages
MAbstract employs a human-based antibody-display technology. We believe that MAbstract allows for the discovery of therapeutic antibodies with several potential advantages over current technologies. These advantages include the following:

- MAbstract technology selects antibodies for possible therapeutic use and discovers novel drug targets using whole cells, tissues or infectious agents.
- MAbstract technology does not have inherent limitations on antibody specificity.
- MAbstract technology has been used to isolate antibodies for numerous disease applications. Selected antibody specificities can be directly reformatted into antibodies for production using PER.C6 technology.

STAR technology

Overview
STAR technology is useful for increasing production of recombinant antibodies and therapeutic proteins on mammalian cell lines. It is a two component system consisting of (a) STAR elements that counteract gene silencing, resulting in increased levels of production and improved stability of recombinant proteins, and (b) STAR-select, a very stringent selection system that is directly coupled to the expression of the gene of interest, resulting in only a few cell lines that all produce the recombinant protein at high levels.

Multiple companies and licensees are investigating whether the STAR technology can increase production yields of biological substances. We acquired STAR technology in 2004 through the purchase of ChromaGenics B.V., a privately held biotechnology company based in Amsterdam. In connection with the purchase, we also entered into a contingent payment agreement with the former shareholders of ChromaGenics that could result in us making additional payments of up to € 7.0 million, based upon our receipt of revenues generated from the STAR technology. In 2007, we paid € 2.0 million to the former shareholders under this agreement.

Key features and advantages
We believe our STAR technology has the following key advantages over other gene expression technologies:

- Established mammalian cell banks for antibody and protein production are the starting point for STAR technology, thus specially engineered mammalian cells are not needed;
- The STAR technology allows for very rapid stable mammalian cell clone generation; and
- The STAR technology typically yields stable mammalian cell clones that produce five- to ten-fold more antibody or other therapeutic proteins compared to cell clones generated without STAR.

Virosomal technology

Overview
One of the challenges in vaccine development is the creation of products that contain defined antigens of high purity that efficiently induce a protective immune response. Many antigen preparations are therefore supplemented with adjuvants to enhance the body's immune response to the specific antigens. The most commonly used and approved adjuvants for human use are aluminum salt derivatives, which are known to cause adverse reactions such as irritation and inflammation at the injection site. Virosomes are a broadly applicable adjuvant and carrier system with prospective applications in areas beyond conventional antigen-based vaccines. Our virosome technology offers a tool for developing novel, predominantly synthetic vaccines applicable to infectious and chronic diseases. These vaccines offer additional benefits because they are effective even in immune-suppressed patients and infants.

Key features and advantages
We believe our Virosome technology has the following key advantages over other antigen delivery technologies:

- Virosome technology provides a broadly applicable delivery system for antigens or DNA/RNA encoding specific immune stimulatory proteins;
- Virosome technology enables target-specific delivery of antigens and amplification of the immune response;

- Virosomes stimulate both arms of the immune system, eliciting both antibody and cellular immune responses, against inserted immune stimulatory proteins derived from human pathogens;
- Virosomes are completely biodegradable and can exert an immune response via different routes of administration; and
- Virosome technology is used in the manufacture of several of Crucell's registered products where it has an excellent safety record.

Other proprietary technologies

In addition to our core proprietary technology platforms the companies employs numerous other technologies. Of these other proprietary technologies we would like to highlight the following two.

Hansenula polymorpha

Overview
The yeast expression technology Hansenula polymorpha provides us with a highly efficient production technology for proteins, which can be used as a basis for developing and manufacturing new vaccines. The yeast Hansenula polymorpha production system provides superior characteristics for a wide range of industrial applications. In particular its lack of pyrogens, pathogens or viral inclusions, its ease of genetic manipulation and its robustness in industrial scale fermentations add to its attractiveness for the synthesis of pharmaceutical compounds. Our registered HBV vaccine Hepavax-Gene is based on recombinant production in this yeast.

Key features and advantages
We believe our Hansenula polymorpha technology has the following key advantages over other yeast expression technologies:

- Hansenula polymorpha provides an expression system with superior characteristics for the synthesis of pharmaceutical compounds, including vaccines;
- Hansenula polymorpha provides a safe production platform lacking pyrogens, pathogens or viral inclusions; and
- Hansenula polymorpha is easy to manipulate genetically and is robust in industrial scale fermentations.

Recombinant Cholera Toxin B sub-unit technology
Cholera Toxin B (CTB) sub-unit is a powerful inducer of immunity both systemically and mucosally. Numerous applications have shown that coupling of antigen to CTB increases the immunogenicity of the antigen. In some applications simple co-administration of CTB with the antigen has been shown to be effective. This has been shown both for parenteral as well as mucosal (intranasal) applications.

CTB is an efficient mucosal carrier for induction of peripheral immunological tolerance. Oral ingestion of antigen coupled with CTB suppresses peripheral T-cell reactivity to the coupled antigen. The Group has a state-of-the-art GMP manufacturing facility for recombinant CTB. The production system is designed so that CTB is produced completely devoid of the toxins.

Partners, agreements, investments and other collaborations

Strategic partners

In addition to our own research and development activities, Crucell collaborates with several leading companies. Through these agreements, our technologies are playing a vital role in the development of a number of vaccine and antibody products.

Merck
Since 2000, Crucell and Merck have developed a close working partnership, entering into a number of agreements. In June 2003, Merck and Crucell expanded an existing cooperation agreement and agreed to work closely on matters related to maintenance of the PER.C6 Cell Substrate BMF. We further expanded the relationship in December 2006, when we signed a cross-licensing agreement for vaccine production technology. The agreement allows Merck to use our technology on an exclusive basis in additional undisclosed vaccine fields. In return, we received access to Merck's large scale manufacturing technology for our AdVac-based vaccines under development. In September 2007, Merck exercised an option for the exclusive use of our PER.C6 technology and access to our AdVac vaccine technology in two infectious disease areas.

DSM Biologics
In December 2002, we formed an alliance with DSM Biologics to license our PER.C6 technology as a production platform for monoclonal antibodies

and recombinant proteins. The combination of the PER.C6 technology and DSM's manufacturing services provides companies with a turn-key biologic manufacturing solution reducing cost, risk and time to market. Furthering this commitment to the PER.C6 technology, Crucell and DSM established PERCIVIA in August 2006. The innovations resulting from this partnership will be available to PER.C6 licensees to further enhance their development capabilities.

Sanofi pasteur
We have a strategic agreement with sanofi pasteur since 2003 to further develop and commercialize novel influenza vaccine products based on our PER.C6 technology. The agreement covers both seasonal and pandemic influenza vaccines. Sanofi pasteur has the worldwide rights to develop, manufacture and commercialize PER.C6-based influenza vaccines. Crucell has the commercial rights for Japan.

In December 2007, we signed an exclusive collaboration and commercialization agreement with sanofi pasteur for our rabies monoclonal antibodies to be used in association with rabies vaccine for post-exposure prophylaxis.

Novartis
Our largest selling vaccine is Quinvaxem. The vaccine is produced by Crucell in Korea and was co-developed with Novartis (formerly Chiron), which provides four of the five vaccine components in bulk. We have a profit sharing agreement with Novartis for this product.

MedImmune
In October 2007, we entered into an exclusive license and research collaboration with MedImmune to further develop and commercialize bacterial antibodies primarily for the treatment and prevention of hospital-acquired bacterial infection. Crucell discovered these antibodies with use of the MAbstract-technology.

Wyeth
In March 2008, we entered into an exclusive agreement with Wyeth pursuant to which we perform contract manufacturing for Wyeth at our Swiss facilities. We will develop and manufacture certain vaccine components that Wyeth will use in clinical studies. The development activities will take place in our facilities in Bern, Switzerland. Wyeth will be responsible for the overall clinical development of the vaccine.

Other collaborations and agreements

Manufacturing service arrangements
We have signed manufacturing service agreements with a number of our licensees and partners. Under these agreements, we have produced and may produce in the future clinical batches of adenoviral materials, antibodies, or other materials using our PER.C6 technology for the applicable licensee. We have received and may receive in the future initial fees upon signing and subsequent payments upon delivery of the batches we produce in accordance with the terms of the agreement.

University collaborations
We collaborate with a number of universities worldwide in the areas of vaccines, antibodies, cell lines, gene therapy, cancer and cardiovascular disease. Some of our collaborations provide for royalty payments to be made to the universities in the event product sales arise out of the collaborations. Generally, these collaboration agreements specify that Crucell provides the applicable university with a specific amount of funding and the Group receives certain intellectual property rights and access to the results of the university research.

Overview licensees and partners
For an overview of our most important licensees and partners subsidiaries please see the 'Appendix Overview licensees and partners'.

Our equity investments

Subsidiaries
The following transactions changed the scope of consolidation in 2008:

- In December 2008 SBL Vaccin Holding AB and Vitec AB Rhein Vaccines B.V. legally merged into SBL Vaccin AB; and
- In November 2008 we sold our fully-owned subsidiary Etna Biotech Srl (Catania, Italy) to Zydus Cadila (Ahmedabad, India).

For a complete overview of our most significant subsidiaries please see '1.1 Corporate information – List of consolidated companies' in the financial statements.

We are not aware of any legal or economic restrictions on the ability of our subsidiaries to transfer funds to the Company in the form of cash dividends, loans or advances other than withholding taxes due in certain countries in which we operate.

Associates and joint ventures
On July 3, 2008 the Group sold all of the 2,625,000 shares it owned in Kenta Biotech AG to Ingro Finanz AG. Prior to this sale, our ownership interest had already been diluted from 37% in 2006 to 22% by the end of 2007. We realized an accounting gain of € 1.6 million on the sale in 2008.

For a complete overview of our associates and joint ventures please see '5.9 Investments in associates and joint ventures' in the financial statements.

Other equity investments
Galapagos N.V. ('Galapagos') is a discovery company focused on the rapid identification of disease modifying drug targets through the functional screening of human disease models, and the subsequent progression of these targets into drug discovery. The company is listed on the NYSE Euronext Brussels and NYSE Euronext Amsterdam stock exchanges (ticker symbol: GLPG).

Galapagos holds a royalty free exclusive license to use our PER.C6 technology for conducting activities in the field of functional genomics research. Under the license, Galapagos uses PER.C6 technology in conjunction with Tibotec's bioinformatics technology to generate adenoviral gene libraries. We have agreed with Tibotec to not compete with the activities of Galapagos, which holds the rights to the products and technologies that it develops. The Group owns 5.8% of Galapagos as of December 31, 2008 (2007: 5.8%).

Marketing and sales partners

We have our own sales and marketing infrastructure in our markets in the Benelux, Switzerland, Italy, Spain, Scandinavia, US and Canada, Argentina, China, Korea, Indonesia and Vietnam. This sales and marketing infrastructure includes a dedicated sales force for supranational organizations. We have also established a strong network of partnerships to ensure broader market access for our products. Through these measures, we have established a global marketing and sales organization with strong presence in the US, US, South-East Asia and supranational organizations.

We also distribute and market other companies' products, to strengthen our presence in vaccine or therapeutic protein markets. The most significant collaborations in terms of current sales value are:

Our partners:	Marketing, sales and distribution partner for:
Sanofi pasteur – MSD	part of the sanofi pasteur – MSD portfolio in Sweden.
Novartis Vaccines and Diagnostics	part of the Novartis vaccine portfolio in Sweden.
Statens Serum Institute Denmark (SSI)	part of SSI's product portfolio in Spain and Sweden.
Green Cross Corporation Korea	Green Cross Corporation's Japanese encephalitis vaccine in Europe.
Netherlands Vaccine Institute (NVI)	part of NVI's product portfolio in the Benelux
Talecris Biotherapeutics	Talecris's product Prolastin in nine Western European countries.

In addition, we developed a network of companies that market and sell our products. The most significant collaborations in terms of current sales value are:

Our Partners:	Marketing, sales and distribution partner for:
Zuellig	several vaccines in China.
Baxter International Inc.	several vaccines in Austria, Germany, Greece and Russia.
Infectopharm Germany	our flu vaccine in Germany.
Masta UK	our travel vaccines in the UK.
Novartis	our travel vaccines in Germany.
Sanofi pasteur	Dukoral in Canada, Australia and a number of other countries outside Europe and the US.
Sanofi pasteur – MSD	our flu vaccine in the UK.
Kedrion	our flu vaccine in Italy.

Intellectual property

Our success and ability to compete depends in large part on our ability to protect our proprietary technology and information, and to operate without infringing on the intellectual property rights of others. We rely on a combination of patent, trademark and trade secret laws, as well as confidentiality, assignment and licensing agreements, to establish and protect our proprietary and intellectual property rights. Our policy is to actively seek patent protection of our intellectual property in the US and Europe, as well as in other jurisdictions as appropriate.

We engage European and Dutch patent attorneys that file, prosecute, defend and enforce patent rights as well as manage our patent portfolio. Our patent portfolio comprised 1677 active cases (i.e. granted patents in force or pending patent applications) as of December 31, 2008. We aggressively protect our inventions and employ a proactive filing strategy with respect to patent applications. Our portfolio management involves active commercialization and enforcement strategies combined with disposal of cases that we no longer consider commercially attractive.

The following table reflects the total number of active cases (pending or granted) through December 31, 2008, organized according to our different fields of operation. All figures include acquired and jointly owned patent cases, but exclude patent positions licensed-in from third parties.

2008 Patent filings

	Pending	Granted	Active
Vaccines [1]	259	367	626
Antibodies [2]	141	77	218
Technology [3]	268	344	612
Gene Therapy	50	171	221
Total	**718**	**959**	**1,677**

[1] Vaccines patent filings relate to AdVac-based, live viral vector vaccines based on our proprietary measles technology, our virosomal technology and classical whole inactivated virus, split and sub-unit vaccines.
[2] Antibodies patent filings relate to antibodies and/or drug targets, excluding the enabling technologies that are classified as technology.
[3] Technology patent filings primarily relate to cell-based production technology, adenoviral vector technology, STAR-technology and related technology, functional genomics and target and antibody discovery technology.

Patent filings

In 2008, we filed patent applications for four new inventions, in the fields of vaccines and technology. Our new filings in the vaccine field in 2008 reflect our efforts to further strengthen our patent portfolio in support of product development programs in that area. The new filings in the technology area relate to our continuing effort to protect and commercialize the PER.C6 technology and related uses of the PER.C6 cell lines, as well as our AdVac technology. Since we are not actively involved in gene therapy research and development, no new filings were made in that area during 2008.

We maintain a geographically diversified filing strategy, depending on our technological and business needs, as well as our view of long-term economic trends and developments in legal systems in various parts of the world. As of December 31, 2008, we had 64 pending applications in the EU[1], 110 pending applications in the US[2], 21 international patent applications (so called Patent Cooperation Treaty (PCT) applications[3]) and 523 applications in the rest of the world[4].

A significant number of our pending patent applications are filed under the PCT, which offers a cost-effective method to seek provisional worldwide protection in more than 100 countries and territories for 30 or 31 months from the filing date. The decision to divide the PCT application into territories in which a granted patent is desired may be postponed until the obtainable scope of protection and the technical and commercial usefulness of the invention becomes clearer. During the pendency of a European patent application, a single application may designate 35 countries but is counted as one pending application. As soon as the European patent application is granted it may be validated for each of the designated countries by filing a translation into the official language of that designated state. Once such a translation has been filed, we count each such patent as a separate patent.

[1] EU refers to filings made under the European Patent Convention. The EU figures do not include European patent applications designated in PCT applications while still in the international phase.
[2] US figures do not include US patent applications designated in PCT applications while still in the international phase.
[3] Figures reflect PCT applications still in the international phase. Our PCT applications routinely designate all territories and contracting states that are party to the PCT per the international filing date.
[4] Rest of world consists of Australia, Brazil, Canada, China, India, Israel, Japan, Hong Kong, Mexico, New Zealand, Norway, Russia, Singapore, South Africa and South Korea. Rest of world figures do not include PCT applications designating these countries while still in the international phase.

Patents
At December 31, 2008, we owned or co-owned 601 granted patents in the EU territory, 83 patents in the US and 275 patents in the rest of the world.

The following is a summary of the intellectual property rights related to our major products and product developments.

Epaxal and Inflexal V
Epaxal and Inflexal V are the two virosomal products which are protected by the patent family 'Immunostimulating and immunopotentiating reconstituted influenza virosomes and vaccines containing them', which will expire in 2012. In addition, the hepatitis A strain used to produce Epaxal is claimed in a patent family which will expire in 2012.

Other products
We have no patent protection for the active substances of Quinvaxem, Hepavax-Gene, Vivotif, Dukoral and MoRu-Viraten.

We seek patent protection, whenever possible, commercially feasible and appropriate, in respect of any technology or product development that is important to our business. Together with our affiliates in Switzerland, Sweden, Italy and Korea, we have several platform technologies and consequently our intellectual property (IP) activities concentrate on protecting these technologies and any improvements thereof in the main worldwide vaccine markets of Europe, the US, Canada, Japan and Australia. However, because some vaccine markets are outside these countries, we have also sought protection in other countries, such as Korea, India and China. The IP portfolio is constantly reviewed to decide on maintenance of individual patents or patent families considering parameters such as actual product performance, product development, patent term, options for commercialization or out-licensing of non-core IP. Our IP tasks are coordinated and patents are filed on a worldwide basis by specialized patent attorneys.

Patent enforcement and proceedings
We may need to litigate or institute administrative proceedings such as oppositions to a patent to enforce or uphold our intellectual property rights or determine the validity and scope of the proprietary rights of others. Likewise, from time to time it may be necessary to defend our patents in litigation or administrative patent proceedings such as opposition proceedings. We believe that litigation can play a significant role in defining and protecting our intellectual property rights. We are aware, however, that legal and administrative proceedings can be costly and time-consuming, and result in a diversion of resources. As an alternative to litigation, we may enter into licensing, including cross-licensing, arrangements as a means of clarifying the status of our intellectual property rights.

Oppositions against patents from the Group
In 2005, each of Probiogen, CEVEC Pharmaceuticals and Serono filed oppositions with the European Patent Office against one or more of our PER.C6 patents. All PER.C6 technology patents were upheld after first instance opposition proceedings. The PER.C6 patents pertaining to protein and virus production are no longer subject to opposition proceedings. The basic PER.C6 patent is currently under appeal, with Crucell as the only appellant and CEVEC Pharmaceuticals as party as of right. The outcome of appeal proceedings can only improve Crucell's position.

Cell Genesys has filed an opposition against our European patent related to our AdVac technology. Following the withdrawal of Cell Genesys from the opposition a swift resolution of the maintain opposition in Crucell's favor is now underway.

In addition to protecting our intellectual property rights, our commercial success also depends on our ability to operate without infringing the intellectual property rights of others. We monitor patent applications to the extent available, patents issued and publications of discoveries in scientific or patent literature to keep abreast of the activities of others in our field and, with the assistance of our internal and external patent counsel and other external advisors, assess whether our activities or products infringe the patents or proprietary rights of third parties. A number of third parties have been granted patents that cover technologies related to ours and similar patents may be granted in the future. We believe that our current activities do not infringe any valid claims of patents or any other proprietary rights of third parties. We will consider the intellectual property rights of others as we continue to identify and develop potential products and may have to enter into licensing or other agreements or use alternative technologies.

Oppositions against patents from competitors
Our subsidiary Berna Biotech Korea Corporation (formerly Green Cross Vaccine Corporation) and our partner Novartis (formerly Chiron) lodged opposition against a patent of GlaxoSmithKline (GSK) in Korea. The patent relates to multivalent vaccine formulations, such as our pentavalent vaccine Quinvaxem. In response to the opposition, the patent was revoked by the Korean Intellectual Property Office in December 2004 on the grounds that the subject-matter claimed in the patent lacks novelty. GSK appealed that decision to the Korean Patent Court. After a hearing which took place in April, 2006, the Korean Patent Court dismissed the appeal in June, 2006. GSK has appealed this decision before the Korean Supreme Court. In 2008, the Korean Supreme Court confirmed the decision by the Korean Patent Court and declared the patent to be invalid. This decision is final.

In 2005, we filed opposition against a European patent held by Novartis Vaccines and Diagnostics (formerly: Chiron) related to certain aspects of the production of influenza viruses in cell culture. The patent was revoked during oral proceedings.

In addition, production of Quinvaxem requires a particular vaccine component that may become the subject of a patent dispute between either GSK and us or GSK and our supplier of that component. The patent on that particular component, held by GSK, is currently under opposition before the patent office and a definitive outcome on the validity of the patent is expected to take a number of years. A negative outcome of this opposition proceeding could lead to infringement proceedings between GSK and us or GSK and our supplier, although we believe that neither we nor our supplier would be held to have infringed or be infringing that patent. The outcome of legal disputes is invariably difficult to predict with accuracy, but in the event GSK were to prevail in infringement proceedings against us, this would adversely affect our business.

Technology licenses from third parties

We licensed numerous technology and patents for specific use as part of our technology platforms from a number of third parties.

We entered into a technology license agreement with Xoma in the field of bacterial expression technology. This license allows us to develop diagnostic and therapeutic antibodies in the field of infectious disease using phage-display technology. The agreement provides us with options to expand the license to cover additional disease fields. Under the terms of the agreement, we pay Xoma milestone payments and royalties on products as and when developed and marketed using the licensed technology.

We also hold a license under the phage antibody display patent portfolio owned or controlled by MedImmune (formerly Cambridge Antibody Technology) and MRC, a cross-license with Transgene S.A. under which we granted to Transgene a non-exclusive PER.C6 license for the manufacture and sale of certain types of vectors for use in gene therapy, and a license for phage antibody-display technology and part human, or chimeric, binding proteins and molecules from Enzon Corporation's subsidiary, SCA Ventures, Inc.

In the field of vaccines, we have concluded an agreement with the Rockefeller University in New York, US. According to the agreement, we have the exclusive rights to use and exploit the Rockefeller patents related to ex vivo and in vivo targeting of dendritic cells with the use of viral vectors.

The Group has licensed adjuvation technology called ISCOMS from Isconova AB for the development, manufacturing and commercialization of improved influenza vaccines.

When licensing our technology to third parties we seek to obtain access to any improvement patents by our licensees via so-called grant-back provisions to reduce the risk of being exempted from using such improvements for our own benefit, or that of our licensees.

Technology licenses to third parties

We have issued certain licenses on an exclusive basis. These licenses generally state that we will not provide the licensed technology to a party other than the exclusive licensee for use in the area covered by the exclusive license. These licenses also generally provide for higher payments than non-exclusive licenses.

Industry and scientific overview

In this section we discuss the development for the biopharmaceutical areas in which we are predominantly active: vaccines and antibodies.

Vaccines

Vaccines are biological substances that stimulate an immune response that allows a vaccinated individual to resist future infections and disease. The immune system recognizes vaccine agents as foreign, destroys them, and 'remembers' them. When the virulent version of an agent comes along the body recognizes the protein coat on the virus, and thus is prepared to respond by neutralizing the target agent before it can enter cells, and by recognizing and destroying infected cells before that agent can multiply to vast numbers.

Scientific progress in vaccines
Vaccines have contributed to the eradication of smallpox, one of the most contagious and deadly diseases known to man. Other diseases such as rubella, polio, measles, mumps, chickenpox, and typhoid are nowhere near as common as they were a hundred years ago. As long as the vast majority of people are vaccinated, it is much more difficult for an outbreak of disease to occur or to spread. Significant developments include the introduction of combination vaccines and the development of new vaccine technologies that may advance vaccine development. Today, research is under way to develop efficacious and safe vaccines against among others: viruses, parasites, bacteria and inherited or acquired diseases.

Vaccine formats
A variety of vaccine formats are in use today and others are evolving through ongoing research and development efforts. Some of the most common vaccine formats include live-attenuated virus vaccines, inactivated whole-killed virus vaccines, sub-unit vaccines, DNA vaccines, recombinant vector-based vaccines, synthetic vaccines and peptide-based vaccines.

Vaccine technology development
A large variety of vaccine technologies are under development in an attempt to improve safety and overall vaccine efficacy. The key objectives of current vaccine technology research and development are to make safer vaccines without compromising efficacy, to generate new vaccines with stronger and broader immunogenicity, to make vaccines using more efficient manufacturing processes and to make vaccines easier to administer.

Antibodies

Antibodies are proteins made naturally by cells of the body's immune system. They function as one of the body's principal defense mechanisms against pathogens, which are disease causing agents such as parasites, viruses or bacteria. Antibodies recognize and bind to invading pathogens, ultimately eliminating them, thus playing a crucial role in protecting humans against disease. Because of their binding characteristics, antibodies can distinguish subtle cell differences between healthy and diseased cells. Antibodies are used to develop therapeutic products that can

- Bind to and block a key interaction of a disease-related cell, such as an inflammatory cell;
- Block infectious agents; and
- Trigger the death of a target cell, such as a cancer cell.

Antibodies may also be used to bind and neutralize toxic products, to develop diagnostic products to detect viruses or bacteria and as tools in scientific research such as genomics and proteomics.

Scientific progress in antibodies
Methods for generating monoclonal antibodies have evolved considerably over the last 25 years. The technology originally involved immunizing mice with a target molecule and isolating relevant antibody-producing cells from the mice. Because monoclonal antibodies of rodent origin are recognized as foreign proteins and are rapidly eliminated when applied in humans, methods were developed to produce therapeutic antibodies that are of human origin. These antibodies can be developed either using transgenic mice or by means of phage antibody-display technology. Transgenic mice are genetically engineered mice that carry human antibody genes. This allows the immune systems of mice to generate human antibodies in response to any administered antigenic material. Phage antibody-display technology allows human antibody genes to be cloned into bacteriophages, which are viruses that only infect bacteria. Phages displaying antibody fragments that attach to specific molecules can be selected, enabling isolation of antibodies against targets and/or enabling the identification of target molecules. Phage antibody-display libraries are large

collections of antibody-phages for use in identifying the targets and related antibodies.

Competition in product and technology development

The biotechnology field is one of rapid change and innovation. We expect that this industry will continue to experience significant technological and other changes in the years ahead. We operate in highly competitive markets and we may experience competition from companies that have similar or other technologies, and other products or forms of treatment for the diseases we are targeting. We also may experience competition from companies that have acquired or may acquire technology from universities and other research institutions. As these companies develop their technologies, they may develop proprietary positions in the areas of our core technologies or obtain regulatory approval for alternative technologies or commercial products earlier than we or our licensees do. Other companies are developing products to address the same diseases and conditions that we and our licensees target and may have or develop products that are more effective than those based on our technologies. We also compete with our licensees in developing new products.

Vaccines

Other biotechnology and pharmaceutical companies that are focused on developing vaccines against infectious diseases include Wyeth, sanofi pasteur, Merck & Co., GlaxoSmithKline, Novartis, Acambis, Baxter, GenVec, Bavarian Nordic, Baxter, Solvay, Vical and Nobilon.

With respect to vaccines, other companies use alternative non-human expression platform technologies. We are aware of licensed vaccines that are produced in cell substrates such as MDCK (Madin Darby Canine Kidney cells) and VERO as well as on production platforms based on embryonated chicken eggs. There are also mouse brain-derived inactivated vaccines that are produced in several Asian countries. We are aware of other human expression technologies for licensed and marketed vaccines, as well as human cell lines supporting products in development.

Adenoviral vector technology and other recombinant vectors

With respect to vector development, we are aware of several competing technologies, including those of GenVec and Merck & Co., which may pose a threat to the commercial viability of our AdVac technology.

Antibodies

Other biotechnology companies, including UCB Celltech and PDL BioPharma, currently generate humanized antibodies, and Medarex, Inc., GenMab, and Regeneron produce fully-human antibodies from transgenic mice. MedImmune, MorphoSys AG and Dyax generate fully-human antibodies using phage antibody-display libraries that are similar to ours. Companies such as XOMA and SCA Ventures, Inc., a subsidiary of Enzon Corporation, are also working in the field of phage display libraries and related technologies.

In the area of infectious disease antibodies, potential competitors include serum antibody companies such as CSL and Baxter, and monoclonal antibody companies like MedImmune.

Regulations applicable to the biopharmaceutical industry

We operate in a highly regulated industry. Our products require approval of government health authorities before they can be sold, and require significant pre-clinical testing before approval will be granted. Our research and development and production activities involve the use of hazardous materials, including biological materials, many of which we need special approval to obtain and all of which are subject to regulation regarding their handling and disposal. Environmental laws and regulations and laws and regulations relating to safe working conditions, laboratory conditions, and laboratory and manufacturing practices also apply to our operations. We conduct our operations in a manner designed to comply with applicable regulations and we believe that we have all the licenses and permits required to carry out our current activities.

Obtaining product approval is a costly and time-consuming process. All of our potential products, and those of our licensees, are either in research or development. Any products our licensees or we develop will require regulatory clearances prior to clinical trials and additional regulatory clearances

prior to being produced and distributed commercially. These regulatory processes are generally stringent and time consuming. We expect the European Medicines Agency (EMEA) in the European Union, the FDA in the US, the College ter Beoordeling van Geneesmiddelen (CBG) in the Netherlands and comparable agencies in other countries to subject new biopharmaceutical products to extensive regulation. These regulatory requirements with which we and our licensees will have to comply will evolve over time due to the novelty of the biopharmaceutical products and therapies currently under development. Fortunately, the harmonization of these requirements is promoted at an international level (International Conferences on Harmonization (ICH)) to avoid unnecessary repetition of studies when seeking approval in various countries. Under the current definitions, we believe that products developed using our technologies will be regulated either as biological products or as drugs.

Before marketing a (bio) pharmaceutical product, companies require regulatory approval from the relevant authorities. To obtain this approval, pre-clinical and clinical trials must be conducted to demonstrate the safety and efficacy of the product candidates. Clinical trials are the means by which experimental drugs or treatments are tested in human volunteers. New therapies typically advance from laboratory research testing through pre-clinical testing and finally through several phases of clinical human testing. On successful completion of the clinical trials and demonstration that the product can be manufactured in a safe and consistent manner, approval to market the biopharmaceutical may be requested from the EMEA in Europe, the FDA in the US or their counterparts in other countries.

Clinical trials are normally done in three phases:

- **Phase I:** First clinical trial of a new compound generally performed in a small number of healthy human volunteers, to assess clinical safety, tolerability as well as metabolic and pharmacologic properties.
- **Phase II:** Clinical studies that test the safety and efficacy of the compound in patients with the targeted disease with the goal of determining the appropriate doses for further testing and evaluating study design as well as identifying common side effects and risks.
- **Phase III:** Large-scale clinical studies with several hundred or several thousand patients to establish safety and effectiveness for regulatory approval for indicated uses and to evaluate the overall benefit/risk relationship.

Our research and development and production activities are undertaken in a number of countries around the world. These activities are subject to strict regulatory requirements of national and supranational authorities in the countries in which they are undertaken such as requirements governing the testing, manufacturing and marketing of pharmaceutical products. In most countries, it is necessary to obtain an approval to market a pharmaceutical or medical product. The grant of such an approval is subject to a detailed evaluation of data submitted by the applicant related to the quality, safety and efficacy of the product. Many countries, including member states of the EU and the US, impose extensive testing and data submission requirements and conduct rigorous technical appraisals of product candidates. In addition, different regulatory authorities may impose different conditions upon the marketing of a given product or may refuse to grant or require additional data before granting an approval to market a product even though the product may have been approved by another regulatory authority. Pre-clinical testing, clinical research and regulatory approval of a pharmaceutical or medical product is a lengthy and costly process.

Once a product is approved, the manufacturing and marketing of the product remains subject to periodic review. Changes in applicable regulations, breaches of regulatory requirements or the discovery of problems related to the manufacturing, safety, quality or efficacy or stability as well as changes in the characteristic of a product inherent to its biological origin may result in the imposition of restrictions upon the manufacturing and sale of such products, including at worst withdrawal of the product from the market and/or the revocation of the relevant regulatory approvals.

Pre-qualification applicable to the biopharmaceutical industry

National and regional governments rely on the pre-qualification granted to biopharmaceutical products by evaluative bodies such as the WHO and, in some cases, simply elect not to purchase products which have not been granted pre-qualification of approval.

The WHO Pre-qualification project is carried out to facilitate access to medicines that meet unified standards of quality, safety and efficacy.

Pre-qualification was originally intended to give United Nations procurement agencies, such as UNICEF the choice of a range of quality medicines. With time, the growing list of medicines that have been found to meet the set requirements has come to be seen as a tool for anyone purchasing medicines in bulk, including countries themselves and other organizations.

Any manufacturer wishing their medicines to be included in the pre-qualified products list are invited to apply. Each manufacturer must present extensive information on the product (or products) submitted to allow qualified assessment teams to evaluate its quality, safety and efficacy. The manufacturer must also open its manufacturing sites to an inspection team that assesses working procedures for compliance with WHO Good Manufacturing Practices (GMP).

The Pre-qualification project does not intend to replace national regulatory authorities or national authorization systems for importation of medicines.

Additional information on the Company

Legal proceedings

In the ordinary course of business, we have been and may become involved in disputes. Neither we, nor any of our subsidiaries, has been party to any legal or arbitration proceedings that may have, or have had during the 12 months preceding the date of this document, a significant effect on our results of operations or any of our subsidiaries nor, as far as we are aware, are any such legal proceedings pending or threatened, except for those disclosed in 'Intellectual Property – Patent Enforcement and Proceedings' in this section and those disclosed in section '5.18 Provisions, commitments and contingencies – legal proceedings' in the financial statements.

Property, plant and equipment

Our corporate offices and research activities are located in facilities of approximately 8,700 square meters in Leiden, the Netherlands. The section of this building that we use in Leiden includes 3,500 square meters of laboratories, with BioSafety Level (BSL) 1, BSL 2 and BSL 3 labs. The remainder of the main building is divided into 2,800 square meters of office space and 2,400 square meters for storage, technical areas, washrooms, waste destruction and sterilization. In addition, we lease 1,200 square meters of space adjacent to the corporate main building.

In 2008, the construction of the Valerio building, which was named after Crucell co-founder Dinko Valerio, was completed. The Valerio building is a GMP Process Technology Center of 5,400 square meters in Leiden. This new facility can be operated as a BSL 3 facility, in which two concurrent products can be produced at the BSL 2 and/or BSL 3 safety levels.

The Valerio Building meets the highest environmental and safety standards recommended for the laboratory activities to be conducted there. The facility has received approval from the Dutch government to produce material for use in humans. Extensive precautions will be taken to ensure safety and continuity of operations. Product quality will be strictly monitored, maintained and administered in-house.

Since our 2006 acquisitions, we also have office space, laboratories, production facilities, pre-clinical facilities and storage space in Switzerland, Spain, Sweden, Korea and Italy.

The following sets out information regarding our main facilities outside the Netherlands.

Bern, Switzerland (owned)
Crucell has two facilities located in the canton of Bern. These facilities are FDA/WHO/EMEA approved and are the primary sites for the manufacturing of Inflexal V, Vivotif, MoRu-Viraten and Epaxal. The combined facilities have a floor space of 45,000 m^2, 33,000 m^2 of which is manufacturing space. The facilities in Bern have the technology to manufacture both viral and bacterial vaccines using various manufacturing platforms within BSL 1 and BSL 2 environments.

In addition to the manufacturing, the facilities also have all the necessary support capabilities including Clinical Affairs, Regulatory Affairs, Quality Control, Quality Assurance, Operations, Finance and Process Development.

The Process Development group has a pilot plant of approximately 2,500 m^2. This facility is GMP certified and allows for work to be carried out on BSL 2 products. The capabilities within this facility are cell banking, up and downstream manufacturing, formulation, filling and lyophilisation for bacterial vaccine production. This facility is currently being used for life cycle management activities as well as conducting CMO activity for one of Crucell's partners.

Seoul, Korea (leased)
Our manufacturing facilities in Korea are KFDA/WHO approved and are used primarily for the production of Quinvaxem and Hepavax-Gene and for formulating and filling vials. The facilities include 3,201 m² of production and development space, 1,305 m² of storage space and 1,818 m² of office space.

In October 2008, we announced that we will relocate the Korean production facility from Yongin City to the Incheon, Free Economic Zone. The investments in the new facility are expected to total approximately €50 million, with the majority of spending in 2009. We entered into a mortgage loan facility in Korea for an amount of KRW 50 billion to partly finance the investments in the new Korean facility in 2009.

Madrid, Spain (owned)
Crucell has its main centre for filling and packaging operations in Madrid as well as local distribution. The facility is EMEA approved and it has the capability to fill syringes on two filling lines, primarily used to fill Inflexal V and Epaxal. The total facility consists of 2,130 m² of manufacturing space, 1,000 m² of office/laboratory space and 2,610 m² of warehousing.

Stockholm Sweden (leased)
In Sweden, our manufacturing facilities are EMEA/WHO approved and are used for the production of Dukoral and the recombinant protein rCTB. The manufacturing capabilities consist of large scale cGMP manufacturing of bulk, comprising both bacterial and mammalian systems, formulation and filling, visual inspection and packaging in vials. The site has a total of 4,866 m² of GMP development and production space, 5,990 m² storage space and 2,662 m² of office space.

In August 2008, we announced the intention to move Dukoral and rCTB bulk production, formulation and fill/finish activities from Sweden to other sites within the Crucell organization. The Group is now going through a feasibility study to determine the scope and timing of the move.

In 2008, € 15,787 was invested in property, plant and equipment compared to € 27,156 in 2007. The investments in 2008 mainly related to our new Korean production facility in the Incheon, Free Economic Zone, investments in our facilities in Bern, Switzerland that will improve current production processes and allow in-house production of materials currently acquired from third parties and investments in our new filling line in Madrid, Spain.

In 2007, € 27,156 was invested in property, plant and equipment compared to € 20,337 in 2006. The investments in 2006 and 2007 mainly related to our new GMP production facility in Leiden, the Netherlands and investments in our facilities in Bern, Switzerland.

Raw materials

We require a reliable supply of materials for the production of our products, including starting materials, like the serum-free medium in which we grow our PER.C6 cells, and antigens that are present in certain of our final products. Some of these materials are provided by a limited number of third party suppliers. Our ability to conduct research and to launch new products also depends on a steady supply of these raw materials. Any adverse changes to our existing supplier relationships will thus likely adversely affect our overall results. Prices for our raw materials are volatile and may change significantly over time. Some of our raw materials are purchased in foreign currencies and are subject to foreign currency exposures. We try to mitigate these exposures by entering in long term purchasing arrangements and by hedging the foreign currency exposures on our purchases.

Insurance

We have in place general third party public and product liability insurance. Our policy has a limit of liability and has certain additional conditions to coverage and deductibles. We do not insure our phage antibody display library or PER.C6 master cell bank, though identical copies of the same cell bank are stored in multiple locations in Europe. We believe we carry adequate insurance relating to theft, fire and damage to the moveable assets within our facilities and other customary insurance coverage for most of our activities, including liability insurance coverage for the members of the Management Board, Management Committee and the Supervisory Board.

Employees

For a breakdown of the employees by function and geography reference is made to note 5.1 ‘Personnel expenses’ in the financial statements.

Material contracts

As of the date of this Annual Report, we are not party to any contracts (not entered into in the ordinary course of business) that are considered material to our results, financial condition or operations.

Dividends and dividend policy

Crucell N.V. did not pay any dividends in 2008. We do not intend to pay dividends on our ordinary shares for the coming years, and thereafter only on the condition that our financial performance is adequate and it is in the shareholders' interest to pay dividends instead of investing the proceeds into the company. Any payment of future dividends and the amounts thereof will depend upon earnings, statutory and financial requirements and other factors deemed relevant by our Management Board, and will be subject to withholding tax in the Netherlands. In the event that we pay dividends in the future, holders of our American Depository Shares (ADSs) will be entitled to receive payments in US dollars in respect of dividends on the underlying ordinary shares in accordance with a deposit agreement dated October 26, 2000 between The Bank of New York Mellon, as depository, and us.

Risk Factors

Our Management Board is responsible for designing, implementing and operating the Company's internal risk management and control systems. The purpose of these systems is to manage in an effective and efficient manner the significant risks to which the Company is exposed. For a more detailed description please see 'Internal risk management and control system' in the Corporate Governance section of this Annual Report.

An integral part of our internal risk management process is the identification of risks that could prevent us from reaching our objectives. To identify these risks we performed a corporate risk assessment with the Disclosure Committee of the Company in 2008. The outcome has been discussed in the Audit Committee and was taken into account in the risk factors described below. We have classified these risk factors in accordance with the categories of objectives identified in the COSO model, an integrated internal control framework established by the Committee of Sponsoring Organizations of the Treadway Commission.

You should carefully consider these material risk factors. The risks we face are not limited to the risks listed here. Some risks are not yet known to us and some of the risks that we currently do not believe to be material to our operations could prove to be material at a later date. All of these risks can materially affect our business, financial condition and results of operations.

Strategic

Concentration of sales

We are dependent on a limited number of products and customers for a majority of our revenues and expect this dependence to continue in the foreseeable future. Our core product portfolio consists of seven vaccines, namely Quinvaxem, Hepavax-Gene and MoRu-Viraten (paediatric vaccines), Inflexal V (influenza), Dukoral, Epaxal and Vivotif (travel vaccines). The aggregated revenues for our core product portfolio represented a significant part of our total product sales in 2008. The sales to our largest customers, which are in the paediatric vaccines area, represented a considerable part of our net product sales in 2008. In particular, we are highly dependent on sales of Quinvaxem and Inflexal V. If these products were to become subject to any problem such as unexpected side effects, product liability litigation, loss of patent protection, supply interruptions, regulatory proceedings, publicity affecting doctor or patient confidence or pressure from competitive products, or if a new more effective treatment is introduced, we could experience a significant decrease in revenues and an adverse effect on our financial results.

Additionally, our results may fluctuate as a result of seasonality in our business. In particular, the market for flu vaccines is highly seasonal so a majority of our distribution and sales tends to occur in the second half of the year. Delays in any step of our regulatory approval, production or distribution processes could result in a significant sales reduction.

Strategic alliances

If our current or prospective partners or licensees do not use our products or technologies, we may not be able to continue to realize revenues related to those partners or licensees. In particular, our current or prospective licensees or partners may use or develop alternative technologies or competing products, independently or in collaboration with others, including our competitors. If any of our licensees or partners becomes involved in a business combination or other major corporate transaction, this could cause a strategic shift in their business focus and lead them to discontinue the use of our products and technologies.

Furthermore, we may have disagreements with our licensees over royalty payments owed to us and may have difficulty collecting these payments. Our existing license arrangements generally entitle us to receive royalty payments for any products developed using our technology. We depend on our licensees to inform us when they develop products using our technology. If our licensees fail to inform us of these developments, we may not otherwise learn of payments to which we are entitled. In addition, our licensees may have difficulties making payments to us given the current economic climate or other factors. We may also incur significant expenses in collecting royalty payments, or in some instances, may not succeed in collecting these payments at all.

Competition and pricing pressures

We face competition from other companies in the development, marketing and licensing of new technologies and products. We operate in competitive markets and compete with companies that have their own technologies, products or other forms of treatment for the diseases we target.

Companies may develop proprietary positions in the areas of our core technologies or obtain regulatory approval for alternative technologies or commercial products earlier than we or our licensees do. Other companies, including our own licensees, may already have or may in the future develop products that are more effective or more effectively marketed and sold than those based on our technologies. We may not be able to compete effectively with these companies, and such competition could hamper our ability to bring products to market or to license and derive revenue from our technologies.

Our existing products may experience pricing pressures from competition with other products on the market. Pricing pressures may further increase due to the introduction of new products, the expansion of production capacity, or decreases in demand. We cannot predict with accuracy the impact of such events on our revenues. Products that compete with Quinvaxem have already been introduced to the market and still others may yet be introduced. Increased competition from these products could result in further pricing pressure on Quinvaxem and a substantially negative impact on our revenues.

We experience pricing pressures in the public markets for our products, which typically operate via a tender system. In a tender system, national governments or supranational organizations request proposals for the terms under which a vaccine manufacturer will provide a large quantity of one or more vaccines. The awarding of the contract is typically based on a number of factors, including price, supply reliability and product quality. Failure to win one of these public contracts may cause us to be ineligible to supply a national government or supranational organization for a period of time, resulting in a negative impact on our revenues. Pricing pressures may have a material adverse effect on our business, results of operations and financial condition.

Operational

Product development and clinical trials

All of our products and those of our licensees and partners may fail at any stage of development or even after market introduction due to factors beyond our control. Such failures could have a material adverse effect on our business and prospects.

Pre-clinical testing, clinical research and regulatory approval of a pharmaceutical or medical product is a very lengthy and costly process, and there is a significant risk of failure at each stage of the process should issues arise with respect to the efficacy or safety of a product. In particular, because pre-clinical and early clinical studies cannot ensure efficacy for humans, actual human studies are required for vaccine development. Such studies may, however, fail to prove the efficacy of the product candidates and are at constant risk of suspension for posing unreasonable health risks. There can be no assurance that any product candidate in our product pipeline will reach or successfully complete the clinical research phase of product development. Although a product that reaches a later stage of development offers a reasonably high probability of success relative to products in earlier stages, the chances of failure remain significant throughout the development process. We have had products fail at later stages of development in the past. Any or all of our current later-stage products could fail to be shown sufficiently safe or effective to be brought to market, or could otherwise fail to receive necessary regulatory approvals.

Regulators have granted certain of our products provisional or conditional marketing approval, requiring us to do follow-up studies to assess the safety and efficacy of the product in all or part of the target population. Poor results in any of these studies may give rise to the withdrawal of market authorization for some or all indications, in part or in all of the targeted population. Even if the products currently in later-stage development are introduced to the market, there can be no assurance that demand for such products will develop or be sustained. If a market does develop, there can be no assurance that our existing facilities and resources will be sufficient to meet demand. Accordingly, there can be no assurance that we will realize any potential benefits that may be associated with our later-stage development product portfolio.

Our success depends on a sufficient pipeline of new products and technologies. We therefore commit substantial resources and efforts towards research and development. We have no assurance that these efforts will succeed. Failure to maintain a healthy flow of new products through our pipeline could result in higher costs without a proportional increase in revenues.

To a certain extent, we are dependent on third parties with whom we contract to perform clinical trials of our products. If we fail to adequately manage the work of these third parties, a regulatory authority may determine that they have not complied with applicable regulations and therefore may not approve a product candidate of ours.

To continue to develop our core technologies and new products, we will need access to biological materials such as virus and tissue samples, which may be in limited supply. If we lose or do not obtain access to these biological materials, or if tighter restrictions are imposed on their use or on the information generated from their study, we could be restricted or prevented from conducting certain research and product development.

Interrupted product supply
Supply interruptions, product recalls or inventory losses caused by unforeseen events such as manufacturing or distribution interruptions or regulatory actions, may reduce sales, delay the launch of new products and adversely affect our operating results and financial condition.

Our products are manufactured and distributed using technically complex processes requiring specialized facilities, highly specific raw materials and other production constraints. The complexity of these processes as well as strict Group and government standards for the manufacture of our products may expose us to risks affecting our production process. Defects in the manufacturing process, including equipment malfunction, labor problems, regulatory action, power outages, natural disasters and environmental factors may all affect production output. The new EU regulation (EC 1907/2006, REACH), requiring registration of all chemical materials by us and our suppliers, may cause supply interruptions of raw materials that may in turn cause production delays if we need to change our sources of certain raw materials or marketing delays due to new validation activities to demonstrate similarities, or differences in comparability studies between old and new suppliers. Our vaccine products in particular are subject to the risks of manufacturing problems and inventory loss because of the difficulties inherent in the manufacture of biological materials, whether in our own facilities or in the facilities of our suppliers. Vaccine components cannot be sterilized nor can preservatives be added to the manufactured vaccine. Contamination of our products could result in the loss of entire batches of finished vaccine, which could lead to lost sales, damage to customer relations, a significant outlay of time and money to investigate the cause of the contamination and possibly a costly product recall if contaminated vaccines have already been shipped to customers. A disruption in the supply of certain key products or our failure to accurately predict the demand for those products could have a material adverse effect on our results.

We rely on a separate facility for the manufacture of each of our products. The marketing and regulatory authorization of biological products, in particular vaccines, is strongly linked to the production facility and equipment that are used to manufacture those products. If any event occurs that interrupts production at one of our facilities we may have to transfer production to a new site, which would be costly and time consuming. Because of the short shelf life of biological products, our existing stocks of product may not be sufficient to supply our customers during such a transition period. For example, our manufacturing facility in Korea is our sole production source of the Quinvaxem vaccine. As such, we are vulnerable to any event that interrupts, reduces or slows production of Quinvaxem at that facility. We intend to relocate our Quinvaxem operations to another site in Korea and preparations for such a move are ongoing. The relocation of the Quinvaxem operations is a complex process, which includes the inherent risk of the new facility not coming online before the old one has shut down. We agreed on the time line and conditions of this relocation with parties involved, enabling a smooth transition to the new production facility, however there can be no assurance that there will be no delay in the transition process.

We require a reliable supply of materials for the production of our products, including starting materials, like the serum-free medium in which we grow our PER.C6 cells, and antigens that are present in certain of our final products. Some of these materials are provided by a limited number of third party suppliers. Any interruption or termination of these supply relationships may have adverse effects on our ability to manufacture and sell products, particularly if we are unable to source new supplies of the same materials or adapt our technologies and manufacturing processes to use different starting materials in a timely manner. Our ability to conduct research and to launch new products also depends on a steady supply of these raw materials.

Any adverse changes to our existing supplier relationships will thus likely adversely affect our overall results.

Regulatory approval
We may be unable to obtain regulatory approval to manufacture and market our new products or may have regulatory approval for the manufacture and marketing of our existing products revoked by regulatory bodies such as the US Food and Drug Administration (FDA), the European Medicines Agency (EMEA), the European Commission or other non-governmental bodies such as the World Health Organization (WHO).

These various regulatory authorities have substantial discretion and may impose different conditions upon the marketing of a given product or may refuse to grant, or require additional data before granting, an approval to market a product even though the product may have already been approved by another regulatory authority. National and regional governments rely on the (pre) qualification and/or approval of biopharmaceutical products by evaluative bodies such as the WHO and, in some cases, simply elect not to purchase products which have not been granted (pre) qualification or approval.

Once a product is approved, its manufacture and marketing remains subject to regulatory requirements including industry code of conduct regulations. Changes in applicable regulations, breaches of regulatory requirements or the discovery of problems related to the marketing, manufacture, safety, quality, efficacy or stability of a product, as well as changes in the characteristics of a manufactured product stemming from alterations in its biological origins, could result in the imposition of fines or restrictions upon the manufacture and sale of such product, including in the worst case scenario withdrawal of the product from the market altogether and/or the revocation of necessary regulatory approvals.

Regulatory requirements could make product development based on new technologies highly uncertain because regulatory review of the underlying technologies is generally required.

If regulatory authorities do not approve our new products or other products developed using our technologies, or if they subsequently revoke their approval, that may impact our revenues generated from the sale of products and/or the licensing of our technologies, which may in turn have a material adverse impact on our business, financial condition, results of operations and prospects.

Intellectual property
Our efforts to protect our intellectual property rights or to defend ourselves against any claims of infringement of third party intellectual property may be costly and, if unsuccessful, we may be barred from using or licensing our technologies, and from developing and commercializing our new products.

Our commercial success depends in part on our ability to obtain and maintain adequate protection of our intellectual property rights, including patents, in our technologies and products in Europe, the US and elsewhere. Our patent-related activities do not afford complete protection to our intellectual property rights. Patents of technology-based enterprises like ours are subject to complex factual and legal issues that may give rise to uncertainty as to the validity, scope and priority of a particular patent. There can be no assurance that we will develop products that are patentable, that patents will be granted under pending or future applications or that patents granted to us or our collaborators will be of sufficient breadth to protect against competitors with similar technologies or products. A patent that is issued to us may be narrower than our application or found to be invalid. Others may make attempts to copy, reverse engineer or design around aspects of our technology, or to obtain and use information that we regard as proprietary. In addition, our patent filings may be subject to challenges. Our inability to adequately protect our products and technologies in emerging economies, such as India and China, may give rise to competition in those countries from manufacturers operating in low-cost economies. Due to compulsory licensing regimes currently in place in many of these underdeveloped and developing jurisdictions, we may not be able to use our intellectual property rights to prevent the low-cost manufacture of competing products. Such competition may adversely affect our ability to maintain viable pricing levels and to sell products in those countries.

In addition, production of Quinvaxem requires a particular vaccine component that may become the subject of a patent dispute between either GSK and us or GSK and our supplier of that component. The patent on that particular component, held by

GSK, is currently under opposition before the patent office and a definitive outcome on the validity of the patent is expected to take a number of years. A negative outcome of this opposition proceeding could lead to infringement proceedings between GSK and us or GSK and our supplier, although we believe that neither we nor our supplier would be held to have infringed or be infringing that patent. The outcome of legal disputes is invariably difficult to predict with accuracy, but in the event GSK were to prevail in infringement proceedings against us, this would adversely affect our business.

For a more detailed discussion of issues surrounding our patent enforcement and related proceedings, see 'Intellectual property – Patent enforcement and proceedings'.

We also endeavor to protect our proprietary technologies, processes, know-how and data by entering into confidentiality agreements with our employees, consultants, partners and certain contractors. We have no assurance that these agreements or other trade secret protections will provide meaningful protection to us.

Our commercial success also depends on not infringing on the patents and other proprietary rights of third parties. As our activities in the biotechnology and biopharmaceutical markets expand and as more patents are issued in the field, the risk that our technologies and products may give rise to claims of alleged infringement increases. Licensing or other arrangements for addressing these infringements or violations may not be available, or may not be available on commercially acceptable terms if we or our licensees are unable to obtain licenses from third parties for the use of their intellectual property in the manufacture of our products, we or our licensees may be unable to develop or market those of our products which are based in part on the intellectual property of others.

Product liability exposure
We may be exposed to product liability and other claims if third parties allege that our technologies or products have caused some harm.

If a third party sues us for an injury caused by our products or by products developed using our technologies, our liability could exceed our total assets. Because our vaccines that constitute our core products are administered to healthy individuals, any adverse health consequences associated with such administration may be more apparent and perceived as less tolerable than similar side effects associated with the treatment of disease.

Lawsuits against us arising out of clinical trials may increase as more and more licensees utilize our technologies, thereby reducing our control over the manner of their use. We maintain product liability insurance in respect of all of our marketed products. We may seek to obtain additional product liability insurance in the future, though it cannot be assured that such additional insurance will not be prohibitively expensive, or that it will cover all of our potential liabilities. If we are unable to obtain sufficient insurance coverage at an acceptable cost or if we are otherwise unable to protect ourselves against potential product liability claims, we and/or our licensees may be prevented or inhibited from commercializing new products.

Product liability cases, claims and even relatively minor potential health risks associated with our products may give rise to adverse regulatory action, and/or a negative market perception of us and our products, resulting in a material adverse effect on our business, financial condition, results of operations and prospects. Though we believe we have strong defenses in these and other cases, including patent infringement cases, there can be no assurance as to the outcome of these matters and we could incur judgments or enter into settlements of claims that could have a material adverse effect on our results of operations.

Qualified personnel
We may not be able to continue to recruit and retain highly qualified management, scientific, manufacturing, sales and marketing and finance personnel. Competition for qualified personnel could be intense and may limit our ability to attract and retain qualified personnel on acceptable terms and may therefore significantly increase our labor costs. The inability to attract and retain highly skilled personnel on acceptable terms could have a material adverse effect on our business, financial condition, results of operations and prospects.

Hazardous biological materials
Our manufacturing, research and development processes involve the controlled use of hazardous biological materials. Certain of our laboratory

facilities are qualified up to Biosafety Level III (BSL-III), which allows us to work on-site with hazardous biological materials. Our operations may also produce hazardous biological waste. Given the inherently dangerous nature of certain biological materials we may work with in our BSL-III laboratory facilities, we cannot eliminate the risk of accidental contamination or discharge or any injuries that result therefrom. Various laws and regulations govern the use, manufacture, storage, handling and disposal of these materials. We could be subject to civil damages and significant adverse publicity in the event of an improper or unauthorized release of, or exposure of individuals to, hazardous materials.

Competition laws
We cannot be certain that our licensing or other agreements are not in breach of applicable competition laws and will not be rendered void by the relevant competition authorities. In the past, we have not notified the European Commission competition authorities of any of our licensing or other agreements or sought clearance from any other competition authority. We take the view that these agreements are unlikely to be found to infringe European Union or other applicable competition regulations. It is possible, however, that current or future licensing or other agreements of ours could be found to infringe applicable competition regulations. If so, among other things, we may be subject to fines and claims of damages and these agreements may be considered void and unenforceable. Under the European Union's 2004 Technology Transfer Block Exemption Regulation, we may be required to review and possibly amend existing license and technology transfer agreements in the future. For example, if certain market share thresholds will be or have been reached in the relevant markets by those third parties that use our technologies to produce their products, the Regulation may require us to revise our agreements with those parties to ensure the agreements are in compliance with applicable European competition law.

Financial

Substantial use of capital
In the past, we have had to raise additional funds to acquire other companies and assets while continuing to research and develop our technologies and products. We also have incurred accumulated net operating losses since our incorporation. Although the Company generated positive cash flow in 2008, we may have cash outflows and net operating losses in the future due to the occurrence of events that would consume our available capital resources. We may seek additional funding through public or private financing (including debt or equity financing), strategic alliances or other arrangements. We may not have access to additional financing and, if we do, it may not be on favorable terms. If we fail to raise sufficient funds, we may have to forego acquisitions, reduce our capital expenditures, scale back our product development, reduce our workforce and/or license products or technologies to others that we might otherwise commercialize ourselves.

Weakness in the global economy could negatively affect our business
The weakness of the global economy in 2008 was a challenge for many companies worldwide. The ongoing financial crisis became prominent in September 2008 with the failure or near-failure of several United States and European based financial institutions and the resulting deterioration in financial and market conditions spread around the globe. In recent months the financial crisis has adversely affected businesses in many industries and geographical areas all over the world at an unexpected pace.

The weakness of the global economy has not had a significant impact on our liquidity or on our ability to derive revenues from our operations. However, there can be no assurance that our liquidity will not be affected by recent and possible future changes in global financial markets and global economic conditions.

Financial distress and bankruptcies experienced by our customers and suppliers resulting from the recent global economic slowdown could impair their ability, as the case may be, to purchase our products, pay for products previously purchased or meet their obligations to us under supply agreements. This could lead to a material adverse effect in our revenues.

We do not know how long the current financial crisis will continue nor how severe it will ultimately be. In the long run, we may be affected if governmental agencies or supranational organizations decide to realign priorities and allocate fewer funds to public health initiatives. The financial crisis may have

a negative impact on the travel pattern, which is the key driver of our travel vaccines.

Foreign currency risk
The majority of our total revenues in 2008 were in currencies other than our functional currency, the Euro. Currency fluctuations may cause significant economic foreign currency exposure and transactional foreign currency exposure. Fluctuations in the currencies in which we do business relative to the Euro have affected our results in the past and, given the current economic climate and the substantial recent fluctuations in interest rates and currency exchange rates, may do so again in the future. Notwithstanding our efforts to foresee and mitigate the effects of changes in fiscal circumstances, we cannot predict with certainty changes in currency and interest rates, inflation or other factors affecting our business. Because of the variability of currency exposures and the potential volatility of currency exchange rates, we may suffer significant foreign currency losses in the future, particularly if the Euro strengthens relative to currencies in which a significant number of our operations are conducted. We engage on a limited basis in derivative transactions to hedge our foreign currency exposure. See section 3.2 'Foreign currency risk' in the financial statements for further details on our foreign currency risk.

Taxation
We are subject to the tax laws of the countries in which we operate as well as to European tax law. We may incur additional tax charges, including penalties, resulting from changes in tax laws or the interpretation of tax laws or from failure to comply with obligations required by relevant tax authorities. Disputes with tax authorities may arise with regard to the interpretation and application of tax laws. If any of these risks materializes, leading to tax costs associated with particular transactions being greater than anticipated, it could affect the profitability of our business as a whole. See note 5.4 'Income tax' in the financial statements for further details on our taxation.

Compliance and other

Ethical, legal and social issues related to the use of genetic technology
The use of genetic technology and materials derived from human fetal tissue, such as our PER.C6 technology, may raise ethical, legal and/or social issues that could hinder regulatory approval, patentability or market acceptance of our technologies and the products developed using them. If these risks materialize they could have adverse consequences for our business since they could reduce or eliminate altogether potential markets for our own or our licensees' products.

Protective measures included in articles of association
Protective measures included in our articles of association, in accordance with Dutch law, may prevent corporate action and/or shareholder transactions that might be in the best interests of our Company or the shareholders. Among other things, our articles of association provide that our Supervisory Board may make binding nominations for the election of its members. Only a shareholders' resolution approved by an absolute majority of the votes cast, representing more than one-third of our total outstanding shares, can override those nominations. Furthermore, under Dutch law, we may issue preference shares to a foundation, Stichting Preferente Aandelen Crucell, or the Preferred Foundation, giving it preferred dividend rights, which may dilute the voting rights held by the holders of other classes of shares. The Preferred Foundation has an option to acquire a number of preference shares equal to the number of our total outstanding shares. The chairman of our Supervisory Board, Jan Oosterveld, and four independent members comprise the board of the Preferred Foundation. These and other provisions in our articles of association may have the effect of delaying, deterring or preventing corporate action that might be in the best interest of the Company or our shareholders and/or preventing our shareholders from selling their ordinary shares or ADSs at a premium to the market price. See 'Other information' and 'Articles of Association and Share Capital' for additional information regarding the preference shares and our articles of association.

US and other non-Dutch holders of our ordinary shares may not be able to exercise pre-emption rights.
In the event of an increase in our share capital, holders of our ordinary shares are generally entitled to certain pre-emption rights unless these rights are excluded by a resolution of the General Meeting of Shareholders or a meeting of the Management Board if so delegated by the General Meeting of Shareholders. However, US holders of our ordinary

shares may not be able to exercise pre-emption rights unless a registration statement under the Securities Act is declared effective with respect to the shares issuable upon exercise of such rights or an exemption from the registration requirements is available. No assurance can be given that any registration statement will be filed or, that if filed, it will be declared effective or that any exemption from registration would be available to enable the exercise of a US holder's pre-emption rights.

Shareholders may have difficulty protecting their interests as shareholders as we are a Dutch limited liability Company.

Dutch law and our articles of association govern issues regarding the legal organization, internal constitution, corporate authority and liability of members of our Management Board and Supervisory Board. Most of our offices and assets are located outside the US. In addition, a majority of the members of our Supervisory Board, all of the members of our Management Board and management team are residents of, and most of their assets are located in, jurisdictions outside the US. As a result, it may be difficult to serve process on these persons within the US. It may also be difficult to enforce a US court judgment against them in a US court or in a Dutch court or to enforce a Dutch court's judgment against them in a US court. This can include actions under the US securities laws. In addition, it may be difficult to enforce, in original actions brought in courts in jurisdictions located outside the US, claims under US securities laws. For a more complete discussion of potential difficulties in protecting your rights, see 'Articles of Association and Share Capital – Enforcement of Civil Liabilities'.

Share price volatility

Our ordinary shares and ADSs may have a highly volatile trading price. Shareholders may not be able to resell their ordinary shares or ADSs at or above the price they pay for them, the ADSs may vary in value and our share price may render us vulnerable to a takeover bid. Our ordinary shares are listed on NYSE Euronext Amsterdam and the SWX Swiss Exchange, and our ADSs are listed on the NASDAQ Global Select Market. The trading prices of ordinary shares of biotechnology companies in general have experienced significant volatility in the past and are likely to continue to be volatile. In addition, any negative change in the public's perception of the prospects of biotechnology companies could depress our ordinary share or ADS price regardless of our results of operations. Other broad market and industry factors, such as discussions on business combinations and a weak global economy may affect the trading price of our ordinary shares and ADSs, regardless of our performance.

Operating and Financial Review and Prospects

The following discussions should be read in conjunction with our financial statements and the notes thereto included elsewhere in this Annual Report. We refer to 'Forward-looking statements' as well as to 'Risk factors' for certain factors that may affect our operating results. Unless otherwise mentioned all amounts in this section are in thousands of Euro, except share and option data.

General

We are a fully integrated biopharmaceutical Company, focused on developing, producing and marketing vaccines and antibodies against infectious diseases for private and public markets worldwide. We have a portfolio of well-known vaccines and a pipeline of potential new vaccines and antibodies. We combine proprietary technologies to discover, develop and produce a variety of vaccines and antibodies to combat infectious diseases.

Summary of the full year financial results

Total revenue and other operating income for the year ended December 31, 2008 were € 283,309, which represent a 32.9% increase over the € 213,116 in revenues and other operating income reported in 2007. The increase in total revenues and other operating income is mainly attributable to increased sales of paediatric vaccines, travel and endemic vaccines and higher license revenues.

Total operating expenses amounted to € 129,691 (2007: € 125,918). R&D expenses of € 70,229 (2007: € 63,995) reflect our continued focus on (pre-) clinical development.

We achieved profitability for the full year 2008, reporting a net profit of € 14,586, compared to a net loss of € 42,910 in 2007. This amounted to € 0.22 net profit per share in 2008, compared to a net loss per share of € 0.66 in 2007.

Cash and cash equivalents at December 31, 2008 amounted to € 170,969 (2007: € 163,248).

Our operating cash flow was € 254 negative in 2008, compared to a positive operating cash flow of € 22,194 in 2007. The reduction is mainly due to the build-up of Quinvaxem inventory for sales in 2009.

Segments

We operate in one reportable segment, which comprises the development, production and marketing of products that combat infectious diseases. The Group early adopted IFRS 8 'Operating Segments', which replaces IAS 14, 'Segment reporting', as of January 1, 2007. The Management Board is identified as the 'chief operating decision maker'. The Management Board reviews the consolidated operating results regularly to make decisions about resources and to assess overall performance.

In 2007, our segmentation was based on the two segments that were reported to our Management Board:

- Vaccines: developing, producing and marketing vaccines worldwide to combat infectious diseases; and
- Proteins: leverage our novel, proprietary technologies to develop monoclonal antibodies to combat infectious diseases.

In 2008, the Management Board decided to integrate both business units and reduce the complexity of our organisation. In 2008, the separate segments were no longer reported to the Management Board.

Retrospective application of newly adopted accounting policies

We adopted IFRIC 14, 'IAS 19 – The limit on a defined benefit asset, minimum funding requirements and their interactions' in 2008. This interpretation provides guidance on assessing the limit of the surplus in a defined benefit pension plan that can be recognized as an asset. It also explains how a pension asset or liability may be affected by a statutory or contractual minimum funding requirement. Our pension fund in Switzerland has a minimum funding requirement and the application of the interpretation resulted in an increase in the assets recorded on the Group's balance sheet of € 7,853 (2007: € 4,918, 2006: € 746) and a corresponding increase in the Group's equity of € 6,165 (2007: € 3,861, 2006: € 586). As a result of the adoption of IFRIC 14, the result for the year increased by € 2,101 (2007: € 3,037, 2006: € 367). As required by IFRS, all comparative figures were adjusted as if the interpretation had always been applied.

Acquisitions and divestments
In 2006, we acquired a controlling interest in the Swiss biotech Company Berna Biotech AG (Berna Biotech), in a share exchange. In September 2006, we acquired the remaining 1.6% minority interest in Berna Biotech. In October 2006, we purchased the assets and liabilities of Florida-based Berna Products Corp. (BPC) from Acambis plc. In November 2006, we acquired Stockholm-based SBL Vaccin Holding AB (SBL) from the private equity firm 3i and the financial group SEB.

2007 is the first year that includes the consolidated results of the acquired companies for a full year. Our 2006 financial results included one month of SBL's financial results, three months of BPC's financial results and ten months of Berna Biotech's financial results.

Economic and industry-wide factors

Various economic and industry-wide factors are relevant to us and could affect our business, including the factors set forth below.

Our financial strength and ability to adapt to the current market and economic conditions are dependent, in part, on the success of our existing products, the cost of bringing novel products to market and the success of our licensees in developing commercial products using our technology. Our industry is subject to extensive government regulation, and we must make significant expenditures to comply with these regulations. Our business success is dependent in a significant part on our success in establishing intellectual property rights, either internally or through licenses of third-party intellectual property rights, and protecting our intellectual property rights.

Our sales are exposed to seasonal variations, and the majority of our sales is made in the second half of the year. This is specifically the case for our influenza vaccines as vaccination programs mainly take place in the second half of the year. Furthermore, our travel vaccines sales are subject to seasonal travel patterns. The 2008 flu season was comparable to 2007 in our major markets in Europe.

To be successful, we must retain qualified clinical, scientific, marketing, administrative and management personnel. We face significant competition for experienced personnel. In 2008, the number of employees of the Group remained stable at 1,126 employees (2007: 1,126).

The above economic and industry-wide factors are discussed in more detail in the section 'Risk factors'.

Result of operations

Revenues

The table below shows our revenues for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Product sales	**226,055**	177,569	103,918	27.3	70.9
License revenues	**30,202**	12,211	16,955	147.3	(28.0)
Service fees	**10,900**	14,006	10,694	(22.2)	31.0
Total revenues	**267,157**	**203,786**	**131,567**	**31.1**	**54.9**

In 2008, total revenues increased by € 63,371 or 31.1% from € 203,786 in 2007 to € 267,157 in 2008. The increase is attributable to an increase in product sales of € 48,486 or 27.3% and license revenues of € 17,991 or 147.3%. The increase is partly offset by a decrease in revenue from service fees of € 3,106 or (22.2%).

Total revenues grew by € 72,219 in 2007 or 54.9 % from € 131,567 in 2006 to € 203,786 in 2007. The increase is primarily attributable to increases in sales of paediatric vaccines by € 41.438 or 115.3 % and travel and endemic vaccines by € 24.210 or 104.9 % and higher revenues related to the acquisitions made in the second half of 2006.

Reference is made to '4.4 Geographical segments' in the financial statements for the breakdown of our revenues by geographic segment.

Product sales
Our product sales by type of product in 2008, 2007 and 2006, as well as the percentage change between the periods, are shown below:

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Paediatric vaccines	**111,039**	77,371	35,933	43.5	115.3
Respiratory vaccines	**32,474**	33,188	40,386	(2.2)	(17.8)
Travel and endemic vaccines	**55,572**	47,282	23,072	17.5	104.9
Other products	**26,970**	19,728	4,527	36.7	335.8
Total product sales	**226,055**	**177,569**	**103,918**	**27.3**	**70.9**

In 2008, product sales grew by € 48,486 or 27.3%. The increase is primarily attributable to increased sales of paediatric vaccines of € 33,668 or 43.5%, travel and endemic vaccines of € 8,290 or 17.5% and other products of € 7,242 or 36.7%.

In 2008, paediatric vaccines grew mainly due to increased Quinvaxem sales. Supranational organizations awarded us additional contracts for Quinvaxem and Hepavax Gene amounting to $ 140 million for the period 2008-2009. Travel and endemic vaccines showed considerable growth on an overall basis. ´Other products´ include sales of vaccine and proteins trade goods that we distribute for third parties and also sales of conjugates to Wyeth. The increase in other products mainly relates to increased sales under our distribution agreement with Talecris as 2008 includes a whole year of sales under this agreement for the first time.

Our core product portfolio consists of seven vaccines: Quinvaxem, Hepavax-Gene, MoRu-Viraten (paediatric vaccines), Inflexal V (respiratory), Dukoral, Epaxal and Vivotif (travel and endemic vaccines). The aggregated revenues for our core product portfolio amounted to € 191,631 in 2008 (2007: € 151,791, 2006: € 92,144) and represented 84.8% (2007: 85.5%, 2006: 88.7%) of our total product sales.

In 2008, sales to our two largest customers, which are in the paediatric vaccines area, amounted to € 85,142 or 37.6% and € 18,390 or 8.1 % of net product sales. In 2007, sales to these customers accounted for € 45,480 or 25.6% and € 23,457 or 13.2% of net product sales, respectively.

In 2007, product sales grew by € 73,651 or 70.9 %. The growth in revenue from product sales was mainly due to increased revenue from sales of paediatric vaccines of € 41,438 or 115.3%, travel and endemic vaccines of € 24,210 or 104.9 % and sales of other products of € 15,201 or 335.8 %. The increase in product sales was partly offset by a decrease in respiratory vaccines of € 7,198, mainly caused by lower influenza vaccine sales as a result of a mild flu-season in 2007.

The majority of our sales are export sales. Domestic product sales amount to € 3,743 or 1.7% (2007: € 717 or 0.4% and 2006: nil). Almost all of our license revenues and service fees are billed to foreign parties.

License revenues
In 2008, license revenues increased by € 17,991 or 147.3% to € 30,202 compared to 2007. This increase mainly results from milestone payments related to the rabies and influenza programs from sanofi pasteur and upfront fees received from Talecris for the exclusive production rights of two specific proteins.

In 2007, our license revenues decreased to € 12,211, a reduction of € 4,744 or 28.0% compared to 2006, which was mainly due to one-off issuance fees included in contracts with DSM and sanofi pasteur in 2006. The underlying agreements with DSM and sanofi pasteur are still in effect. The decrease was partly offset by recognized issuance fees on contracts signed in 2007 with MedImmune, ADImmune and Wyeth that totaled € 4.3 million and numerous other smaller contracts.

In December 2007, we signed an exclusive collaboration and commercialization agreement with sanofi pasteur related to our rabies monoclonal antibodies. We received a payment of € 10.0 million, which will be recognized as license revenues over the period that the development activities are performed. We will be eligible for additional potential milestone payments of up to € 66.5 million.

Service fees
In 2008, service fees amount to € 10,900, a decrease of € 3,106 or 22.2 % compared to 2007. In 2008, service fees on the sanofi pasteur influenza project were less compared to 2007. Service fees include revenues relating to various collaboration agreements. Typically we do not retain the residual interest on products developed under these agreements. We are more selective in the programs that we want to carry out and we tend to put more focus on the profitability of these types of programs.

In 2007, service fees amounted to € 14,006, an increase of € 3,312 or 31.0% compared to 2006. This increase was mainly attributable to consulting services provided to ADImmune and increased service fees in Sweden realized on miscellaneous projects.

Cost of goods sold
The following table shows our cost of goods sold for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Cost of product sales	**138,790**	124,557	83,518	11.4	49.1
Cost of service fees	**6,965**	10,327	6,971	(32.6)	48.1
Total cost of goods sold	**145,755**	**134,884**	**90,489**	**8.1**	**49.1**

Cost of product sales
Costs of product sales comprise direct labor, materials, and overhead costs incurred in performing work under various collaboration agreements directly related to product sales. The cost of product sales increased in 2008 mainly due to an increase in product sales of 27.3%. This increase was partly offset by the reduction in purchase price allocation charges in 2008. The 2008 cost of product sales includes additional expenses of € 3,473 (2007: € 10,191) relating to the purchase price allocations of the businesses acquired by the Group. The gross margin on product sales amounts to 38.6% (2007: 29.9%). The percentage increase in gross margin is mainly due to the strengthening of the US Dollar in the second half of 2008, product-mix changes, improvements in production performance and a reduction of the purchase price allocation charges in 2008.

Cost of service fees
Cost of service fees comprises direct labor, materials and overhead costs related to work under various collaboration agreements. We do not retain the residual interest on products developed under the agreements and will normally not have ownership of intellectual property rights on these products.

In 2008, the cost of service fees decreased by € 3,362 or 32.6 % compared to 2007. The decrease reflects the lower level of service fee revenues, which reduced our expenses. The gross margin on service fees was 36.1% in 2008 compared to 26.3% in 2007. In 2008, there has been a shift in strategy to focus more on programs that generate higher margins.

In 2007, the cost of service fees increased by € 3,356 or 48.1% compared to 2006, which is primarily attributable to the increase of the service fee revenues by 31.0%. The gross margin on service fees was 26.3 % in 2007 compared to 34.8% in 2006.

Other operating income

The following table shows our other operating income for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Government grants	**5,380**	7,086	6,901	(24.1)	2.7
Other operating income	**10,772**	2,244	2,455	380.0	(8.6)
Total other operating income	**16,152**	**9,330**	**9,356**	**73.1**	**(0.3)**

Government grants
In 2008, government grants decreased by € 1,706 or 24.1% compared to 2007. The grants decreased as several projects were completed in 2007. The most significant grants in 2008 were received from NIH and from SenterNovem, an agency of the Dutch Ministry of Economic Affairs, for numerous research projects.

In 2007, government grants were stable compared to 2006. The most significant grants in 2007 were received from NIAID for further research on HIV and from SenterNovem.

Other income
Other income mainly consists of the reimbursement of development costs and funding received from non-governmental agencies. Other income also includes non-core business transactions such as the sale of property, plant and equipment and income generated from training courses. Other income increased by € 8,528 or 380.0% mainly due to reimbursement of development costs on the rabies program, for which the partnership with sanofi pasteur started in 2008, and increased funding from non-governmental agencies in 2008.

The amount of other income in 2007 was stable compared to 2006.

Other operating expenses

The following table shows our other operating expenses for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Research and development	**70,229**	63,995	67,606	9.7	(5.3)
Selling, administrative and general	**64,350**	61,752	46,732	4.2	32.1
Restructuring	**—**	—	3,120	—	—
(Reversal of impairment)/ impairment	**(4,888)**	171	30,416	(2,958.5)	(99.4)
Total other operating expenses	**129,691**	**125,918**	**147,874**	**3.0**	**(14.8)**

Research and development expenses
Research and development expenses consist of personnel expenses, laboratory expenses, technology purchases, patent related fees, technology license fees, depreciation of property, plant and equipment and amortization of intangible assets related to research and development, and lease expenses for lab space and equipment lease. Research and development expenses also include fees we pay to third parties who conduct research on our behalf.

Research and development expenses increased in 2008 by € 6,234 or 9.7% compared to 2007. This increase is mainly attributable to increased expenditures on the rabies program for which two phase II clinical trials were performed.

Research and development expenses comprised 54.2% of total other operating expenses in 2008 (2007: 50.8%). We expect that research and development expenses will continue to be a significant portion of our overall expenses in the future.

In 2007, research and development expenses decreased by € 3,611 or 5.3% compared to 2006, which was primarily attributable to the cost-saving effect of the restructuring program that took place in 2006 to centralize research and development activity in Leiden and phasing out work on both a vaccine candidate as well as on programs at the Center of Mammalian Cell Culture.

Selling, general and administrative expenses
Selling, general and administrative expenses consist of personnel expenses and other operating expenses in marketing and sales, finance, human resources, investor relations, legal and general management.

These expenses increased in 2008 by € 2,598 or 4.2% to € 64,350 in 2008 compared to € 61,752 in 2007. This increase is primarily due to the overall growth of the Group as a whole. Specific items are the increased distribution and sales expenses as a result of increased revenues, annual salary increases and the recognition of specific provisions. The increase in selling, general and administrative programs is partly offset by cost reductions realized through our Healthy Ambition program.

Selling, general and administrative expenses increased in 2007 by € 15,020 or 32.1% to € 61,752 in 2007, compared to € 46,732 in 2006. Selling costs increased as a result of the cost base of the companies acquired in 2006, which are for the first time included for a whole year in 2007. General and administrative expenses also included integration costs of the 2006 acquisitions and additional costs relating to compliance with internal control over financial reporting requirements under US law.

Restructuring
A restructuring program in our Italian subsidiary Berna Biotech Italia Srl. was executed in 2008. A total provision of € 684 was recognized, of which € 610 is recorded in restructuring provisions as per year-end

2008. The majority of this provision was paid in the first quarter of 2009. The costs for the restructuring are included in the applicable operating expenses as they have an operating nature.

There were no restructuring expenses in 2007.

The restructuring expense in 2006 is related to centralizing R&D functions in Leiden and phasing out R&D projects in Switzerland, including the candidate vaccine Aerugen, and the Center of Mammalian Cell Culture. The decision to concentrate R&D in Leiden was made to increase efficiency in R&D spending. The provision was recognized in 2006 as recognition criteria were met at that time. The actual reduction in the number of staff employed was effected in the first quarter of 2007.

Impairment
In the first quarter of 2008, we reversed € 5,219 of previously impaired property, plant and equipment. In 2008, we entered into an exclusive agreement with Wyeth Pharmaceuticals in which we will develop and manufacture certain components of a vaccine for use by Wyeth in clinical studies. The contract manufacturing takes place in one of the two buildings that were impaired in 2006 as described below. We reassessed the recoverable amount of the asset and as the outcome exceeded the carrying value of nil, we partially reversed the previously recognized impairment loss on this building.

In the fourth quarter of 2008, we recognized an impairment charge of € 331 for the animal housing facility in Bern, Switzerland that was not in use anymore. As there was no alternative use for this building for any of the Group's other activities and the building cannot be sold directly to other parties as it is on our campus, the Group impaired the carrying value to zero.

In 2007, we recognized an impairment charge of € 171 for a warehouse in Korea that was demolished to make way for the construction of a light railway.

In 2006, we recognized a total impairment of € 30,416. The impairment related to two buildings in Switzerland including installed equipment, for an amount of € 19,568 and to acquired in-process research and development related to the Tetra vaccine for an amount of € 10,848.

Operating profit/ (loss)

The following table shows our operating profit/ (loss), for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Operating profit/ (loss)	7,863	(47,686)	(97,440)	(116.5)	(51.1)

The movements in operating loss are explained by the operating results discussed above.

Financial income and expense, net

The following table shows our financial income and expenses, net, for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Financial income and expenses	(2,662)	1,378	1,747	(293.2)	(21.1)
Results investments non-consolidated companies	(128)	(996)	(1,956)	(87.1)	(49.1)
Results on disposal non-consolidated companies	1,570	2,186	—	(28.2)	—
Disposal of subsidiaries	(367)	—	—	—	—
Total financial income/ (expense), net	(1,587)	2,568	(209)	(161.8)	(1,328.7)

Financial income and expenses
Financial income and expenses mainly consist of interest income and expenses, foreign exchange losses and other financial expenses.

In 2008, the negative result on net financial income and expenses totaled € 2,662 and consists of interest income of € 5,021, foreign exchange losses of € 3,926, interest expenses of € 2,719 and other financial expenses of € 1,038.

The net financial income and expenses decreased by € 4,040 or 293.2 % compared to 2007. The decrease is primarily attributable to foreign exchange losses of € 3,926. These losses mainly resulted from a weaker Euro in conjunction with Euro receivables in Switzerland, as the Swiss Franc is the functional currency of our subsidiary Berna Biotech AG. In addition, foreign exchange losses were realized on Euro liabilities and losses on US Dollar transactions in Korea.

See – 'Financial risk management – 3.2 Foreign currency risk' in the financial statements for more details on foreign currency risk management including the use of hedging instruments by the Group.

Other changes in the net financial income and expenses were:

- A reduction of interest income by € 690, mainly caused by a lower average cash balance in 2008 compared to 2007;
- Increased interest expenses of € 438 as a result of increased finance leases and short-term financial liabilities; and
- An increase other financial expenses of € 292 primarily due to factoring arrangements engaged in during 2008.

In 2007, net financial income and expenses decreased by € 369 or 21.1% compared to 2006. The decrease was primarily attributable to:

- Increased negative foreign exchange results of € 1,142 as the foreign currencies in which we traded lost value compared to the Euro;
- Increased interest expenses of € 544 as a result of additional charges relating to leasing and the full year effect of our 2006 acquisitions; and
- An increase in other financial expenses of € 402 primarily due to factoring arrangements engaged in during 2007. The decrease was partly offset by increased interest income of € 1,993 resulting primarily from higher interest rates in 2007.

Results investments non-consolidated companies
At December 31, 2008, we had one associate, ADImmune Corp and one joint venture, Percivia. In July 2008, we sold our investment in Kenta Biotech AG. The results of investments in non-consolidated companies include the results of Kenta Biotech AG up to the moment of the sale. The results of investments in non-consolidated companies are accounted for under the equity method and amount to a total loss in 2008 of € 128 (2007: € 996). The decrease of € 868 or 87.1% compared to 2007 year is mainly due to the reduced losses on Kenta Biotech AG.

In 2007, the losses from investments in non-consolidated companies were reduced by € 960 or 49.1%. The decrease was primarily attributable to the reduced losses in Pevion Biotech AG and Kenta Biotech AG.

Results on disposal non-consolidated companies
On July 3, 2008 the Group sold all of the 2,625,000 shares it owned In Kenta Biotech AG to Ingro Finanz AG. Prior to this sale, our ownership interest had already been diluted from 37% in 2006 to 22% by the end of 2007. We realized an accounting gain in 2008 of € 1,570 on the sale.

On November 5, 2007 the Group sold all of the 2.9 million shares it owned in Pevion Biotech AG for an amount of € 6,081 to other shareholders of Pevion Biotech AG. The Group realized an accounting gain in 2007 of € 2,186 on the sale.

Disposal of subsidiaries
In November 2008, we sold our fully-owned subsidiary Etna Biotech Srl to Zydus Cadila. The sale resulted in net proceeds of € 182 and an accounting loss on disposal of € 367.

Income tax

The table shows our income tax for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Income tax	8,310	2,208	10,451	276.4	(78.9)

In 2008, tax income increased by € 6,102 or 276.4%. The increase resulted from a change in deferred tax of € 11,503 (2007: € 3,024) that mainly consists of carry forward losses not previously recognized in our subsidiary Berna Biotech AG for € 8,585 and a reduced expected tax realization rate on our deferred tax liabilities of € 3,384 in Korea. The increase is partially offset by current tax charges of € 3,200 compared to € 811 in 2007 as a result of taxable income in Sweden, Korea, Spain and the US.

The Group has a negative effective tax rate of 132.4% in 2008 compared to positive effective tax rates of 4.9% in 2007 and 10.7% in 2006. Our effective tax rate was impacted by numerous items.

The effective tax reconciliation starts with our IFRS profit/ (loss) per subsidiary multiplied by the domestic rate of tax in the country in which our subsidiaries are domiciled. In 2008, our total profit under IFRS of € 6,276 had a negative correlation with our total taxes based on domestic rates of € 820. This effect was mainly caused by a loss under IFRS in our Dutch operation at a tax rate of 25.5% and a profit of our Korean subsidiary at a lower average tax rate of 21.0%.

In addition, the following transactions significantly affected our effective tax rate reconciliation:

- We reached an agreement with the Dutch tax authorities to retroactively change the valuation of our intellectual property, to avoid the evaporation of unrecognized tax carry forward losses. This agreement allows us to recognize € 72,000 of our intellectual property as assets for tax purposes. Under IFRS no deferred tax assets were recognized on these temporary differences, which on a combined basis with the utilization of previously unrecognized carry forward losses in our Dutch fiscal unity in 2008, causes a net negative tax effect of € 6,103;
- We reassessed the valuation of our carry forward losses and recognized previously unrecognized carry forward losses in our subsidiary Berna Biotech AG, which resulted in a taxation gain of € 8,585;
- As of the year 2012, we will benefit from a tax holiday to our investment in the Incheon, Free Economic Zone, Korea, which will significantly reduce the effective Korean income tax rate for a period of 5 years. The reduced expected realization rate for our deferred tax liabilities in Korea resulted in a taxation gain of € 3,384;
- In 2008, we benefited in Korea from a research and development tax credit for an amount of € 2,916; and
- Non-deductible stock-option expenses are recognized in the Netherlands for an amount of € 1,251 in 2008.

See – '1 General information – 1.4 Use of estimates and judgments' in the financial statements section for a description of estimates and management judgments in determining the tax position and '5.4 Income tax' in the financial statements for a numerical reconciliation of our effective tax rates.

Changes in the underlying timing differences in 2007 resulted in a taxation income of € 3,024 in 2007 compared to € 10,922 in 2006.

Liquidity

We have a strong cash position, which we believe makes it possible to continue financing important development programs. Our cash and cash equivalents amounted to € 170,969 and € 163,248 as of December 31, 2008 and 2007, respectively. We believe that our liquidity is sufficient for our present requirements.

In 2009, we entered into a mortgage loan facility in Korea for an amount of KRW 50 billion to partly finance the investments in the new Korean facility.

Cash flows

The following table shows our cash flow statement for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Profit/ (loss) of the period	**14,586**	(42,910)	(87,198)	(134.0)	(50.8)
Adjustments for non-cash items	**18,801**	44,593	58,505	(57.8)	(23.8)
Changes in net working capital	**(30,381)**	24,208	(23,174)	(225.5)	(204.5)
Interest and taxes paid	**(3,260)**	(3,697)	(2,087)	(11.8)	77.1
Net cash flows from/ (used in) operating activities	**(254)**	**22,194**	**(53,954)**	**(101.1)**	**(141.1)**
Net cash flows from/ (used in) investing activities	**(8,907)**	**(24,241)**	**23,159**	**(63.3)**	**(204.7)**
Net cash flows from financing activities	**16,626**	**11,244**	**78,731**	**47.9**	**(85.7)**
Effect of exchange rates on cash and cash equivalents	**256**	(3,786)	(1,833)	(106.8)	106.5
Net increase/ (decrease) in cash and cash equivalents	**7,721**	**5,411**	**46,103**	**42.7**	**(88.3)**
Cash and cash equivalents at beginning of period	**163,248**	157,837	111,734	3.4	41.3
Cash and cash equivalents at end of period	**170,969**	163,248	157,837	4.7	3.4

Net cash flows from/ (used in) operating activities

In 2008, our net cash flow from operating activities decreased by € 22,448 or 101.1% compared to 2007. The decrease resulted from an increase of our working capital by € 54,589 and a reduction in the adjustments for non-cash items by € 25,792. The decrease is partly offset by € 57,496 due to improved results in 2008 compared to 2007.

In 2008, the decrease in changes in the net-working capital compared to 2007 amounted to € 54,589. The year 2008 had relatively stable cash flows on the monetary working capital items compared to positive cash flows in 2007. The decrease in 2008 compared to 2007 mainly resulted from inventories for € 30,993 due to build-up of Quinvaxem inventory for 2009 sales, and other current liabilities for € 22,327.

In 2008, adjustments for non-cash items were reduced by € 25,792. This reduction was mainly caused by:

- One-off cash receipts in 2007 in the amount of € 11,500 in 2007 relating to the non-current deferred revenue on the ADImmune technology license and the rabies program;
- Non-cash revenues realized in 2008 for an amount of € 4,728 that related to the above transactions; and
- Partial reversal of the impairment loss on one of our buildings in Switzerland in 2008 for an amount of € 5,219 as we now perform contract manufacturing at this location.

In 2007, our net cash flow from operating activities increased by € 76,148 or 141.1 % compared to 2006. The increase resulted from a reduction of our working capital by € 47,382 and a reduction of our net loss by € 44,288. The increase is partly offset by a decrease in the adjustments for non-cash items of € 13,912 and an increase in interest and taxes paid by € 1,610 in 2007.

Net cash flows from/ (used in) investing activities
Our cash flow used in investing activities amounted to € 8,907 in 2008, compared to € 24,241 in 2007.

In 2008, the most significant cash flows used in investing activities resulted from investments made in property, plant and equipment for an amount of € 15,787. These investments mainly related to our new Korean production facility, investments in our facilities in Bern, Switzerland that will improve current production processes and allow in-house production of materials currently acquired from third parties, as well as investments in our new filling line in Madrid, Spain.

In 2008, the most significant cash flows from investing activities were from the following transactions:

- Interest received of € 4,395 in 2008 (2007: € 5,274);
- The sale of all shares owned by the Group in Kenta Biotech AG for € 1,570 to Ingro Finanz AG; and
- Restricted deposits that were transferred to cash and cash equivalents for € 1,500.

In 2007, the most significant cash flows used in investing activities were from the following transactions:

- Investments were made in property, plant and equipment for an amount of € 27,156, which mainly related to our new GMP production facility in Leiden, the Netherlands and investments in our facilities in Bern, Switzerland to improve production processes and allow in-house production of materials currently acquired from third parties; and
- The Group acquired a 20% equity-stake in ADImmune Corp. in March 2007 for € 8,553.

In 2007, the most significant cash flows from investing activities were from the following transactions:

- The sale of all shares owned by the Group in Pevion Biotech AG, Switzerland for € 6,081 to other shareholders of Pevion Biotech; and
- Interest received of € 5,274 in 2007.

Net cash flows from/ (used in) financing activities
Our cash flow from financing activities amounted to € 16,626 in 2008, € 11,244 in 2007 and € 78,731 in 2006.

In 2008, the cash flow from financing activities increased by € 5,382 or 47.9% compared to 2007 and, mainly related to:

- Additional short-term financing facilities in Korea for an amount of € 22,222; and
- Finance leases with proceeds of € 12,368 relating to our GMP-facility in Leiden, the Netherlands and our Spanish filling-line.

The most significant cash flows used in financing activities mainly related to:

- Redemption of a Korean Won-denominated privately placed bond in Korea for € 11,869 and a partial redemption of a short-term Euro loan also in Korea for € 1,455;
- Settlement of financial liabilities relating to factored Italian trade accounts receivable by € 5,653 for which the Group did not substantially transfer all the risks and rewards in 2007; and
- Repayment of finance lease liabilities for an amount of € 1,922.

In 2007, the cash flow from financing activities decreased by € 67,487 or 85.7% compared to 2006 as we limited the use of additional financing and funded our operations and investments with our own resources. The cash flow from financing activities in 2007 mainly related to:

- Factoring of trade accounts receivable in Italy for an amount of € 5,653; and
- Finance leases with proceeds of € 4,247. These finance leases mainly related to equipment for the new production and development facility in Leiden.

Critical accounting policies and estimates

The methods, estimates and judgments we use in applying our most critical accounting policies have a significant impact on the results we report in our financial statements. Please see '1 General information – 1.4 Use of estimates and judgments' in the financial statements for further details on our most critical policies and the methods, estimates and judgments used.

In addition to the critical accounting policies and estimates, the Group chooses to disclose the impact of discounts, rebates and returns.

Discounts, rebates and returns

At the time sales revenue is recognized, we also record estimates for revenue deductions, including discounts, rebates and product returns. We report net sales after deducting all sales deductions from gross sales revenue. The following table identifies the items that reduced our gross product revenue as at the end of the periods ended December 31, 2008, 2007 and 2006.

In thousands of Euro

	2008	2007	2006
Product sales, gross	**227,791**	179,395	105,059
Discounts and rebates	**945**	626	291
Returns	**791**	1,200	850
Total discounts, rebates and returns	**1,736**	1,826	1,141
Product sales, net	**226,055**	**177,569**	**103,918**

Discounts and rebates

Discounts include prompt payment discounts and charge backs. In 2008, our discounts and rebates amounted to € 945.

We generally offer our US wholesalers a prompt-pay cash discount as an incentive to remit payment in full within one month after the date of an invoice. Prompt-pay discount calculations are based on the gross amount of each invoice. We account for these discounts by reducing product sales by the estimated discount amount when the product is sold.

Wholesaler charge backs, customary in our industry, are arrangements that relate to contractual agreements to sell products to Group Purchasing Organizations (GPOs) in the US at fixed prices that are lower than the list prices we charge wholesalers. When the GPOs purchase our products through wholesalers at these reduced prices, the wholesaler charges us for the difference between the price the wholesaler paid to us and the price at which they sold the products to the GPO. Accruals for wholesaler charge backs closely approximate actual results because charge back amounts are fixed at the date of purchase by the GPOs. As the charge backs are settled within a short time of incurring the liability, the outstanding accruals are relatively low.

We offer rebates primarily in connection with attainment of sales targets by wholesalers and large retailers in contractually agreed percentages. The rebates are accrued as the underlying sales transactions are recognized and are based on reasonable estimates on the attainment of the sales targets.

Returns

Returns that reduce our gross product revenue may arise from the following:

- Customers return of products defective upon delivery;
- Specific right of return in accordance with contractual terms; and
- Returns via the normal distribution channels if the product is in good condition, pursuant to local law in certain jurisdictions.

In 2008, returns amounted to € 791 (2007: € 1,200) or approximately 0.4% (2007: 0.7%) of our net product sales.

The following table shows the percentage of products returned as a percentage of the gross product sales per country during 2008 based on the country from which the products were originally sold.

Country	Returns 2008	Returns 2007	Returns 2006
Spain	3.0%	2.5%	1.7%
Italy	1.1%	1.4%	0.1%
Switzerland	0.1%	0.1%	0.7%
US 2.1%	1.9%	0.9%	
Sweden	0.9%	0.1%	0.2%
Korea	—	—	—
Netherlands	—	—	—

Roll-forward information
The table below shows the roll-forward information of our discounts, rebates, and product returns:

In thousands of Euro

	Accrual for discounts and rebates	Accrual for returns	Total
January 1, 2008	(190)	(1,117)	(1,307)
Additions – current period	(945)	(791)	(1,736)
Actual returns/ credits – current period	762	240	1,002
Actual returns/ credits – prior period	160	975	1,135
Release of accruals – current period	—	—	—
Release of accruals – prior period	—	—	—
Effect of movements in exchange rates	24	18	42
December 31, 2008	(189)	(675)	(864)

Discounts and rebates
We base our estimates for discounts and rebates primarily on historical experience and contractual agreements, supplemented by management's judgment. In 2008, our estimates for rebates based on historical experience did not differ materially from actual results. With respect to discounts, we have limited uncertainties in determining our estimates, because these deductions generally occur within a short time frame of incurring the liability.

For calculating our rebates estimates we make use of quantifiable contractual rebates data. In general, our rebates are based on fixed rebate percentages on product sales to customers that have been granted rebates.

Returns
We base our estimates of product returns on the percentage of returns that we have experienced historically. We may adjust these return estimates if we are aware of other factors that we believe could meaningfully impact our expected return percentages. For example, in respect of our influenza vaccine, we specifically take into account the development of the flu season, in particular, the number and impact of outbreaks. While we do not have a formula that estimates the impact of the number and impact of outbreaks on the level of the accrual for returned vaccines, an increased number of outbreaks will generally result in a lower accrual for returned influenza vaccines, because it becomes more unlikely that vaccines will be returned. Alternatively, a lower number of outbreaks can result in a higher accrual, because it becomes more likely that influenza vaccines will be returned unused at the end of a mild flu season.

In addition, in our estimates of returns, we take into account other information, such as media coverage of vaccination programs, estimates of inventory levels of our product in the distribution channel, vaccine shelf life and known sales and market trends. These are reflected in the accruals by means of management's judgment.

Increased media coverage of vaccination programs, either by advertising campaigns or coverage of flu outbreaks, results in an increased public awareness. Consequently, this may lead to an increased number of flu vaccinations and fewer unsold doses with our customers, which limits the level of accruals for product returns.

Relatively high levels of inventory of our product in the distribution channel and short shelf life of product sold can be indicators for an increased level of returns.

Sales and market trends are taken into account by reference to the life cycle phase of products. If product sales show a decreasing revenue pattern over time, this can be an indicator for an increased level of returns. We do not rely on quantitative externally sourced information in our calculation of returns estimates. We are not aware of any available external quantitative information or other quantifiable data that would provide us the benefit of a more reliable estimate.

The rate of product returns is quantifiable. We monitor returns primarily on a per country basis based on the country from which the product was sold because our accruals are determined at this level. Within the individual countries, we monitor the returns on a product-by-product basis. In 2008, our estimates for returns did not differ materially from actual results.

Tabular disclosure of contractual obligations

Future minimum payments for all contractual obligations for years subsequent to December 31, 2008 are as follows:

In thousands of Euro

	Total	Less than one year	1-3 years	3-5 years	More than 5 years
Contractual obligations					
Debt obligations (excluding finance lease obligations)	40,225	22,677	2,239	861	14,448
Finance lease obligations [1]	20,526	2,777	6,381	7,911	3,457
Interest payments on debt obligations	12,580	2,105	3,512	2,314	4,649
Derivative financial instruments [2]	45,560	45,560	—	—	—
Accounts payable	59,205	59,205	—	—	—
Other liabilities	21,114	20,523	591	—	—
Recognized obligations	**199,210**	**152,847**	**12,723**	**11,086**	**22,554**
Commitments					
Operating lease obligations [3]	24,662	3,830	6,575	3,498	10,759
Capital expenditure commitments [4]	20,380	16,163	4,217	—	—
Total commitments	**45,042**	**19,993**	**10,792**	**3,498**	**10,759**
Total recognized obligations and commitments	244,252	172,840	23,515	14,584	33,313

[1] Finance lease obligations
Certain of the Group's fixtures and equipment are finance leases. The finance leases relate to equipment for the new production facility in Leiden, the Netherlands and to the filling line in Spain. Interest rates are fixed at the contract date. All leases are on a fixed repayment basis and no arrangements have been entered into for contingent rental payments.
[2] Derivative financial instruments are foreign exchange contracts. The contractual obligations are € 45,060. The corresponding receivables are € 46,442.
[3] Operating lease obligations
The operating lease obligations include rental obligations. Crucell concluded long-term rental agreements for premises in Sweden and the Netherlands. In addition, Crucell leases certain motor vehicles and items of machinery and equipment.
[4] Capital expenditure commitments
The contractual commitments for purchases of property, plant and equipment as per December 31, 2008 amount to approximately € 20,380 (2007: € 4,696, 2006: € 11,693). These commitments mainly relate to our new production facility in Incheon, Free Economic Zone, Korea.
See note '5.19 Short and long-term financial liabilities' in the notes to the financial statements for details on the maturity profile and the interest rate environment of our financial liabilities.

Off-balance sheet arrangements

As of December 31, 2008, we have no unconsolidated special purpose financing or partnership entities or other off-balance sheet arrangements that have or are reasonably likely to have a current or future effect on our financial condition or lead to changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources, that is material to investors.

The Group has investments in one associate and in one joint venture that are both non-consolidated companies. Details are provided in '5.9 Investments in associates and joint venture' in the financial statements.

Further details on our off-balance sheet arrangements such as our guarantees and covenants are disclosed in note 3 'Financial risk management' in our financial statements.

Quantitative and qualitative disclosure about market risk

Market risk is the risk of loss related to adverse changes in market prices, including currency risk, interest rate risk and risk of financial instruments. During the ordinary course of business, the Group is exposed to various financial market risks, primarily from foreign exchange, interest rates and credit risk. Details on our market risks are disclosed in '3 Financial risk management' in the financial statements.

Impact of inflation

Crucell does not operate subsidiaries in countries with hyperinflation. Sales to customers in hyperinflationary countries are made in hard currency, mainly Euro, US Dollar, Swiss Franc and Swedish Crown.

Corporate Governance

Corporate governance at Crucell

Corporate governance concerns the relationship between management and the shareholders, and more generally the stakeholders, of the Company. It is the formal codification of the manner in which the Company is governed, of the accountability of its management and its supervision, of the manner in which stakeholders, and more particularly shareholders, are able to gain an insight into the state of affairs within the Company, and finally, of the way in which they can influence the decision-making process. With regard to this final issue, voting rights and the manner in which votes can be exercised, play an important role.

As a Dutch corporation, Crucell is subject to the Dutch Corporate Governance Code (the 'Code'). As a foreign private issuer whose ADSs trade on NASDAQ Global Select Market (NASDAQ), we are also subject to US securities laws (including the provisions of the Sarbanes-Oxley Act of 2002) and the NASDAQ rules.

As a foreign private issuer Crucell may follow its home country practice in lieu of the requirements of certain rules of NASDAQ. Our Annual Report discloses those requirements that are not followed and describes the home country practice that is followed instead, see 'Exemptions from certain NASDAQ Corporate Governance Rules' in this section.

Also under the rules of the SWX Swiss Exchange, where Crucell has a secondary listing, it is allowed to apply the Code.

Corporate governance developments

We monitor and assess applicable corporate governance rules, including recommendations and initiatives regarding principles of corporate governance. These include those that have been developed in the US, both by NASDAQ and by the SEC pursuant to the Sarbanes-Oxley Act of 2002, as well as in the Netherlands, through the Code, which came into effect as of the financial year starting on or after January 1, 2004.

Dutch Corporate Governance Code

The Code has been instituted by government decree. According to Dutch law, a public company should include in its annual report a statement about the compliance with the principles and best practice provisions of the Code that regard the Management Board and Supervisory Board. If a corporation does not, or does not intend to comply with one or more of the principles and best practice provisions, it must explain its motivation in the annual report. According to the Code, substantial amendments to the Company's existing corporate governance structure and compliance with the Code should be submitted for discussion to the General Meeting of Shareholders.

Important principles of the Code are:

- Strengthening the role of the Supervisory Board and its committees and increasing its independence, quality and expertise;
- Strengthening the role of the shareholders with respect to control of the functioning of the Management Board and the Supervisory Board, as well as with respect to nomination and remuneration of members of the Management Board and the Supervisory Board;
- Facilitating and stimulating shareholders to use their voting power and to actively participate in the General Meeting of Shareholders;
- Defining the role of the external auditor vis-à-vis the Supervisory Board as its principal contact; and
- Maintaining an appropriate internal risk and control system.

For an overview of Crucell's conformity with the Code, please refer to our website (www.crucell.com), where the following documents can be consulted:

- Corporate governance at Crucell;
- By-laws of the Management Board;
- Remuneration policy Management Board;
- By-laws of the Supervisory Board; and
- Code of Conduct (Crucell's company code) including whistle-blower policy.

In 2003, we adopted a code of business conduct and ethics (Code of Conduct) that applies to all employees of the Company, including our principal executive officer and principal financial officer. The Code of Conduct underlines that one of the most valuable assets of Crucell is its integrity. The Code of Conduct was amended in 2008 and has been filed as an exhibit to our Form 20-F for the fiscal year ended December 31, 2008. The amended Code of Conduct adheres to the same underlying principles as the original Code of Conduct, but reflects that we are a fully integrated company that operates in numerous countries. No waivers of the Code of Conduct were granted during 2008.

We have a whistle blower policy in place, which encourages employees to report abuses and non-compliance with our Code of Conduct, anonymously if necessary.

Compliance with the Code
In June 2005, the General Meeting of Shareholders approved our current corporate governance structure. Except for the three provisions of the Code referenced below Crucell has fully implemented the recommendations set forth in the Code and incorporated them into its corporate governance policies.

Exceptions to compliance with the Code
The Code contains a 'comply-or-explain' principle, offering the possibility to deviate from the Code as long as any such deviations are explained. Crucell complies with all of the principles and best practice provisions of the Code, except for the following:

Remuneration of Management Board members

Under the Code, the maximum severance pay for a Management Board member should be no more than one year's salary, unless this is manifestly unreasonable. We do not apply this principle in the event of a dismissal arising from an unwanted change of control for Management Board members. The employment contracts of those members of the Management Board that were already in place as at 1 January 2004 (the date on which the Code took effect) remain unchanged. In other cases agreed severance payments can be higher if otherwise this would obstruct the recruitment of the right person for a Management Board position.

Loans to the Company's management

We do not apply the provision in the Code that no personal loans shall be granted to a company's Management Board member because, prior to the Code's development and passage of similar legislation in the US, loans were made to Management Board members and one such loan currently remains outstanding. Reference is made to note 5.23 'Related parties' in the financial statements. We have not granted additional loans to Management Board members since 2002.

Remuneration of Supervisory Board members

We do not apply the provision that remuneration of the members of the Supervisory Board should not include share grants. Crucell deems this form of remuneration adequate because this is customary among biotechnology companies operating internationally, and it helps attract well-qualified supervisory directors with specific expertise in biotechnology and international business fields.

Exemptions from certain NASDAQ corporate governance rules

NASDAQ rules provide that NASDAQ may provide exemptions from the NASDAQ corporate governance standards to a foreign issuer when those standards are contrary to a law, rule or regulation of any public authority exercising jurisdiction over such issuer or contrary to generally accepted business practices in the issuer's country of domicile. We are exempt from certain NASDAQ corporate governance standards that are contrary to the laws, rules, regulations or generally accepted business practices of the Netherlands. These exemptions and the practices followed by our Company are described below:

- We are exempt from NASDAQ's quorum requirements applicable to meetings of shareholders. In keeping with Dutch law and generally accepted business practice, our articles of association provide that there are no quorum requirements for the general meeting of shareholders.
- We are exempt from NASDAQ's requirements regarding the solicitation of proxies and provision of proxy statements for meetings of shareholders. We inform shareholders of meetings in a public notice, but we do not solicit proxies for the General Meeting of Shareholders. Dutch law does not have a regulatory regime for the solicitation of proxies and the solicitation of proxies is not a generally accepted business practice in the Netherlands. In connection with our American Depositary Shares (ADSs), the Bank of New York Mellon, as depositary, distributes proxy materials to holders of our ADSs.
- NASDAQ requires shareholder approval or prior to the issuance of securities when a stock option or purchase plan is to be established or materially amended or other equity compensation arrangement made or materially amended, pursuant to which stock may be acquired by officers, directors, employees, or consultants. Under Dutch Company law and the Code shareholder approval is only required for equity compensation plans (or changes thereto) for members of the Management Board and

Supervisory Board, and not for equity compensation plans for other groups of employees. Our articles of association provide that a resolution of the General Meeting of Shareholders to amend our articles of association, to dissolve the Company, or to merge or demerge the Company shall only be adopted on a proposal of the Supervisory Board.

- We do not distribute Annual Reports to all of our shareholders in accordance with NASDAQ rules. As our shares are bearer shares, according to Dutch law we are not required to distribute copies of annual and interim reports to all shareholders. Copies of such reports are available to shareholders at our corporate headquarters, and are filed with NASDAQ and the Bank of New York Mellon as depositary under our depositary agreement relating to our ADSs. Upon request the Bank of New York Mellon distributes our Annual Reports to holders of our ADSs.
- The Company has a two-tiered board structure, in contrast to the one-tier board structure used by most US companies. In the Netherlands, a public limited liability company has a Management Board as its management body and a Supervisory Board which advises and supervises the Management Board. In general, Management Board members are employees of the company while members of the Supervisory Board are often former state or business leaders and sometimes former members of the Management Board. Members of the Management Board and other officers and employees cannot simultaneously act as members of the Supervisory Board. The Supervisory Board must approve certain specified decisions of the Management Board. Under the Code all members of the Supervisory Board with the exception of not more than one person, shall be 'independent'. The definition of 'independence' under the Code however, differs from the definition of 'independence' under the NASDAQ listing standards (e.g. employment by the Company in the three years prior to the appointment as member of the Supervisory Board versus five years under NASDAQ and the Code respectively).
- Dutch law requires that the external auditors be appointed at the General Meeting of Shareholders and not by the Audit Committee.
- Our Audit Committee currently consists of two Supervisory Board members whereas the NASDAQ listing rules require three. The Company is currently recruiting a third Supervisory Board member with financial expertise to fill the vacancy in the Audit Committee.

Directors, senior management and board practices

Crucell has a 'two-tier' governance structure, in which executive and supervisory responsibilities are clearly segregated. Our Management Board is responsible for managing the Company's daily affairs and business and, as such, is responsible for achieving Crucell's goals, strategy, policy, and results.

Supervisory Board

The Supervisory Board, which consists solely of independent directors, supervises the Management Board. In the execution of their duties, the members of the Supervisory Board must be guided by the best interests of Crucell and its stakeholders.

The Supervisory Board reports to the General Meeting of Shareholders with regard to the corporate governance of Crucell, its structure and the compliance with applicable internal and external rules and regulations.

The principal duty of the Supervisory Board is to supervise the policies of the Management Board and to provide advice. The Supervisory Board oversees the corporate strategy, the risks inherent in the Company's activities and supervises the structure and operation of the internal risk management and control systems, the financial reporting process and the Company's compliance with relevant legislation and regulations.

Our Supervisory Board must approve certain categories of resolutions of our Management Board, which categories are specified in our articles of association. In addition, our Supervisory Board may give our Management Board written notice of other corporate actions that it wishes to approve. The division of duties and the procedures within the Supervisory Board are set forth in the by-laws of the Supervisory Board and can be found on Crucell's website (www.crucell.com).

Our articles of association provide that at least three Supervisory Board members must serve on our Supervisory Board. We must fill any vacancies on the Supervisory Board as soon as possible, but until they are filled, the remaining members of our Supervisory Board constitute a competent board. Under Dutch law, Supervisory Board members cannot serve as members of our Management Board.

The members of our Supervisory Board are appointed for terms ending on the date of the first General Meeting of Shareholders that is held four years

after the date of their appointment. They may be reappointed for two additional consecutive terms of four years each. Our Supervisory Board nominates its own members. To be binding, there must be at least two nominees for each vacancy on the Supervisory Board. The nominee earning the highest number of votes of Supervisory Board members becomes a binding nomination. The General Meeting of Shareholders can override these binding nominations by a vote of an absolute majority of the votes cast. This vote must represent more than one third of our total issued and outstanding share capital. If the Supervisory Board does not make any nominations within three months after a vacancy has occurred, our General Meeting of Shareholders can fill Supervisory Board vacancies. If the Supervisory Board makes a non-binding nomination (i.e., only one nominee is presented to the Supervisory Board for any particular vacancy), then such nomination can only be overturned by a resolution of the General Meeting of Shareholders taken by an absolute majority of the votes cast, representing at least one third of the Company's total issued and outstanding share capital. The Supervisory Board members retire according to a rotation plan established by the Supervisory Board itself.

Our Supervisory Board appoints its own chairman and must adopt rules for its own internal governance, including the creation of committees. The Supervisory Board must, in any event, establish an Audit Committee, a Remuneration Committee and a Nomination Committee. Passing Supervisory Board decisions requires a majority of the votes cast at a meeting of our Supervisory Board, unless otherwise provided for in the articles of association or the by-laws of the Supervisory Board. The company secretary assists the Supervisory Board.

A Supervisory Board member can be suspended or dismissed at any time by a resolution of a General Meeting of Shareholders passed by an absolute majority of the votes cast. This vote must represent more than one third of our total issued and outstanding share capital if the resolution to suspend or dismiss a Supervisory Board member is not proposed by the Supervisory Board itself. Within three months after a suspension, a General Meeting of Shareholders must either dismiss the Supervisory Board member, terminate or extend the suspension. The total suspension may not exceed three months.

The General Meeting of Shareholders determines the Supervisory Board members' compensation. In contrast to the provisions of the Code, until the end of our 2004 fiscal year we paid our Supervisory Board members in options on our ordinary shares as well as in cash. Starting in 2005, we began paying them in ordinary shares and cash, or cash only, at the member's discretion. We also reimburse Supervisory Board members for their expenses incurred in work relating to Crucell. The remuneration policy is intended to be able to attract and retain qualified and expert Supervisory Board members. It is in line with what is customary in the US biotechnology industry and is in line, as much as possible, with the best practice provisions of the Code.

According to the best practice provisions of the Code, an individual may hold a maximum of five Supervisory Board memberships in Dutch listed companies, with the chairmanship of a Supervisory Board counting as two memberships. All members of our Supervisory Board comply with this provision.

All members of the Supervisory Board comply with the criteria for independence as set out in the NASDAQ rules, the Code and the requirements of applicable EU and Swiss rules.

The business address of each Supervisory Board member is the address of our principal executive office in Leiden, the Netherlands. As of April 17, 2009 our Supervisory Board members held an aggregate of 0.17% of our ordinary shares.

As of December 31, 2008 the Supervisory Board of Crucell consisted of:

Name	Age	Position	End of current term
Jan Oosterveld	64	Chairman	2010
Phillip Satow	67	Member	2009
Claes Wilhelmsson	69	Member	2011
Seán Lance	61	Vice-Chairman	2011
Arnold Hoevenaars	59	Member	2009
Steve Davis [1]	51	Member	2012

[1] Mr. Davis was appointed as member of the Supervisory Board at the Company's General Meeting of Shareholders on May 30, 2008.

Mr. Jan Oosterveld has served as chairman of our Supervisory Board since June 2006 and as a member of the Supervisory Board since his appointment at the General Meeting of Shareholders on June 3, 2004. He retired from Royal Philips Electronics N.V. on April 1, 2004, after an international career of 32 years. At his retirement he was responsible for Corporate Strategy, Corporate Alliances and the joint

ventures with LGE, Korea, relating to Cathode Ray Tubes (CRTs) and Liquid Crystal Displays (LCDs). In the latter responsibility, he was the Chairman of the board of LG Philips Ltd, which went public in April 2004, and Vice-Chairman of the board of LG Philips Displays B.V. He was also the CEO of Philips Asia Pacific. He graduated with a degree in mechanical engineering from the Technical University Eindhoven and holds an MBA from the Instituto de Estudios Superiores de la Empresa (IESE) in Barcelona. He was appointed Professor at IESE in 2003. He is also a Member of the Board of Barco, Kortrijk, Belgium, Cookson Group, London, U.K., Candover, London, U.K. and Continental, Hannover, Germany. Mr. Oosterveld is a Dutch citizen.

Mr. Phillip Satow has served as a member of our Supervisory Board since our incorporation. He worked 14 years with Pfizer, Inc. where his last position was Vice President, Pfizer Europe. From 1985 to 1997, he was Executive Vice President Marketing at Forest Laboratories, Inc. From 1998 to 1999 he was President of Forest Pharmaceuticals, and Executive Vice President of Forest Laboratories Inc. In addition to the Forest Laboratories Board which he served on from 1999 to 2005, Mr. Satow is a former Board member of Eyetech Pharmaceuticals Inc. Mr. Satow co-founded, and served as Chairman and CEO of JDS Pharmaceuticals LLC, a privately held company that was sold to Noven Pharmaceuticals Inc. in 2007. Mr. Satow is currently a Member of the Board of Directors of Noven Inc. Mr. Satow is a US citizen.

Mr. Claes Wilhelmsson has served as a member of our Supervisory Board since May 2003. He was previously the Executive Director of Research and Development of AstraZeneca plc from 1999 to July 2002, responsible for AstraZeneca's global R&D. He joined Astra in 1985 and held various positions until the company merged with Zeneca in 1999. Prior to working for Astra, he was a lecturer and researcher at the University of Göteborg in Sweden, where he also completed his medical education and PhD. He currently serves on the boards of a number of biotechnology and start-up companies. Dr. Wilhelmsson previously served on the board of AstraZeneca plc. Mr. Wilhelmsson is a Swedish citizen.

Mr. Seán Lance has served as a member of our Supervisory Board since January 2004. Mr. Lance is a former Chairman of Chiron Corporation. He joined Chiron as President and Chief Executive Officer in 1998. From 1985 to 1998 he was employed at Glaxo Holdings where his last position was group Chief Operating Officer and CEO designate. He is a former President of the International Federation of Pharmaceutical Manufacturers Association. Mr. Lance is a chartered company secretary and administrator and also holds a post-graduate degree in Advanced Financial Management. Mr. Lance is a South African citizen.

Mr. Arnold Hoevenaars has served as a member of our Supervisory Board since June 2005. Mr. Hoevenaars is a chartered accountant in the Netherlands and his previous positions include, among others, Chairman of the Management Board of the Achmea Group; Chairman of the Board of Directors and Chairman/CEO of the Executive Board of Eureko B.V.; and Member of the Management Board and CFO of Royal Boskalis Westminster N.V. Mr. Hoevenaars is a Dutch citizen.

Mr. Steve Davis has served as a member of our Supervisory Board since June 2008. Mr. Davis is a Senior Advisor to McKinsey & Company's Social Sector Office based in Seattle, Washington, US. He is also a Lecturer in Intellectual Property at the University of Washington Law School. He recently served as the Interim CEO of IDRI (Infectious Disease Research Institute) and is now Chairman of its Board of Directors. Previously, Mr. Davis was CEO of Corbis Corporation and presently acts as a senior advisor to the company. He has held positions with the United Nations High Commission for Refugees and several refugee resettlement programs. Currently, he is a member of the Board of Trustees for PATH, a non-profit organization focused on improving public health in the developing world, and the Fred Hutchinson Cancer Research Center, one of the world's leading cancer centers. He also holds board positions with Intrepid Learning Solutions, The Seattle Foundation and Global Partnerships. Mr. Davis holds a Bachelor of Arts from Princeton University, a Master of Arts from the University of Washington and a Doctorate in Law from Columbia University School of Law. Mr. Davis is a US citizen.

Committees

The Supervisory Board appoints from its members an Audit Committee, a Remuneration Committee, a Nomination Committee and a Scientific Advisory Committee. The function of these committees is to advise and assist the Supervisory Board to make decisions.

Audit Committee

Arnold Hoevenaars (chairman) and Seán Lance.

The Audit Committee currently consists of two Supervisory Board members who are independent

within the meaning of the NASDAQ listing rules and the Code. The Company is in the process of recruiting a Supervisory Board member with financial expertise to fill the vacancy in the Audit Committee. The Audit Committee is responsible for, among other things, reviewing our annual and interim reports and accounts and for securing and monitoring our external auditors' involvement in that process. The Audit Committee is the first point of contact of the external auditor when irregularities are found in the contents of the financial reports. Ultimate responsibility for reviewing our Annual Report and interim financial reporting lies with our Supervisory Board. At the request of the Audit Committee, the chairman of the Supervisory Board may be invited to attend its meetings.

Our Audit Committee is in compliance with all of the relevant rules and regulations of the Netherlands. We believe that the members of our Audit Committee have sufficient financial and other experience to perform their responsibilities on the Committee. Mr. A. Hoevenaars is a 'financial expert' as defined in the rules promulgated under the Sarbanes-Oxley Act of 2002.

Remuneration Committee
Phillip Satow (chairman), Claes Wilhelmsson and Jan Oosterveld

The Remuneration Committee advises on policies and reviews and determines objectives relevant to the compensation of the members of the Management Board and members of the Management Committee. The Remuneration Committee evaluates the performance of members of the Management Board and Management Committee in view of these objectives and advises on the compensation of the members. In advising on short and long-term incentive compensation, the Remuneration Committee considers, among other factors, our financial and commercial performance, scientific performance and progress and any increases in the value of the Company. External compensation survey data available for the biotechnology industry is also used as a benchmark for determining compensation levels. It is the aim of the Remuneration Committee to position the remuneration packages for members of the Management Board and Management Committee at competitive levels. Bonuses are paid to members of the Management Board in connection with achievement of certain objectives set by the Supervisory Board.

Crucell maintains stock option plans whereby the Remuneration Committee may grant options to employees and members of the Management Board and Supervisory Board as well as non-employees in exchange for consulting services, subject to approval by the shareholders.

In addition, the Remuneration Committee reviews the general compensation and benefit policies for all of our employees.

Nomination Committee
The Nomination Committee consists of all of the Supervisory Board members. This committee (a) draws up selection criteria and appointment procedures for members of the Supervisory Board and the Management Board, (b) periodically assesses the size and composition of the Supervisory Board and the Management Board and makes proposals of nominees to the Supervisory Board, (c) periodically assesses the functioning of individual members of the Supervisory Board and the Management Board, and reports on this to the Supervisory Board and (d) supervises the policy of the Management Board on the selection criteria and appointment procedures for senior management. The committee also makes proposals for appointments of Management Board members to the Supervisory Board.

Scientific Advisory Committee
Claes Wilhelmsson (chairman)

The Scientific Advisory Committee consists of one Supervisory Board member who is independent within the meaning of the NASDAQ listing rules. This committee is responsible for, among other things, reviewing progress in our research and development activities. The committee reports to the Supervisory Board on a regular basis.

Management Board
Our Management Board manages our general affairs and business, under the supervision of our Supervisory Board. Under our articles of association, the Management Board requires prior approval of the Supervisory Board to:

- Expand into a new, or cease an existing, line of business;
- Participate, sell an interest, change its participation, or otherwise take an interest in, or assume the management of, another business enterprise;
- Enter into, terminate or amend any joint venture or pooling arrangement;
- Acquire fixed assets exceeding price limits set by the Supervisory Board; and

- Enter into financial commitments, other then in the ordinary course of business and/ or exceeding price limits set by the Supervisory Board or for longer than a year.

Under Dutch law, in certain circumstances, Management Board actions may require the approval of the General Meeting of Shareholders.

Our Supervisory Board determines the size of our Management Board after consultation with our Chief Executive Officer. The General Meeting of Shareholders appoints the members of our Management Board from a list of candidates nominated by our Supervisory Board. If the list of members contains the names of at least two persons it shall be binding. However, the general meeting of shareholders may at any time, by resolution passed with an absolute majority of the votes cast representing more than one third of the Company's issued capital, resolve that such list shall not be binding. If our Supervisory Board does not nominate anyone for a specific position within three months after a vacancy occurs, our General Meeting of Shareholders can appoint a member at its own discretion. If the Supervisory Board makes a non-binding nomination (i.e., only one nominee is presented to the Supervisory Board for any particular vacancy), then such nomination can only be overturned by a resolution of the General Meeting of Shareholders taken by an absolute majority of the votes cast, representing at least one third of the Company's total issued and outstanding share capital. A member of the Management Board may be appointed or reappointed for a term of not more than four years at a time.

Our Management Board may establish rules governing its internal organization. Our Supervisory Board must approve the adoption of and any changes to these rules. Our Management Board may charge each member of the Management Board with particular duties. The allocation of duties requires the approval of the Supervisory Board. Resolutions of our Management Board are passed by a majority of votes cast, unless provided otherwise in the by-laws of the Management Board. The Management Board shall appoint a Company Secretary who will assist the Management Board. The appointment and dismissal of the Company Secretary requires the approval of the Supervisory Board.

Each member of the Management Board may be suspended or removed by the General Meeting of Shareholders at any time. A resolution to suspend, remove or revoke the suspension of a member of the Management Board other than at the proposal of the Supervisory Board may only be passed by the General Meeting of Shareholders with an absolute majority of the votes cast representing at least one third of the Company's total issued and outstanding share capital.

Our Supervisory Board may also suspend (but not dismiss) a member of our Management Board. We must hold a General Meeting of Shareholders within three months after a suspension to either terminate or extend it. Any suspension may be extended one or more times, but may not last longer than three months in the aggregate. If at the end of that period no decision has been taken on termination of the suspension, or on removal, the suspension shall cease.

Our Supervisory Board determines the compensation and benefits of the members of our Management Board, based on a proposal by the Remuneration Committee, within the scope of the remuneration policy adopted by the General Meeting of Shareholders. The business address of the members of our Management Board is the same as the address of our principal executive office in Leiden, the Netherlands.

Pursuant to the Code, members of the Management Board are allowed to hold a maximum of two Supervisory Board positions in other listed companies. The members of the Management Board did not hold any such positions in 2008.

The name, date of appointment and position of the members of our Management Board are:

Name/Position	Date of appointment
Ronald Brus Chairman of the Management Board, President and Chief Executive Officer	May 30, 2008
Leonard Kruimer Chief Financial Officer	May 30, 2008
Cees de Jong Chief Operating Officer	May 30, 2008
Jaap Goudsmit Chief Scientific Officer	May 30, 2008

Management Board service contracts

The contracts for the Management Board members have been entered into for an indefinite period and provide for a notice period of up to six months upon termination by us and a notice period of three months upon termination by the individual. Nominations for a seat on the Management Board members are for a period of four years.

A dismissal arising from an unwanted change of control will result in a severance arrangement limited to a maximum of two years' worth of base salaries for the Management Board members.

The contracts of the Management Board members contain non-compete provisions that would apply for a period of one year after the end of their employment with us.

Management Committee

For its day-to-day operations Crucell has established a Management Committee that is responsible for the design, implementation and management of long and short-term strategy under the ultimate responsibility of the Management Board. The Management Board determines the number of members of the Management Committee. Members of the Management Committee are appointed and dismissed by the Management Board, with the approval of our Supervisory Board. The Management Committee generally meets once a month, and works closely with other members of our management. Our Management Board may establish rules governing its relationship with our Management Committee. Our Supervisory Board must approve the adoption of and any changes to these rules.

The following table sets forth the name, age and position of each of the members of our Management Committee:

Name/position	Age
Ronald Brus Chairman of Management Committee, President and Chief Executive Officer	45
Leonard Kruimer Chief Financial Officer	50
Cees de Jong Chief Operating Officer	47
Jaap Goudsmit Chief Scientific Officer	57
René Beukema General Counsel and Corporate Secretary	44
Björn Sjöstrand Chief Business Officer	40
Arthur Lahr Chief Strategy Officer & Executive Vice President Business Development	40

The following paragraphs contain brief biographies of the members of our Management Board and the members of our Management Committee:

Mr. Ronald Brus is chairman of the Management Board and President and Chief Executive Officer since January 2004, and has been a member of our Management Committee since incorporation. He was Executive Vice President, Business Development at IntroGene from 1997 to 2000 and Chief Operating Officer at Crucell from March 2003 until his appointment as President and Chief Executive Officer. From 1994 to 1996, he was product-planning physician at Forest Laboratories (New York) and from 1990 to 1994 he was medical director for Zambon B.V. He holds a medical degree (MD) from the University of Groningen. Mr. Brus is a Dutch citizen.

Mr. Leonard Kruimer became a member of the Management Board in January 2005. He has been our Chief Financial Officer and a member of our Management Committee since incorporation. He held the same position at IntroGene from 1998 to 2000. From 1996 to 1998 he was an independent consultant with companies such as Pepsico and Royal Boskalis Westminster N.V. From 1988 to 1995, he held senior executive positions at Continental Can Europe, GE Capital/TIP Europe and Kwik-Fit Europe B.V. He was a consultant at McKinsey & Co. and has worked with Price Waterhouse & Co. He holds a Masters in Business Administration from the Harvard Business School, a degree from the University of Massachusetts, Amherst, and is a CPA in New York State. Mr. Kruimer is a Dutch citizen.

Mr. Cees de Jong joined Crucell as Chief Operating Officer in 2007. Prior to joining Crucell Mr. De Jong was with Quest International in Naarden, the Netherlands as a member of the Board and responsible for the Flavours Division. Mr. De Jong has also worked as Managing Director of DSM Anti-infectives. In 1989 Mr. De Jong started his career at Gist Brocades, holding a variety of roles in business development, strategy and general management before the company's acquisition by DSM in 1998. Mr. De Jong holds a Medical Degree from the Erasmus University of Rotterdam and an MBA from the RSM Erasmus University.

Mr. Jaap Goudsmit is a member of the Management Board since January 2004. He was Senior Vice President Vaccine Research from September 2001 until July 2002 and member of the Management Committee from July 2002 as Executive Vice President Vaccine R&D. In September 2002 he was appointed Chief Scientific Officer. He chaired the Academic Medical Center of the University of Amsterdam, the Research Institute for Infectious Diseases and the Institute for Science Education. He was the founding Chairman of the Scientific

Advisory Committee of the International AIDS Vaccine Initiative (IAVI) and the founding co-Chairman of the European Vaccine Effort against HIV/AIDS (EuroVac). Since 1989, he has been a professor at the University of Amsterdam and the Academic Medical Center. He holds a medical degree (MD) and a PhD from the University of Amsterdam. Mr. Goudsmit is a Dutch citizen.

Mr. René Beukema has been our General Counsel and Company Secretary since our incorporation. He held the same position at IntroGene from 1999 to 2000. From 1994 to 1999 Mr. Beukema was senior legal counsel for GE Capital/TIP Europe. From 1991 to 1994, he was legal counsel for TNT Express Worldwide N.V. He has a Masters in Law from the University of Amsterdam.

Mr. Arthur Lahr is Crucell's Chief Strategy Officer and Executive Vice President Business Development. He joined Crucell in April 2001 as Executive Director Business Development, was appointed Vice President Business Development in December 2003, a member of the Management Committee in January 2004; Executive Vice President in January 2006; and assumed responsibility for European marketing and sales and company strategy in 2006. From 1994 to 2001, he was a consultant with McKinsey & Co. Prior to that, he worked with Unilever. He holds a Masters in Business Administration from INSEAD and a Masters in Science, Applied Physics, from the University of Delft.

Mr. Björn Sjöstrand joined Crucell in 2007 and is Crucell's Chief Business Officer. He was Chief Executive Officer of SBL Vaccines before it merged with Crucell in November 2006. Mr. Sjöstrand successfully headed the Crucell-SBL integration committee while directing the travel franchise and the Nordic sales force for the Crucell Group. He initiated and led a management buyout of SBL Vaccin AB funded by 3i and SEB Företagsinvest. At SBL, he successfully turned around the company from loss-making to a growth-focused, profit-making company between 2004 and 2006. Between 1999 and 2001, he was Vice President Operations & IT at Active Biotech, where he was also a member of the senior management team. Mr. Sjöstrand completed a Bachelor of Science (BSc) degree in Economics and Business Administration at the University of Örebro. He also studied Financial Investment Theory and Commercial Law at the same university.

Disclosure Committee

The Disclosure Committee is designed to help senior management, particularly the Chief Executive Officer and Chief Financial Officer, in the maintenance and evaluation of our disclosure controls and procedures. The Disclosure Committee gathers all relevant financial and non-financial information and assesses materiality, timeliness and necessity of disclosure of such information. The Disclosure Committee is comprised of the members of the Management Committee and selected senior managers. Members of the Disclosure Committee have direct access to our external legal counsel and our external auditor. The Disclosure Committee reports to the Chief Executive Officer and Chief Financial Officer.

The Disclosure Committee is an integrated part of our organization and is essential to our internal control over financial reporting. The Disclosure Committee and additional actions taken to further improve disclosure and internal control are intended to help us comply with the requirements of the Sarbanes-Oxley Act of 2002 and regulations promulgated by the Securities and Exchange Commission under that Act.

Remuneration policy for Management Board and Supervisory Board

The Remuneration Committee advised the Supervisory Board in 2008 to make certain changes to the remuneration policy for the Management Board, based on developments in the market as well as recommendations by the Monitoring Commission on Corporate Governance (Commissie Frijns). The main objectives of these changes are to:

- Decrease the complexity of the existing policy; and
- Re-balance the variable components (Short, and Long-Term Incentive bonus) to better reflect the responsibility of the Management Board to achieve both short-term goals and long-term strategy, following market practice.

The Supervisory Board reviewed the changes in the remuneration policy as proposed by the Remuneration Committee. The general meeting of shareholders in 2008 approved the changes in the existing remuneration policy, which took effect in 2008 and are described below.

Remuneration structure

The Management Board members receive fixed remuneration in the form of a base salary as well as performance-based compensation in the form of a short-term incentive plan and a long-term incentive plan.

The incentive for achieving target performance for the Chief Executive Officer equals 115% of base salary (65% in short-term incentive and 50% in long-term incentive). For other Management Board members the incentive is 90% of base salary (50% in short-term incentive and 40% in long-term incentive). For the Chief Executive Officer, this breaks down to 46.5% of salary in fixed compensation and 53.5% of salary in performance-based compensation. For the other three Management Board members, the breakdown is 52.6% fixed compensation compared to 47.4% performance-based compensation.

Base salary
In 2009, the base salary levels of the Management Board have been increased by 3 to 5% in order to keep up with inflation. Each year the Supervisory Board considers whether base salary levels should be adjusted according to external and internal business factors.

Short-term incentive
At the General Meeting of Shareholders in 2008, our shareholders approved the implementation of short-term cash-based incentive plans (STI). The STI bonus is now payable in cash, which is different from the share-based STI bonus in the previous years. In the approved policy, payment of the bonus begins upon 70% achievement of certain milestones. In order to compensate higher achievement of certain milestones, the payment limit was increased from 100% to 130%.

The STI bonus is linked to the achievement of predetermined collective and individual milestones. The collective milestones are based on predetermined annual goals for research, development, business development, finance, intellectual property and corporate legal affairs. We do not disclose specific details of these goals as this is commercially sensitive information. The individual milestones depend on the specific responsibilities of the individual Management Board member. Milestones linked to the STI bonus plan are revised annually and approved by our Supervisory Board.

The table below shows the relative weight of the collective and individual milestones in the STI bonus plan structure:

Management Board	Collective milestones	Individual milestones
CEO, CFO, CSO, COO	70%	30%

The target bonus of the Chief Executive Officer amounts to 65% of base salary and for the Chief Financial Officer, Chief Operational Officer and Chief Scientific Officer a target bonus of 50% of base salary is applicable. The bonus can be increased with a maximum of 30% in the event performance exceeds expectations to a considerable extent. The Supervisory Board has the discretionary power to increase or decrease the bonus by 25%.

Long-term incentive
At the General Meeting of Shareholders in 2008, our shareholders approved certain proposed changes in the long-term incentive (LTI) plan. The main changes in the LTI plan are as follows:

- Shift from payment in shares to payment in conditionally granted options; and
- Reduction of complexity by removing the circuit breaker and the ranking of the Company on Total Shareholder Return (TSR) in the Goldman Sachs European Biotech Index as performance indicators.

Target LTI compensation levels amount to 50% of base salary for the Chief Executive Officer and 40% for the other Management Board members. The LTI compensation can be increased up to 200% of the target award when achieving maximum performance.

Under the terms of the LTI plan, options are conditionally granted and vest at the end of a four-year performance period. The number of LTI options that vests depends on the fulfilment of the LTI performance condition.

On a vesting date Crucell's Total Shareholder Return (TSR) performance is measured against the performance of the NASDAQ Biotechnology Index during the applicable performance period. The positive difference in percentages, if any, between Crucell's TSR compared to the performance of the NASDAQ Biotechnology Index, determines the number of LTI options which vest, in accordance with the table set out opposite:

NASDAQ Biotech Index Vesting Scheme

Positive difference between TSR performance Crucell and the NASDAQ Biotech Index	Vesting as % of target award
≥ 50	200%
≥ 35 and < 50	150%
≥ 20 and < 35	100%
≥ 10 and < 20	50%
≥ 0 and < 10	25%
< 0	0%

Ad-hoc option grant

At the General Meeting of Shareholders in 2008 the shareholders of the Company approved an additional one-off stock option grant to members of the Management Board. The objective of the additional option grant is to increase the alignment of interests of shareholders and the Management Board and to provide an extra retention incentive.

In total, 800,000 additional options were granted to the members of the Management Board and these options were allocated as follows: the CEO received 300,000 options, the Chief Operational Officer 200,000 and the other Management Board members 150,000.

The options are conditionally granted and vest at the end of a three-year performance period. The options are granted conditionally as they include a predetermined performance condition. The performance condition is a TSR of at least 50% as of the vesting date.

Pension

At the beginning of our 2005 fiscal year a new pension plan for our Management Board was introduced. The plan is a defined contribution plan, with a pensionable age of 65 years. The employee contribution is set at 7% of the pensionable salary (base pay minus an offset). The table below outlines the annual contribution rates, including the employee contribution. The risk premium for the survivor's pension is financed separately by the employer.

Total contribution rates for our Management Board members are:

Age	Contribution rate
25 to 30	8.4%
30 to 35	10.2%
35 to 40	12.5%
40 to 45	15.2%
45 to 50	18.7%
50 to 55	23.0%
55 to 60	28.6%
60 to 65	36.1%

Shareholdings of the Management and Supervisory Boards

As of April 17, 2009 members of our Management Board and Supervisory Board held the following ordinary shares and options.

Name of Holder	Ordinary shares held per April 17, 2009	Options held per April 17, 2009	Year of expiration	Exercise price (€)
R.H.P. Brus	239,202	200,000	2011	3.49
		90,000	2011	2.64
		125,000	2011	5.94
		300,000	2013	12.23
		36,170	2016	10.82
L. Kruimer	28,195	30,000	2011	3.49
		125,000	2011	5.94
		150,000	2013	12.23
		19,490	2016	10.82
C. de Jong	2,406	185,000	2012	14.58
		200,000	2013	12.23
		20,655	2016	10.82
J. Goudsmit	169,276	125,000	2011	5.94
		150,000	2013	12.23
		23,388	2016	10.82
Totals	**439,079**	**1,779,703**		
J.P. Oosterveld	12,000	10,000	2009	8.81
		10,000	2009	11.55
S.P. Lance	12,500	10,000	2011	7.86
		10,000	2009	11.55
P.M. Satow	66,300	10,000	2009	11.55
		22,000	2011	3.49
		10,000	2011	6.48
C.E. Wilhelmsson	10,000	10,000	2009	11.55
		10,000	2011	6.48
A. Hoevenaars	10,000	5,000	2009	8.81
		10,000	2009	11.55
S. Davis	5,000	–	–	–
Totals	**115,800**	**117,000**		

During the period December 31, 2008 and April 17, 2009, a number of 250,000 options with an exercise price of € 9.4 were exercised by Ronald Brus and 85,000 options were exercised by Jaap Goudsmit with an exercise price of € 9.4. There were no other changes in the number of options held by members of the Management Board or Supervisory Board.

For additional details on remuneration of members of the Management and Supervisory Boards reference is made to note 5.23 'Related parties' in the financial statements.

Principal accountant fees and services

Deloitte Accountants B.V. audited the accompanying consolidated balance sheets of Crucell N.V. and subsidiaries (the 'Group') as of December 31, 2008 and 2007 and the related consolidated income statements, shareholders' equity, and cash flows for the years then ended.

The Sarbanes-Oxley Act of 2002 requires that Audit Committees pre-approve all services provided by the Company's external auditor. This process is critical to the auditor maintaining independence. Our process requires that all services provided by the external auditor are pre-approved by the Audit Committee.

During 2008 and 2007, we paid the following amounts to our external auditors for audit services, audit related services and tax services.

Year ended December 31,	2008	2007
Audit fees	840	904
Audit related fees	75	64
Fees for services related to Consultations on tax matters	–	–
Total	915	968

Audit fees include fees associated with the annual audit, interim reviews, required statutory audits and services that only the external auditor can reasonably provide, such as services associated with documents issued in connection with securities offerings.

Audit-related fees include accounting consultations on financial and accounting reporting standards.

Responsibility statement

Crucell's Management Board, as required by section 5.25c paragraph 2c of the Dutch Act on Financial Supervision (Wet op het Financieel Toezicht), confirms that to the best of their knowledge:

- The financial statements of 2008 give a true and fair view of the assets, liabilities, financial position and the profit or loss of the Group;
- The Annual Report gives a true and fair view of the Group's position and the state of affairs as per December 31, 2008; and
- The Annual Report contains a description of the material risk factors that the Group faces.

Controls and procedures

Internal risk management and control system

Crucell's Management Board is responsible for designing, implementing and operating the Company's internal risk management and control systems. The purpose of these systems is to manage in an effective and efficient manner the significant risks to which the Company is exposed. Crucell's internal and risk management and control systems with respect to financial reporting are in line with the guidance set forth in the COSO model, an integrated internal control framework established by the Committee of Sponsoring Organizations of the Treadway Commission. The Company's internal risk management and control systems are designed to provide reasonable assurance that strategic objectives can be met. Such systems can never provide absolute assurance regarding achievement of Company objectives, nor can they provide an absolute assurance that material errors, losses, fraud, and the violation of laws or regulations will not occur. A summary of the risks that could prevent Crucell from realizing its objectives is included in the section 'Risk Factors' of this report.

Our internal risk management and control systems make use of various measures including:

- Annual strategic evaluations of our business;
- Periodic operational review meetings of the Management Board with the Management Committee;
- Quarterly financial planning meetings of the Management Board with the Supervisory Board;
- A planning and control cycle consisting of annual, quarterly and monthly procedures, including subsequent follow-up on achievements of targets set;
- Advice of Crucell's Disclosure Committee to our Chief Executive Officer and Chief Financial Officer with respect to the timely review, disclosure and evaluation of periodical (financial) reports as well as with respect to the maintenance and evaluation of disclosure controls and procedures;
- Letters of representation that are signed by selected key-management members on a quarterly basis in which they confirm that for their area of responsibility based upon their knowledge:
  - An effective system of internal controls and procedures is maintained; and
  - The financial reports fairly present the financial position, results of operations and cash flows;
- Management letters and audit reports provided by our external auditor;
- Crucell's standardized and formalized working practices, including the Biological Safety Manual which was developed in-house to meet the specific needs of Crucell's working environment; and
- The Code of Conduct of Crucell.

The Management Board has discussed the internal risk management and control system with the Audit Committee and the Supervisory Board.

As a result of its listing at NASDAQ, Crucell is also obliged to comply with Section 404 of the Sarbanes-

Oxley Act of 2002 and related regulations (Section 404). Section 404 addresses the responsibility of the Management Board for establishing and maintaining an adequate system of internal control over financial reporting. Internal control over financial reporting is a process to provide reasonable assurance regarding the reliability of our public financial reporting.

Evaluation of disclosure controls and procedures
We have evaluated, with the participation of our Chief Executive Officer and Chief Financial Officer, the effectiveness of our disclosure controls and procedures as of December 31, 2008. There are inherent limitations to the effectiveness of any system of disclosure controls and procedures, including the possibility of human error and the circumvention or overriding of the controls and procedures. Accordingly, even effective disclosure controls and procedures can only provide reasonable assurance of achieving their control objectives. Based upon our evaluation, our Chief Executive Officer and Chief Financial Officer concluded that the disclosure controls and procedures as of December 31, 2008 were effective to provide reasonable assurance that information required to be disclosed in the reports we file or submit under the US. Securities Exchange Act of 1934, as amended, is recorded, processed, summarized and reported, within the time periods specified in the applicable rules and forms, and that it is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting
Management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the US Securities Exchange Act of 1934. The Company's internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. The Company's internal control over financial reporting includes those policies and procedures that:

- Pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and disposition of the assets of the Company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only by authorized employees in accordance with documented authorizations; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness for future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

As required by Section 404 of the Sarbanes-Oxley Act of 2002, Management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2008. In making this assessment, Management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework.

Based on its assessment and those criteria, Management concluded that the Company maintained effective internal control over financial reporting as of December 31, 2008.

Deloitte Accountants B.V., the independent registered public accounting firm that audited the financial statements included in this Annual Report, has issued an attestation report on the effectiveness of the Company's internal control over financial reporting as of December 31, 2008 as stated in their report beginning on page 116 of this report.

Changes in internal control over financial reporting
There has not been any change in the internal controls over financial reporting of the Company that occurred during the period covered by this report that has materially affected, or is reasonably likely to materially affect, such internal controls over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Supervisory Board and Shareholders of Crucell N.V. Leiden, the Netherlands

We have audited the internal control over financial reporting of Crucell N.V. and subsidiaries (the 'Company') as of December 31, 2008, based on criteria established in Internal Control – *Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A Company's internal control over financial reporting is a process designed by, or under the supervision of, the Company's principal executive and principal financial officers, or persons performing similar functions, and effected by the company's board of directors, management, and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and Directors of the Company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of the inherent limitations of internal control over financial reporting, including the possibility of collusion or improper management override of controls, material misstatements due to error or fraud may not be prevented or detected on a timely basis. Also, projections of any evaluation of the effectiveness of the internal control over financial reporting to future periods are subject to the risk that the controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on the criteria established in *Internal Control – Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated financial statements as of and for the year ended December 31, 2008 of the Company and our report dated April 21, 2009 expressed an unqualified opinion on those financial statements and included an explanatory paragraph regarding the adoption of IFRIC 14 by the Company.

Deloitte Accountants B.V.
Amsterdam, The Netherlands
April 21, 2009

Articles of Association and Share Capital

Memorandum and Articles of Association

Set out below is a summary of material information concerning our shares, which are our ordinary shares together with our preference shares, and related material provisions of our articles of association and of Book 2 of the Dutch Civil Code (Boek 2 van het Burgerlijk Wetboek). This summary is not complete and is qualified in its entirety by reference to our articles of association and to Dutch law.

General

We were incorporated as a limited liability company (naamloze vennootschap) on October 9, 2000 by deed executed before Mr. R.J.J. Lijdsman, civil law notary. Our corporate seat is in Leiden, the Netherlands, and we have offices at Archimedesweg 4-6, 2333 CN Leiden, the Netherlands. We are registered in the trade register of the Chamber of Commerce and Industry for Leiden under number 28087740. The statement of no objection of the Minister of Justice in respect of our deed of incorporation was issued on October 9, 2000 under number N.V. 1133178. Our agent in the US is CT Corporation, 111 Eighth Avenue, New York, New York 10011. Our articles of association were last amended on 23 July 2008 before Mr. R.J.J. Lijdsman, civil law notary.

Corporate purpose

The objects of the Company are set out in Article 3 of the articles of association. Our objects include acquiring, establishing and managing companies in our field, controlling and using intellectual property, and funding of our operations as well as to do all that is connected therewith or may be conducive thereto.

Limitation of liability and indemnification matters

Pursuant to Dutch law, each member of our Supervisory and Management Boards is responsible to us for the proper performance of his or her assigned duties. They are also responsible for taking measures to prevent the consequences of any improper performance of duties by another member of our Supervisory Board or our Management Board. Our articles of association provide that our Management Board members and our Supervisory Board members are released from liability for the exercise of their duties as board members, if our General Meeting of Shareholders adopts a resolution to that effect. This discharge extends only to the exercise of the duties reflected in the annual accounts or otherwise disclosed to our General Meeting of Shareholders prior to the adoption of the annual accounts.

This release of liability may be limited by virtue of Dutch law, such as in the case of bankruptcy. Under Dutch law, our Supervisory Board members and members of our Management Board generally cannot be held personally liable for actions taken in their capacity as such, provided, however, that the foregoing shall not eliminate or limit the liability (1) for any breach of such individual's duty of loyalty to the Company or its shareholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) for any transaction from which the member derived an improper personal benefit or (4) for personal liability which is imposed by Dutch law, as may be amended from time to time.

Our articles of association provide that we shall generally indemnify any person who is or was a member of our Supervisory Board or our Management Board, and suffers any loss as a result of any action in connection with the execution of his duties for us, provided he acted in good faith and in a manner he reasonably believed to be in or not opposed to our best interests, and with respect to criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful or beyond his mandate.

This indemnification generally will not be available if the person seeking indemnification was adjudged liable for acting with gross negligence or wilful misconduct in the performance of his duties to us, unless the court in which the action was brought, determines that indemnification is appropriate nonetheless.

Share capital

Our authorized share capital amounts to € 40.8 million divided into: 85,000,000 ordinary shares and 85,000,000 preference shares, each with a par value of € 0.24.

At December 31, 2008, there were 65,833,242 ordinary shares issued and outstanding. No preference shares are currently issued and outstanding. The ordinary shares can be issued in bearer or registered form. The preference shares can only be issued in registered form. Only bearer ordinary shares can trade on NYSE Euronext Amsterdam. No share certificates will be issued for shares in registered form.

Ordinary shares
Our ordinary shares may be in registered or bearer form and will be in bearer form unless the shareholder indicates otherwise in writing.

Bearer ordinary shares
All of our bearer ordinary shares are embodied in a single global share certificate which will not be exchanged for single or multiple physical securities and which we will deposit with the Dutch Securities Depository (NECIGEF) for safekeeping on behalf of the parties entitled to the ordinary shares in bearer form.

The ordinary shares represented by the single global share certificate may only be transferred through the book-entry system maintained by NECIGEF. A participant in the collective deposit (verzameldepot) of a securities institution admitted to NECIGEF may, at his own expense, require conversion of one or more of his bearer ordinary shares into ordinary shares in registered form.

Registered ordinary shares
We enter holders of registered ordinary shares in the register of shareholders. We do not issue share certificates. However, the shareholder may request an extract from the shareholders' register regarding the ordinary shares registered in his name. We are required to provide this free of charge. Dutch law requires that transfers of registered ordinary shares be recorded in a written instrument to which we are a party or which is served on us, or that the transaction is acknowledged by us.

Preference shares
As of the date of this Annual Report, we have not issued any preference shares. On October 25, 2000, we established a foundation called Stichting Preferente Aandelen Crucell, also referred to as the Preferred Foundation. The Preferred Foundation's objective is to safeguard our interests, our business and parties connected therewith by blocking any influences that may threaten these interests, which interests may include the continuity of the Company, identity of the proposed acquirer or identity of us, our business and the parties connected therewith. The Preferred Foundation can safeguard these interests through acquiring and managing our preference shares and by exercising the rights attaching to these shares, in particular, the voting rights.

The Preferred Foundation has an option to acquire preference shares up to 100% of the number of our outstanding shares, necessary to match the total number of statutory votes on all of the ordinary shares outstanding at the time of an acquisition. The Preferred Foundation must pay at least 25% of the nominal value of the preference shares it acquires from us. If we acquire any preference shares, they may be cancelled.

A board of governors of up to five persons directs the Preferred Foundation. Jan Oosterveld, in his capacity as chairman of our Supervisory Board, and Pieter Bouw, Mick W. den Boogert, Sweder van Wijnbergen and Gerard P. Krans, have been appointed to the board of governors. A majority of these members may not be members or former members of our Management or Supervisory Board, or an employee of any of our advisers, any of our banks or us. These independent members are appointed by the board of governors. The non-independent members are appointed by our Supervisory Board after consultation with our Management Board.

Membership of the board of governors of the Preferred Foundation terminates upon:

- Voluntary retirement, reaching the age of 72, death or bankruptcy;
- For our non independent members, resignation, or dismissal by the members of our Supervisory Board;
- For our independent members, if they cease to be independent;
- Dismissal by the complete board of the Preferred Foundation; or
- Periodic retirement in accordance with a rotation plan to be drawn up by the Preferred Foundation's board of governors, however, these members may be reappointed.

Issue of shares and pre-emptive rights
Our General Meeting of Shareholders, or our Management Board if the General Meeting of Shareholders has delegated the power to it, has the authority to decide on any further issuance of shares or rights to subscribe for shares and on the terms and conditions of such issuance. Our Management Board is the authorized corporate body (orgaan) for this purpose until November 30, 2009, and the authorization may at any time be extended by the General Meeting of Shareholders for periods of up to five years. Our Management Board's authority to issue shares is limited to a maximum of 10% of the issued share capital at the time of issue, plus a further issue up to 10% of the issued share capital at the time of issue in case the issue takes place in relation to a merger or an acquisition.

Our Management Board can issue shares of any class if it has the approval of our Supervisory Board. Without specific authorization from our General Meeting of Shareholders our Management Board may not issue preference shares or grant options for such shares if, as a result, more preference shares than ordinary shares will or could become outstanding.

Each holder of ordinary shares has pre-emptive rights to subscribe for any ordinary shares that we issue and has pre-emptive rights to subscribe if we grant rights to subscribe for ordinary shares. Pre-emptive rights are in proportion to the percentage of our outstanding ordinary shares that the holder owns. Pre-emptive rights do not apply to ordinary shares issued for a non-cash contribution, to ordinary shares issued to our employees or ordinary shares issued to a person who exercises a previously acquired right to subscribe for ordinary shares. Holders of preference shares do not have pre-emptive rights if we issue ordinary shares, and holders of ordinary shares have no pre-emptive rights to purchase preference shares if we issue preference shares.

If our Management Board has been delegated the authority to issue shares, it can limit or exclude any pre-emptive rights as long as the general meeting of shareholders has granted it that power and our Supervisory Board approves. At present, our Management Board is authorized to do this. This authorization is valid until November 30, 2009 and the General Meeting of Shareholders may at any time extend this authorization for periods of up to five years.

Our shares cannot be issued below par. The ordinary shares must be fully paid up upon issue. Preference shares may be issued without being fully paid up, but at least one-quarter of the nominal amount must be paid up upon subscription, and each issue of preference shares must have the same amount paid up. Our Management Board may determine the day and the amount of a further call for payment on preference shares.

Acquisition by us of shares in our own capital
We may acquire our own fully paid up shares if the following conditions are met:

- Our General Meeting of Shareholders has authorized our Management Board to acquire the shares;
- The authorization specifies the number of shares that we may acquire, the manner in which they may be acquired and the limits within which the price must be set;
- Our shareholders' equity, after deduction of the price of acquisition, is not less than the sum of the paid and called up portion of the share capital and the reserves that provisions of Dutch law or our articles of association require us to maintain; and
- The aggregate par value of the shares to be acquired, together with the shares in our share capital that we already hold directly, indirectly or as pledgee, does not equal more than one-tenth the aggregate par value of our total issued share capital.

An authorization by the General Meeting of Shareholders for a term of a maximum of 18 months is needed in the event of an acquisition for valuable consideration. Currently an authorization is granted to the Management Board by the General Meeting of Shareholders to repurchase fully paid up ordinary shares up to 10% of our outstanding share capital until November 30, 2009. The repurchase price lies between the nominal value of the shares and an amount equal to 110% of the highest price officially quoted on the NASDAQ National Market and the NYSE Euronext Amsterdam stock exchange on any of five (5) banking days preceding the date of the repurchase.

We and our subsidiaries may not vote shares that we or they hold. We may acquire shares to transfer them to our employees or the employees of our group companies under designated stock option plans without authorization.

Capital reduction
If our Management Board proposes, our Supervisory Board approves and Dutch law permits, the General Meeting of Shareholders can reduce our issued share capital by cancellation of shares or reduction of the nominal value of shares.

Other key provisions of our articles of association

Voting rights and shareholders' meetings
We must hold annual general meetings of shareholders within six months of the end of our financial year. The annual meeting is held, among other things, to adopt our annual accounts. We must hold extraordinary general meetings of shareholders whenever:

- Shareholders and holders of American depositary receipts for shares together representing at least one- tenth of our outstanding share capital request it in writing, listing the topics to be discussed; and
- Our Management Board or our Supervisory Board deems appropriate.

General meetings of shareholders may only be held in the municipalities of Leiden, Amsterdam, Haarlemmermeer (including Schiphol Airport and Schiphol-Rijk), Utrecht, Rotterdam and The Hague.

Each shareholder can attend general meetings in person or by proxy, address the meeting and vote. Each share, whether ordinary or preference, confers one vote on the shareholder. The Management Board must be notified in writing of a registered shareholder's intention to attend the General Meeting of Shareholders. The holders of bearer ordinary shares can vote if a NECIGEF participant sends a written statement as to their shareholdings to our offices. Resolutions are passed by absolute majority of votes cast unless stated otherwise in Dutch law and our articles of association.

Shareholders representing alone, or in aggregate, at least one percent (1%) of our issued capital or – according to the Euronext Official Price List – at least a value of 50 million Euro, have the right to request the Management Board and the Supervisory Board to place items on the agenda of the General Meeting of Shareholders. These requests shall be honoured on the condition:

- That the shareholders have a reasonable interest in the items to be considered;
- That the placing on the agenda is not in conflict with the orderly course of the meeting and that there shall be no material interest against placing the item on the agenda; and
- That the request has been filed in writing with the Management Board or the Chairman of the Supervisory Board at least 60 days prior to the date of the General Meeting of Shareholders.

The General Meeting of Shareholders can amend our articles of association, dissolve us, merge us or demerge us only if proposed by the Supervisory Board.

Dutch law and our articles of association do not impose any limitations on non-Dutch ownership or voting of our ordinary shares.

Approval rights of the Supervisory Board
Our Supervisory Board must approve certain resolutions of our Management Board, which are specified in our articles of association.

Annual Report
We have a calendar financial year. Dutch law requires that within four months after the end of our financial year, unless the general meeting of shareholders has extended this period for a maximum of six months, our Management Board must make available to the shareholders a report with respect to that financial year. This report must include the financial statements and a report of an independent accountant. The Annual Report is submitted to the annual General Meeting of Shareholders for adoption. See 'Information for Shareholders and Investors – Limitation of Liability and Indemnification Matters'.

Dividends
Annual dividends may only be paid out of profits as shown in the adopted annual financial statements. We may not make distributions if the distribution would reduce our shareholders' equity below certain reserves required by Dutch law or by our articles of association. The profits must first be used to set up and maintain reserves required by Dutch law and must then be set off against certain financial losses. The dividends for the preference shares will be a certain percentage of their nominal value. These will be paid first. With Supervisory Board approval, our Management Board then decides whether and how much of the remaining profit they will reserve. Any profits remaining shall be paid as a dividend on the ordinary shares, if the retained earnings are negative or are to be used to form a statutory reserve no dividend will be paid out. With the approval of our Supervisory Board and subject to Dutch law, our Management Board can pay an interim dividend.

We can make distributions to shareholders at the charge of one or more of our reserves. Holders of shares are entitled to the full dividend for the financial year 2000 and subsequent financial years. Any dividends that are not claimed within five years of their declaration revert to us.

Amendment of our articles of association and liquidation rights
The General Meeting of Shareholders may only resolve to amend our articles of association or to dissolve, merge or demerge us on the proposal of our Supervisory Board. The class of shareholders

affected must approve a resolution to amend the articles of association to change the rights of the class. If we are dissolved and liquidated, after we pay all debts and liquidation expenses, the holders of preference shares have first rights to payment of any dividends not fully paid to them in previous years and of the nominal value of their preference shares. Any remaining assets will be distributed to the holders of ordinary shares.

Enforcement of civil liabilities
We are incorporated under the laws of the Netherlands, and the majority of the members of our Supervisory Board, all of the members of our Management Board and management team and all of the experts named in this document are residents of, and most of our and their assets are located in, jurisdictions outside the US. As a result, it may not be possible for you to effect service of process within the US upon us or these persons, or to enforce against us or these persons in courts in the US, judgments of these courts predicated upon the civil liability provisions of US securities laws. In addition, it is not clear whether a Dutch court would impose civil liability on us, members of our Management Board or Supervisory Board or management team or any of the experts named in this document in an original action based solely upon the federal securities laws of the US brought in a court of competent jurisdiction in the Netherlands. Dutch law, furthermore, does not recognize a shareholder's right to bring a derivative action on behalf of a corporation.

Our legal counsel in the Netherlands, Allen & Overy, has advised us that because there is no treaty on the reciprocal recognition and enforcement of judgments in civil and commercial matters between the US and the Netherlands, courts in the Netherlands will not automatically enforce a final judgment rendered by a US court. In order to obtain a judgment enforceable in the Netherlands, claimants must litigate the relevant claim again before a Dutch court of competent jurisdiction. Under current practice, however, a Dutch court will recognize a final and conclusive judgment rendered by a US court if the Dutch court finds that:

- The US court assumed jurisdiction on grounds that are acceptable from an international law perspective;
- The final judgment results from proceedings compatible with Dutch concepts of due process; and
- The final judgment does not contravene public policy of the Netherlands.

If the Dutch court recognizes the final US judgment, that court generally will grant the same judgment without the parties having to litigate again on the merits.

Obligations of shareholders to disclose holdings under Dutch law
Under the Financial Supervision Act any person who, directly or indirectly, acquires, or disposes of, an interest in the capital and/or the voting rights of a public limited liability company incorporated under Dutch law with an official listing on a stock exchange within the European Economic Area must immediately give written notice to the Dutch securities regulator AFM by means of a standard form, of such acquisition or disposal if, as a result of such acquisition or disposal, the percentage of capital interest and/or voting rights held by such person meets, exceeds or falls below the following thresholds: 5%, 10%, 15%, 20%, 25%, 30%, 40%, 50%, 60%, 75% and 95%.

The notification requirement also applies if a person's capital interest or voting right meets, exceeds or falls below the above mentioned thresholds as a result of a change in the share capital or voting rights, and the notification must be made no later than the fourth trading day after the AFM has published the notification as described in the following sentence. Crucell is required to notify the AFM immediately if its share capital or voting rights change by 1% or more since the previous notification. Other changes must be notified periodically.

In addition, the members of the Management Board and Supervisory Board are required to immediately notify the AFM of any change in the number of Crucell shares or options they hold or voting rights in respect of these shares. The AFM will disclose this information in a public register on its website. Non-compliance with the obligations of the Financial Supervision Act can lead to criminal prosecution. In addition, a civil court can issue orders against any person who fails to notify or incorrectly notifies in accordance with the Financial Supervision Act, including suspension of the voting rights in respect of such person's ordinary shares.

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Report of Independent Registered Public Accounting Firm

To the Supervisory Board and Shareholders of Crucell N.V. Leiden, the Netherlands

We have audited the accompanying consolidated balance sheets of Crucell N.V. and subsidiaries (the 'Company') as of December 31, 2008 and 2007, and the related consolidated statements of income, changes in equity, and cash flows for each of the three years in the period ended December 31, 2008. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of Crucell N.V. and subsidiaries as of December 31, 2008 and 2007, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2008, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

As discussed in note 1.5.1 to the financial statements as of January 1, 2008, the Company changed its method of accounting for pension assets to conform to IFRIC 14, and retrospectively, adjusted the 2007 and 2006 financial statements for the change.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the Company's internal control over financial reporting as of December 31, 2008, based on the criteria established in *Internal Control – Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated April 21, 2009 expressed an unqualified opinion on the Company's internal control over financial reporting.

Deloitte Accountants B.V.
Amsterdam, The Netherlands
April 21, 2009

Consolidated Income Statements

Year ended December 31, (Amounts in thousands of Euro, except per share data)	Notes	2008	2007	2006
Product sales		**226,055**	177,569	103,918
License revenues		**30,202**	12,211	16,955
Service fees		**10,900**	14,006	10,694
Total revenues	4	**267,157**	**203,786**	**131,567**
Cost of product sales		**(138,790)**	(124,557)	(83,518)
Cost of service and license fees		**(6,965)**	(10,327)	(6,971)
Total cost of goods sold	5.1	**(145,755)**	**(134,884)**	**(90,489)**
Gross margin		**121,402**	**68,902**	**41,078**
Government grants		**5,380**	7,086	6,901
Other income		**10,772**	2,244	2,455
Total other operating income		**16,152**	**9,330**	**9,356**
Research and development	5.1	**(70,229)**	(63,995)	(67,606)
Selling, general and administrative	5.1	**(64,350)**	(61,752)	(46,732)
Restructuring	5.18	**—**	—	(3,120)
Reversal of impairment/ (impairment)	5.6/5.7	**4,888**	(171)	(30,416)
Total other operating expenses		**(129,691)**	**(125,918)**	**(147,874)**
Operating profit/(loss)		**7,863**	**(47,686)**	**(97,440)**
Financial income	5.2	**6,935**	13,190	13,453
Financial expenses	5.3	**(9,597)**	(11,812)	(11,706)
Results investments non-consolidated companies	5.9	**(128)**	(996)	(1,956)
Results disposal of non-consolidated companies	5.9	**1,570**	2,186	—
Disposal of subsidiaries	1.1	**(367)**	—	—
Profit/ (loss) before tax		**6,276**	**(45,118)**	**(97,649)**
Income tax	5.4	**8,310**	2,208	10,451
Profit/ (loss) for the year		**14,586**	**(42,910)**	**(87,198)**
Attributable to:				
Equity holders of the parent		**14,586**	(42,910)	(86,946)
Minority interest		**—**	—	(252)
		14,586	(42,910)	(87,198)
Profit/ (loss) per share – basic and diluted	5.5	**0.22**	**(0.66)**	**(1.52)**
Weighted average shares outstanding – basic (in thousands)	5.5	**65,593**	65,103	57,064
Weighted average shares outstanding – diluted (in thousands)	5.5	**66,315**	65,103	57,064

Following the adoption of IFRIC 14 as of January 1, 2008, the equity in 2006 and the entries for defined benefit post-employment plans and corresponding deferred tax liabilities have been adjusted for the years 2006 and 2007. The impact of this retrospective application on the financial statements is provided in note 1.5.

The accompanying notes are an integral part of these financial statements.

Consolidated Balance Sheets

Year ended December 31, (Amounts in thousands of Euro)	Notes	2008	2007
Assets			
Non-current assets			
Property, plant and equipment	5.6	**151,206**	145,525
Intangible assets	5.7	**79,004**	94,045
Goodwill	5.8	**46,076**	44,377
Investments in associates and joint ventures	5.9	**9,239**	9,070
Pension asset	5.10	**8,612**	7,397
Available-for-sale investments	3.5	**4,922**	10,009
Other financial assets	5.11	**14,920**	16,153
		313,979	326,576
Current assets			
Cash and cash equivalents	5.12	**170,969**	163,248
Trade accounts receivable	5.13	**40,108**	47,563
Inventories	5.14	**91,847**	67,233
Other current assets	5.15	**19,394**	25,218
		322,318	303,262
Total assets		**636,297**	**629,838**
Liabilities and equity			
Equity attributable to equity holders of the parent	5.16	**453,492**	441,103
Non-current liabilities			
Long-term provisions	5.18	**4,577**	4,573
Long-term financial liabilities	5.19	**35,297**	28,030
Deferred tax liabilities	5.4	**16,985**	29,267
Other non-current liabilities and deferred income	5.20	**7,645**	12,123
		64,504	73,993
Current liabilities			
Short-term provisions	5.18	**1,581**	761
Short-term financial liabilities	5.19	**25,454**	24,765
Other current liabilities and deferred income	5.20	**29,284**	37,897
Income tax payable		**2,777**	349
Trade accounts payable	5.21	**59,205**	50,970
		118,301	114,742
Total liabilities		**182,805**	188,735
Total liabilities and equity		**636,297**	**629,838**

Following the adoption of IFRIC 14 as of January 1, 2008, the equity in 2006 and the entries for defined benefit post-employment plans and corresponding deferred tax liabilities have been adjusted for the years 2006 and 2007. The impact of this retrospective application on the financial statements is provided in note 1.5.

The accompanying notes are an integral part of these financial statements.

Consolidated Statements of Changes in Equity

(Amounts in thousands of Euro)

	Issued capital	Share premium	Net unrealized gains reserve	Hedging reserve	Translation reserve	Accumulated deficit	Total	Minority interests	Total equity
At January 1, 2006	**9,946**	**278,592**	**9,630**	**—**	**—**	**(160,559)**	**137,609**	**—**	**137,609**
Change in accounting methodology – IFRIC 14	**—**	**—**	**—**	**—**	**(13)**	**232**	**219**	**—**	**219**
Foreign currency translation	—	—	—	—	(7,920)	—	(7,920)	(814)	(8,734)
Unrealized result on available for sale securities	—	—	1,040	—	—	—	1,040	—	1,040
Total income and expense for the year recognized directly in equity	**—**	**—**	**1,040**	**—**	**(7,920)**	**–**	**(6,880)**	**(814)**	**(7,694)**
Loss for the year	—	—	—	—	—	(86,946)	(86,946)	(252)	(87,198)
Total recognized income and expense for the year	**—**	**—**	**1,040**	**—**	**(7,920)**	**(86,946)**	**(93,826)**	**(1,066)**	**(94,892)**
Issue of shares	5,458	433,104	—	—	—	—	438,562	12,093	450,655
Costs share based payment transactions	—	4,000	—	—	—	—	4,000	—	4,000
Issue of warrants and non – employee stock options to acquire ordinary shares in exchange for services	149	10,878	—	—	—	—	11,027	(11,027)	—
Stock based incentive plan	—	295	—	—	—	—	295	—	295
At December 31, 2006	**15,553**	**726,869**	**10,670**	**—**	**(7,933)**	**(247,273)**	**497,886**	**—**	**497,886**
Foreign currency translation	—	—	—	—	(20,384)	—	(20,384)	—	(20,384)
Unrealized result on available for sale securities	—	—	(2,330)	—	—	—	(2,330)	—	(2,330)
Total income and expense for the year recognized directly in equity	**—**	**—**	**(2,330)**	**—**	**(20,384)**	**—**	**(22,714)**	**—**	**(22,714)**
Loss for the year	—	—	—	—	—	(42,910)	(42,910)	—	(42,910)
Total recognized income and expense for the year	**—**	**—**	**(2,330)**	**—**	**(20,384)**	**(42,910)**	**(65,624)**	**—**	**(65,624)**
Issue of shares	132	2,185	—	—	—	—	2,317	—	2,317
Costs share based payment transactions including non-employee stock options	—	6,524	—	—	—	—	6,524	—	6,524
At December 31, 2007	**15,685**	**735,578**	**8,340**	**—**	**(28,317)**	**(290,183)**	**441,103**	**—**	**441,103**
Foreign currency translation	—	—	—	—	(4,709)	—	(4,709)	—	(4,709)
Unrealized result on available for sale securities	—	—	(5,086)	—	—	—	(5,086)	—	(5,086)
Result unrealized cash flow hedges	—	—	—	(685)	—	—	(685)	—	(685)
Total income and expense for the year recognized directly in equity	**—**	**—**	**(5,086)**	**(685)**	**(4,709)**	**—**	**(10,480)**	**—**	**(10,480)**
Profit for the year	—	—	—	—	—	14,586	14,586		14,586
Total recognized income and expense for the year	**—**	**—**	**(5,086)**	**(685)**	**(4,709)**	**14,586**	**4,106**	**—**	**4,106**
Issue of shares	115	3,115	—	—	—	—	3,230	—	3,230
Costs share based payment transactions including non-employee stock options	—	5,053	—	—	—	—	5,053	—	5,053
At December 31, 2008	**15,800**	**743,746**	**3,254**	**(685)**	**(33,026)**	**(275,597)**	**453,492**	**—**	**453,492**

Following the adoption of IFRIC 14 as of January 1, 2008, the equity in 2006 and the entries for defined benefit post-employment plans and corresponding deferred tax liabilities have been adjusted for the years 2006-2007. The impact of this retrospective application on the financial statements is provided in note 1.5.

The accompanying notes are an integral part of these financial statements.

Consolidated Cash Flow Statements

Year ended December 31, (Amounts in thousands of Euro)	Notes	2008	2007	2006
Cash flows from (used in) operating activities				
Profit/ (loss) of the year		**14,586**	(42,910)	(87,198)
Adjustments for non-cash items				
Income tax	5.4	**(8,310)**	(2,208)	(10,451)
Results of investments in associates and joint ventures	5.9	**128**	996	1,956
Financial income and expenses	5.2/ 5.3	**3,963**	(1,378)	(1,747)
Depreciation	5.6	**16,629**	14,453	14,275
Amortization	5.7	**11,674**	11,894	7,560
(Reversal of impairment)/impairment	5.6/ 5.7	**(4,888)**	171	30,416
Fair value adjustments on inventory	5.14	**1,165**	8,493	11,272
Change in long-term liabilities, receivables and provisions	5.11/5.18/5.19	**(5,309)**	7,591	(287)
Gain on disposal of assets	5.6/5.9	**(1,304)**	(2,236)	(176)
Stock-based compensation	5.17	**5,053**	6,817	5,687
Changes in net working capital				
Trade accounts receivable		**(912)**	8,583	(25,755)
Inventories		**(37,121)**	(6,128)	(15,674)
Other current assets		**5,103**	(615)	1,136
Trade accounts payable		**15,978**	16,274	18,509
Other current liabilities		**(14,080)**	8,247	(3,211)
Short-term provisions		**1,218**	(1,191)	1,821
Interest paid		**(2,684)**	(2,152)	(2,211)
Income taxes paid		**(576)**	(1,545)	124
Payments out of provisions		**(567)**	(962)	—
Net cash flows from (used in) operating activities		**(254)**	**22,194**	**(53,954)**
Cash flows from (used in) investing activities				
Purchase of property, plant and equipment	5.6	**(15,787)**	(27,156)	(20,337)
Proceeds from sale of equipment	5.6	**—**	113	197
Acquisition of intangible assets	5.8	**(237)**	—	(12,371)
Proceeds from sale intangible assets	5.7	**—**	—	225
Acquisition of Berna Biotech AG, Switzerland, net of cash acquired	5.8	**—**	—	67,784
Acquisition of SBL, Sweden, net of cash acquired	5.8	**—**	—	(33,386)
Investments/capital increase in joint ventures	5.9	**—**	(8,553)	(1,427)
Proceeds from disposal joint ventures/associates/subsidiaries	5.9	**182**	6,081	—
Assets classified as held for sale		**—**	—	11,772
Proceeds from financial assets		**2,540**	—	7,627
Interest received	5.2	**4,395**	5,274	3,075
Net cash flows from (used in) investing activities		**(8,907)**	**(24,241)**	**23,159**
Cash flows from financing activities				
Proceeds from issue of share capital	5.16	**3,230**	2,281	82,797
Proceeds from financial liabilities	5.19	**35,732**	10,309	14,703
Repayment of financial liabilities	5.19	**(22,336)**	(1,346)	(18,769)
Net cash flows from financing activities		**16,626**	**11,244**	**78,731**
Effect of exchange rates on cash and cash equivalents		**256**	(3,786)	(1,833)
Net increase (decrease) in cash and cash equivalents		**7,721**	**5,411**	**46,103**
Cash and cash equivalents at beginning of the year	5.12	**163,248**	157,837	111,734
Cash and cash equivalents at end of the year	5.12	**170,969**	**163,248**	**157,837**

The accompanying notes are an integral part of these financial statements.

Notes to the Consolidated Financial Statements

1 General information

1.1 Corporate information

General

Crucell N.V. ('Crucell' or the 'Company') is incorporated and domiciled in Leiden, the Netherlands. Its shares are publicly traded on NYSE Euronext Amsterdam (CRXL), and SWX Swiss Exchange Zurich (CRX). Its American Depositary Shares (ADSs) are publicly traded on NASDAQ New York (CRXL). Crucell and its subsidiaries together constitute the Crucell Group, or the 'Group'. The Company has subsidiaries in the Netherlands, Switzerland, Spain, Italy, Sweden, Korea and the US. Crucell employed 1,126 people at December 31, 2008 (2007: 1,126).

Crucell is a fully integrated biopharmaceutical company, focused on developing, producing and marketing products to combat infectious diseases. Its core vaccine portfolio includes Inflexal V, a vaccine against influenza, paediatric vaccines Hepavax-Gene, Quinvaxem and MoRu-Viraten, and travel vaccines Vivotif, Dukoral, and Epaxal. In addition to these portfolio vaccines, the Group has a broad pipeline of new potential vaccines and proteins. The Group has developed various proprietary technologies such as PER.C6, MAbstract, AdVac, STAR and virosome-adjuvanted technologies. Crucell licenses these proprietary technologies to other companies in the biopharmaceutical industry.

List of consolidated companies

Changes in the scope of consolidation

The consolidated financial statements include the results of the acquired companies for the period from the date of acquisition unless mentioned otherwise. There have been the following changes in the scope of consolidation in 2008.

- In November 2008, the Group sold its fully-owned subsidiary Etna Biotech Srl (Catania, Italy) to Zydus Cadila (Ahmedabad, India). The sale resulted in net proceeds for Crucell of € 182;
- In December 2008, SBL Vaccin Holding AB and Vitec AB legally merged into SBL Vaccin AB;

On November 30, 2007, Rhein Vaccines B.V. legally merged into Berna Rhein B.V. and ceased to exist as of that date.

In 2006, the most significant changes in the scope of consolidation were due to:

- The acquisition of the shares of Berna Biotech AG (February 2006);
- The establishment of Crucell Vaccines Inc. followed by the acquisition of the assets and liabilities of Berna Products Corporation (October 2006); and
- The acquisition of the shares of SBL Vaccin Holding AB (November 2006).

Further details on these acquisitions are provided in note 5.8.

The Company's most significant subsidiaries as of December 31, 2008 were:

Name	Legal seat ownership	Country	2008 ownership	2007 ownership	2006 ownership
Crucell Holland B.V.	Leiden	the Netherlands	100%	100%	100%
U-BiSys B.V.	Utrecht	the Netherlands	100%	100%	100%
ChromaGenics B.V.	Amsterdam	the Netherlands	100%	100%	100%
Berna Biotech AG	Bern	Switzerland	100%	100%	100%
Berna Biotech España SA	Madrid	Spain	100%	100%	100%
Berna Biotech Italia Srl	Milano	Italy	100%	100%	100%
Etna Biotech Srl	Catania	Italy	—	100%	100%
Berna Rhein B.V.	Leiden	the Netherlands	100%	100%	100%
Rhein Vaccines B.V.	Maastricht	the Netherlands	—	—	100%
Berna Biotech Korea corp.	Seoul	Korea	100%	100%	100%
Crucell Holding Inc.	Wilmington, DE	United States	100%	100%	100%
Crucell Vaccines Inc.	Wilmington, DE	United States	100%	100%	100%
Crucell Biologics Inc.	Wilmington, DE	United States	100%	100%	100%
SBL Vaccin Holding AB	Stockholm	Sweden	—	100%	100%
SBL Vaccin AB	Stockholm	Sweden	100%	100%	100%
Vitec AB	Stockholm	Sweden	—	100%	100%

Joint venture and associated companies (not consolidated)

Name	Joint venture/ associate ownership	Legal seat ownership	Country	2008 ownership	2007 ownership	2006 ownership
Percivia LLC	Joint venture	Cambridge, MA	United States	50.0%	50.0%	50.0%
ADImmune corp.	Associated company	Taipei	Republic of China	11.8%	20.0%	—
Kenta Biotech AG *	Sold	Bern	Switzerland	—	22.0%	37.0%
Pevion Biotech AG **	Sold	Bern	Switzerland	—	—	50.0%

* On July 3, 2008 the Group sold all of the 2,625,000 shares it owned in Kenta Biotech AG to Ingro Finanz AG.

** On November 5, 2007 the Group sold all shares it owned in Pevion Biotech AG to other shareholders of Pevion Biotech.

1.2 Basis of preparation

The consolidated financial statements of the Group have been prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the IASB and are prepared on a historical cost basis unless stated otherwise. As the Group adopted IFRIC 14 there are no differences between IFRS applied by the Group and IFRS as endorsed by the EU.

As permitted by article 362 of Book 2 of the Netherlands Civil Code, the company financial statements have been prepared applying the same IFRS accounting policies as used in the consolidated financial statements. In conformity with article 402, Book 2 of the Dutch Civil Code, the Company income statement is presented in abbreviated form.

The consolidated financial statements for the year ended December 31, 2008 on form 20-F were authorized for issue in accordance with a director's resolution on April 17, 2009.

Foreign currency translation
The functional and presentation currency of the Company is the Euro. All values are rounded to the nearest thousand (€ 000) unless indicated otherwise.

Each entity in the group determines its own functional currency based on the primary economic environment in which the entity operates. Items included in the financial statements of each entity are measured using that functional currency. Transactions in foreign currencies are initially recorded in the functional currency rate ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies are retranslated at the functional currency rate of exchange ruling at the balance sheet date. All differences are taken to the income statement. Non-monetary items that are measured in terms of historical cost in a foreign currency are translated using the exchange rates as at the dates of the initial transactions. Non-monetary items measured at fair value in a foreign currency are translated using the exchange rates at the date when the fair value was determined.

At the reporting date, the assets and liabilities of subsidiaries with different functional currencies are translated into Euro at the rate of exchange ruling at the balance sheet date and their income statements and cash flow statements are translated into Euro at the weighted average exchange rates for the year. The exchange rate differences arising on the translation are taken directly to the translation reserve, a separate component of equity.

1.3 Basis of consolidation

The consolidated financial statements comprise the financial statements of the Company and its subsidiaries per December 31 and for the period then ended. The financial statements of the subsidiaries are prepared for the same reporting year as the Group, using consistent accounting policies. All intra-group balances and transactions are eliminated in full.

Subsidiaries
Subsidiaries are entities controlled by the Company. Control is achieved where the Company has the power to govern the financial and operational policies of an enterprise so as to obtain benefits from its activities. Subsidiaries are fully consolidated from the date of acquisition, which is the date on which the Group obtains control, and continue to be consolidated until the date such control ceases.

Minority interests represent the portion of profit or loss for the year and net assets at the end of the year not held by the Group and are presented separately in the consolidated income statement and within equity in the consolidated balance sheet, separately from the equity attributable to equity holders of the parent.

Joint ventures
A joint venture is a contractual arrangement whereby two or more parties undertake an economic activity that is subject to joint control. A jointly controlled entity is a joint venture that involves the establishment of a separate entity in which each venturer has an interest. The Group recognizes its interest in joint ventures using the equity method. Under the equity method, the investment in the joint venture is carried in the balance sheet at cost plus post-acquisition changes in the Group's share of net assets of the joint venture. The income statement reflects the share of the results of operations of the joint venture. Periodically the Group determines whether it is necessary to recognize an impairment loss with respect to the Group's net investment in the joint venture. The reporting dates of the joint ventures are the same as those of the Group and the accounting policies of the joint ventures conform to those used by the Group.

Associates
The Group's investments in associates are accounted for under the equity method of accounting and are initially recognized at cost. An associate is an entity in which the Group has significant influence and which is neither a subsidiary nor a joint venture. The reporting dates of the associates are the same as those of the Group and the associates' accounting policies conform to those used by the Group.

1.4 Use of estimates and judgments

The preparation of financial statements requires Management to make judgments, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets, liabilities, income and expenses. Actual results may differ from these estimates.

Estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognized in the period in which the estimate is revised and in any future periods affected. In particular, information about significant areas of estimation uncertainty and use of critical judgments in applying accounting policies that have the most significant effect on the amount recognized in the financial statements are described below.

Revenue recognition
Sales transactions concluded by the Group may be complex as the underlying sales agreements can contain multiple components whose accounting treatment may be affected by the other components. Reviewing these agreements requires due care and a degree of management's judgment. Revenue is not recognized before it is assessed that significant risks and rewards of ownership have been transferred and that the Group retains no continuing managerial involvement or effective control over the goods sold. For some transactions this can result in cash receipts being initially recognized as deferred income and then released to income over subsequent periods on the basis of the performance of the conditions specified in the agreement. The Group is also subject to various licensing agreements that contain milestones that may only be recognized if they are 'substantive'. Determining whether a milestone is substantive also requires management judgment.

Valuation of deferred tax assets and liabilities
Determination of income taxes in jurisdictions in which the Group operates, requires exercising judgment. This involves estimating the actual current tax exposure together with assessing the valuation of carry forward losses and temporary differences. The temporary differences mainly relate to intangible assets, property, plant and equipment, inventories and pension assets.

In assessing the valuation of the deferred tax assets and liabilities the following items are considered: the future taxable profit projections, historical results, tax planning strategies, changes (substantially) enacted in tax laws and the specific timing of the recovery of deferred tax positions. In the event that actual results differ from these estimates due to future changes in income tax law or after final review of our tax returns by tax authorities, the Group may need to adjust the valuation of our deferred tax assets and liabilities, which could materially impact the financial position and results of operations. Management believes that the estimates are reasonable.

As at December 31, 2008, the Group had unrecognized tax carry forward losses of € 172,732 (2007: € 254,511, 2006: € 222,338) that are available, with certain restrictions in time, for offset against future taxable profits of the companies in which the losses arose. Management assessed the likelihood that the carry forward losses will be recovered from future taxable profit. To the extent Management believes that recovery is probable, a deferred tax asset was recognized, which at December 31, 2008

was € 9,060 (2007: € 678, 2006: € 749). To the extent the likelihood of recovery of deferred tax assets changes, an expense or a gain within the tax charge in our income statement for the relevant period will be included.

Accounting for business combinations
Business combinations are accounted for using the purchase method. This involves recognizing identifiable assets (including previously unrecognized intangible assets) and liabilities (including contingent liabilities) of the acquired business at the estimated fair values at acquisition date. Judgments, made in identifying and valuating assets and liabilities assumed in a business combination and in determining the useful life of any acquired assets, can significantly affect both current period as future periods operating results. Estimated fair values in a business combination are based on information available at the date that the purchase price allocation is completed. Assets and liabilities may be adjusted or recognized retrospectively within the period of one year if management receives additional information about facts and circumstances that existed at the acquisition date.

Goodwill is measured as the excess of the total consideration over the net of the acquisition-date amounts of the identifiable assets acquired and the liabilities assumed. Goodwill includes intangible assets that were identified in a business combination, but not valued separately because the assets were either not separable or could not be measured reliably. Assets identified and included as part of goodwill can be specific customer relationships, supply contracts not meeting the recognition requirements or the workforce acquired. Goodwill recognized can significantly affect both current period as future periods operating results as goodwill is subject to an annual impairment review and not to periodical amortization.

Goodwill at December 31, 2008 amounted to € 46,076 compared to € 44,377 at the end of 2007. Goodwill increased due to a strengthening of the foreign currencies underlying the investment in the foreign operations. The increase is mainly caused by the appreciation of the Swiss Franc and the US Dollar against the Euro in 2008.

Impairment reviews of property, plant and equipment, intangible assets and goodwill
An asset's recoverable amount is the higher of the asset's fair value less costs to sell and its value in use. For goodwill, the recoverable amount is tested at the level of the cash generating unit. The Group starts its impairment reviews of property, plant and equipment, intangible assets and goodwill by determining the asset's (or cash generating unit's) recoverable amount based on the fair value less costs to sell of an asset. If the fair value less costs to sell does not exceed the carrying amount, the Group will also consider the value in use before an asset is impaired. The best evidence of an asset's fair value less costs to sell is a price in a binding sale agreement in an arm's length transaction, adjusted for incremental costs that would be directly attributable to the disposal of the asset. However for most of the Group's assets there are typically no observable market prices as the assets have a level of specificity for which no active market exists. The fair values less costs to sell are predominantly based on discounted net present value calculations that use assumptions applicable in the current market. Key assumptions are those regarding the discount rates, the estimated terminal growth rate, expected changes to market share and the selling prices and costs in the forecasted period. Where applicable, the forecasted cash flows for pre-clinical programs are adjusted for the risk of failure of the program.

Property, plant and equipment and intangible assets
The Group assesses for its property, plant and equipment and intangible assets at each reporting date whether there is an indication that an asset may be impaired. If there is such an indication of impairment or when an annual impairment test for an asset is required, an impairment test is performed.

In the year ended December 31, 2006, an impairment loss of € 19,568 was recognized for two buildings, including installed equipment, that were acquired in the business combination with Berna Biotech AG. Both buildings are located in Switzerland. Berna Biotech AG performed contract manufacturing and conducted a candidate vaccine development program in those buildings. The development of the candidate vaccine and the contract manufacturing were phased out during 2007. The buildings are specially configured for biotechnology purposes and it is impracticable to separate the equipment from the buildings. Since at the time there was no direct use for these buildings for any of the Group's other activities, no market for the sale of the buildings to third parties and no expectation that these buildings

could be utilized in the foreseeable future, an impairment was recorded for the total carrying amount of € 19,568 as at December 31, 2006.

In the fourth quarter of 2006 an impairment loss of € 10,848 was recognized on the in-process research and development of the Tetra vaccine which was acquired in February 2006 when the Company acquired Berna Biotech AG. Management decided to stop the development of Tetra after Quinvaxem received approval by the WHO. Consequently, the carrying value of Tetra was impaired for the total amount of € 10,848.

An impairment loss recognized in prior periods for an asset other than goodwill shall be reversed if, and only if, there has been a change in the estimates used to determine the asset's recoverable amount since the last impairment loss was recognized. In the first quarter of 2008, the Group entered into an exclusive agreement with Wyeth Pharmaceuticals. The Group develops and manufactures certain components of a vaccine for use by Wyeth in clinical studies. The contract manufacturing takes place in one of the two buildings that was impaired in 2006, as discussed above. The Group reassessed the recoverable amount of the asset and reversed € 5,219 of the previously recognized impairment loss in the 2008 financial statements.

In the fourth quarter of 2008, the Group also recognized an impairment charge of € 331 for the animal housing facility in Bern, Switzerland, that is no longer in use.

Goodwill
Goodwill is reviewed annually or more frequently when changes in circumstances indicate that the carrying amount may be impaired. The discounted net present value calculations are derived from the Group's most recent long range plan, which forecasts the period for the next five years. Beyond this five year window, cash flows are extrapolated based on the estimated terminal growth rate.

Management exercised judgment in determining the segments and the subsequent allocation of the goodwill. In 2008, the Group reorganized its reporting structure in a way that changes the composition of one or more cash-generating units to which goodwill has been allocated, as the Vaccines and Proteins business units were integrated. In the prior year, all goodwill was allocated to the Vaccines Unit. As a result of the change in composition, Management had to reallocate the goodwill and decided to assign all goodwill to the 2006 business acquisitions that led to the recognition of the goodwill. Management decided not to allocate the goodwill to the individual business acquisitions as the operations are integrated and the allocation would be arbitrary.

Valuation of defined benefit plans
Under defined benefit plans, the pension entitlements are calculated using the projected unit credit actuarial method. The pension liability recognized in the balance sheet is the present value of the defined benefit obligation at the balance sheet date, less the fair value of the plan assets after adding or subtracting unrecognized actuarial gains or losses and past-service costs.

The defined benefit obligation is calculated separately for each plan by estimating the amount of future benefit that employees have earned in return for their service in the current and prior periods. That benefit is discounted to determine its present value and any unrecognized past service costs and the fair value of any plan assets are deducted.

The weighted average of the principal assumptions used in determining the employee benefit obligations for the defined benefit plans of the Group are shown below:

	2008	2007	2006
Discount rate	**3.37%**	3.40%	3.32%
Expected return on plan assets	**4.53%**	4.53%	4.55%
Future salary increases	**1.19%**	1.22%	1.19%
Future pension increases	**0.71%**	0.78%	0.66%

Share based payments
Option plans
The Company operates share-based payment programs, whereby in consideration for equity instruments both employees and non-employees render services.

The cost of equity-settled share-based option programs are measured by reference to the fair value at the date on which they are granted. The Company accounts for its stock options under the fair value method. The following weighted average assumptions were used in determining the fair value of the stock options.

Year ended December 31,	2008	2007	2006
Risk-free interest rate	**4.3%**	4.1%	3.6%
Expected dividend yield	**–**	–	–
Expected volatility	**36.7%**	33.3%	41.8%
Expected life (years)	**4.76**	4.25	4.25

Expected volatilities are based on historical volatilities of the Company's stock measured over a period commensurate with the expected term of the grants. The expected term used is based on the anticipated exercise behavior. Dividend yields used are based on historical information as to dividends declared by the Company. Risk-free interest rates used are equal to the implied yield available on zero-coupon Dutch government bonds with a remaining term equal to the expected term of the share-based instrument.

Some of our share-based option programs include specific market-based conditions that are estimated at the time of the grant, as IFRS 2 does not allow updates to the original estimate for market-based conditions during the vesting period. Estimates of market based conditions that have an effect on the fair values of any shares or options allocated in our share based payment plans are share price growth on the stock markets and our Total Shareholder Return ('TSR') compared to a index of biotech companies. TSR reflects the return received by a shareholder, taking into account both the change in share price and dividends received, while assuming dividends are re-invested in the Company.

Recognition of provisions for litigations and claims
Provisions are recognized when the Group has a present obligation (legal or constructive) as a result of a past event, it is probable that an outflow of resources embodying economic benefits will be required to settle the obligation and a reliable estimate can be made of the amount of the obligation. Management uses judgment in determining the provision for litigations and exposure to contingent liabilities related to pending litigation or other outstanding claims. Judgment is used in assessing the likelihood that a pending claim will succeed or a liability will arise and in quantifying the possible range of the final settlement.

The Group is subjected to (potential) lawsuits and other legal proceedings, resulting from the ordinary course of business. The current status of pending proceedings has been reviewed with legal counsel. Upon consideration of known relevant facts and circumstances, provisions were recognized for losses that are considered to be more likely than not and that can reasonably be estimated as of the balance sheet date.

Valuation of inventories
Inventories are stated at the lower of cost and net realizable value. Management exercises judgment in determining the allowance for obsolete inventory. Inventories are usually written down to net realizable value item by item. In some circumstances, however, it may be appropriate to group similar or related items. In these cases, the Group considers numerous items, which include test results by quality control, review by local supply chain, historic scrapping and rejection percentages per product and the current product portfolio. The allowance recognized in 2008 is € 3,218 (2007: € 6,428).

1.5 Changes in accounting policies

1.5.1 New adopted accounting policies in the financial year 2008

IFRIC 14, 'IAS 19 – The limit on a defined benefit asset, minimum funding requirements and their interactions', as issued by the IASB is effective in periods beginning on or after January 1, 2008. This interpretation is endorsed by the EU with the change that it should be applied at the latest, as from the commencement date of its first financial year starting after 31 December 2008. The difference in the effective date would for the Group cause a difference in equity and results between IFRS as issued by the IASB and IFRS as endorsed by the EU. Foreign private issuers that are unable to assert compliance with IASB-issued IFRS have to reconcile their financial information to US GAAP. To avoid a mandatory reconciliation between IFRS as endorsed by the EU and US GAAP, the Group adopted IFRIC 14 effective as of January 1, 2008.

The interpretation provides guidance on assessing the limit of the surplus in a defined benefit pension fund that can be recognized as an asset. It also explains how the pension asset or liability may be affected by a statutory or contractual minimum funding requirement. The pension fund in Switzerland has a minimum funding requirement with economic benefits from overfunding being available as a reduction of future contributions. The application of the interpretation results in an increase in the assets recorded on the Group's balance sheet and a corresponding increase in the Group's equity.

As required by the transition provisions of IFRIC 14, the Group has applied the revised standard retrospectively as of the beginning of the first period presented in the first financial statements to which the interpretation applies. The impact on the December 31, 2008, 2007 and 2006 consolidated balance sheets and the consolidated income statements are as follows:

In thousands of Euro

	2008			2007			2006		
	Before IFRIC 14	Impact	IFRIC 14 adopted	Before IFRIC 14	Impact	After retrospective application	Before IFRIC 14	Impact	After retrospective application
Income statement									
Gross margin	**121,402**	**—**	**121,402**	68,902	—	68,902	41,078	—	41,078
Operating expenses	**(132,367)**	**2,676**	**(129,691)**	(129,787)	3,869	(125,918)	(148,341)	467	(147,874)
Profit (loss) before tax	**3,600**	**2,676**	**6,276**	(48,987)	3,869	(45,118)	(98,116)	467	(97,649)
Income Tax	**8,885**	**(575)**	**8,310**	3,040	(832)	2,208	10,551	(100)	10,451
Profit/(loss) for the year	**12,485**	**2,101**	**14,586**	**(45,947)**	**3,037**	**(42,910)**	**(87,565)**	**367**	**(87,198)**
Balance sheet									
Pension asset recognized	**759**	**7,853**	**8,612**	2,479	4,918	7,397	2,555	746	3,301
Deferred tax liabilities	**(15,297)**	**(1,688)**	**(16,985)**	(28,210)	(1,057)	(29,267)	(33,586)	(160)	(33,746)
Equity attributable to equity holders of the parent	**(447,327)**	**(6,165)**	**(453,492)**	(437,242)	(3,861)	(441,103)	(497,300)	(586)	(497,886)
Profit (loss) per share – basic	**0.21**	**0.01**	**0.22**	**(0.71)**	**0.05**	**(0.66)**	**(1.53)**	**0.01**	**(1.52)**
Profit (loss) per share – diluted	**0.21**	**0.01**	**0.22**	**(0.71)**	**0.05**	**(0.66)**	**(1.53)**	**0.01**	**(1.52)**

The following standard was not yet effective at December 31, 2008, but has been early adopted by the group:

- IFRS 8, 'Operating segments' (effective from January 1, 2009). IFRS 8 replaces IAS 14 'Segment reporting' and aligns segment reporting with the requirements of the US standard SFAS 131, 'Disclosures about segments of an enterprise and related information'. The new standard requires a 'management approach', under which segment information is presented on the same basis as that used for internal reporting purposes. The Group applies IFRS 8 from January 1, 2007. The impact of the early adoption is described in note 4 'Segment information'.

1.5.2 Other new accounting pronouncements

The following amendments to existing standards and interpretations were not yet effective at the balance sheet date and were not early adopted by the Group:

- IAS 23 (Amendment), 'Borrowing costs' (effective from January 1, 2009). The amendment requires an entity to capitalize borrowing costs directly attributable to the acquisition, construction or production of a qualifying asset (one that takes a substantial period of time to get ready for use or sale) as part of the cost of that asset. The option of immediately expensing those borrowing costs will be removed. The Group will apply IAS 23 (Amended) from January 1, 2009, but adoption will have no impact on the Group's financial statements as borrowing costs directly attributable to qualifying assets are already capitalized in line with the allowed alternative treatment of IAS 23.
- IAS 1 (Revised), 'Presentation of financial statements (effective from January 1, 2009). The revised standard will prohibit the presentation of items of income and expenses (that is, 'non-owner changes in equity') in the statement of changes in equity, requiring 'non-owner changes in equity' to be presented separately from owner changes in equity. All non-owner changes in equity will be required to be shown in a performance statement, but entities can choose whether to present one performance statement (the statement of comprehensive income) or two statements (the income statement and statement of comprehensive income). The Group will apply IAS 1 (Revised) from January 1, 2009.
- IFRS 2 (Amendment), 'Share-based payment' (effective from January 1, 2009). The amended standard deals with vesting conditions and cancellations. It clarifies that vesting conditions are service conditions and performance conditions only. Other features of a share-based

payment are not vesting conditions. These features would need to be included in the grant date fair value for transactions with employees and others providing similar services; they would not impact the number of awards expected to vest or valuation thereof subsequent to grant date. All cancellations, whether by the entity or by other parties, should receive the same accounting treatment. The Group will apply IFRS 2 (Amendment) from January 1, 2009 and currently assesses the impact of the amended standard.

- IFRS 3 (Revised), 'Business combinations' (effective from July 1, 2009). The revised standard continues to apply the acquisition method to business combinations, with some significant changes. For example, all payments to purchase a business are to be recorded at fair value at the acquisition date, with contingent payments classified as debt subsequently re-measured through the income statement. There is a choice on an acquisition-by-acquisition basis to measure the non-controlling interest in the acquiree either at fair value or at the non-controlling interest's proportionate share of the acquiree's net assets. All acquisition-related costs should be expensed. The Group will apply IFRS 3 (Revised), 'Business combinations' from January 1, 2010 and currently assesses the impact of the amended standard.
- IAS 36 (Amendment), 'Impairment of assets' (effective from January 1, 2009). The amendment is part of the IASB's annual improvements project published in May 2008. Where fair value less costs to sell is calculated on the basis of discounted cash flows, disclosures equivalent to those for value-in-use calculation should be made. The Group will apply the IAS 36 (Amendment) and provide the required disclosure where applicable for impairment tests from January 1, 2009.

Not all amendments to existing standards and interpretations that are not yet effective and not early adopted by the Group have been listed above as they may not be applicable to the operations of the Group or are not likely to have a significant impact on the financial statements of the Group. The Group currently assesses in detail the impact of the amendments and interpretations.

2 Summary of significant accounting policies

2.1 Revenue recognition

General

In general, revenue is recognized to the extent that it is probable that the economic benefits will flow to the Group and the amount of revenue and the costs (to be) incurred in the transaction can be measured reliably. Revenue is measured at the fair value of the consideration received excluding discounts, rebates, value added taxes and duties.

Revenues are recognized on a gross basis when the Group acts as the principal in an arrangement, and recognized on a net basis when the Group acts as agent.

Goods or services traded for items of a similar nature are not regarded as transactions that generate revenue. Goods or services traded for dissimilar items are regarded as transactions that generate revenue.

Product sales

Revenue from product sales is recognized when:

- Significant risk and rewards of ownership of the products have passed to the buyer;
- The Group does not retain either managerial involvement to the degree usually associated with ownership or effective control over the goods sold;
- The amount of revenue and the costs (to be) incurred in the transaction can be measured reliably; and
- It is probable that the economic benefits associated with the transaction will flow to the Group.

Products could include a specific right to return, either pursuant to the sales contract or local law. Revenue from that sale is recognized at time of sale only if all of the following conditions are met in addition to the general revenue recognition terms described above:

- The customer is obligated to pay and that obligation is not contingent on resale of the product;
- The customer's obligation to pay will not be changed in the event of theft or physical destruction or damage of the product;

- The customer acquiring the product for resale has economic substance apart from that provided by the Group, e.g. the customer sells other products besides the products the Group delivers to it;
- The Group does not have significant future performance obligations to directly ensure resale of the product by the buyer; and
- The amount of future returns can be reasonably estimated.

Revenue and cost of sales that are not recognized at the time of the sale because the foregoing conditions were not met are recognized on the earlier of either the substantial expiration of the customer's right to return the product or the subsequent satisfaction of those conditions.

License revenues
The Group recognizes initial fees to the licensing of the technology as revenues over the period of the significant continuing performance obligations, if any, and upon transfer of the significant risks and rewards to the buyer.

Under certain arrangements, the Group has no continuing performance obligations after delivery of the associated technology under the license agreement or any other arrangement with the licensee. In such arrangements, initial license fees are recognized as revenue when significant risks and rewards pass to the buyer, which is the moment the transfer of developed technology is completed. The Group's arrangements provide for continuing support of its technology at standard consulting rates. Revenues derived from consulting services that are not essential to licensee's ability to use the Group's technology, are recognized as earned during the period that the consulting services are performed.

In certain arrangements, the Group collaborates with third parties to develop novel products or processes using its proprietary technology. These arrangements generally include an initial license fee upon the delivery of the proprietary technology and additional fees for providing ongoing research and development activities. The research and development activities performed are substantive and critical to the licensees' exploitation of the delivered technology. When significant risks and rewards pass to the buyer, initial fees from these arrangements are recognized as revenues over the period of continuing performance obligations.

Additional fees from research and development activities are recognized as revenues earned over the period of the development collaboration or the manufacturing obligation. All fees received under collaboration agreements are non-refundable.

Certain of the Group's license agreements provide for additional non-refundable fees to be paid to the Group upon the achievement of milestones by the licensee. These milestone payments may be included in license agreements regardless of whether the Group has continuing performance obligations under a particular agreement.

For license agreements where there are no continuing performance obligations, milestone revenue is recognized when those amounts become due and payable upon achievement of the milestone. The licensee has to confirm the achievement of a milestone in writing before the revenue is recognized.

The Group also has license agreements with continuing performance obligations. License revenues from the achievement of these research and development milestones, if deemed substantive (as described below), are recognized as revenue when the milestones are achieved, and the milestone payments are due and collectible under the terms of the agreement.

Milestones are considered 'substantive' if all of the following conditions are met:

- The milestone payments are non-refundable under the terms of the agreement;
- Achievement of the milestone involved a degree of risk and was not reasonably assured at the inception of the arrangement;
- Substantial effort is involved in achieving the milestone;
- The amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with achievement of the milestone; and
- A reasonable amount of time passed between the upfront license payment and the first milestone payment as well as between each subsequent milestone payment.

If any of these conditions are not met, the Group would recognize the proportionate amount of the milestone payment upon receipt as revenue that

corresponds with the percentage of work already completed. The remaining portion of the milestone payment would be deferred and recognized as revenue as performance obligations are completed.

In addition to the initial fee, the Group's arrangements generally provide that the licensee makes semi-annual or annual payments (called 'license maintenance fees') to maintain the license for a subsequent term. Generally, licensees may terminate the license and related maintenance fees upon 30 to 90 days' notice. License maintenance fees are recognized as revenues when the amounts become fixed and payable. The aggregate of license maintenance fees paid are generally deductible from any earned royalty payments which may be due on future product sales of the licensee, if any, under the license agreement. Royalties are recognized as revenue when they become fixed and payable.

Service fees
As part of various collaboration agreements, the Group receives service fees for work performed under such agreements. The Group does not retain the residual interest on products developed under the agreements and will normally not have ownership of intellectual property rights on these products. Revenues and related costs associated with completing performance services are recognized when the service is completed and the collectibility of the receivable is deemed probable. Revenues associated with time and material performance contracts are recognized when the costs incurred and the costs to complete the transaction can be measured reliably.

2.2 Cost of product sales and cost of service fees

Cost of product sales and cost of service fees both comprise direct labor, materials and overhead costs, incurred in performing work under various collaboration agreements that directly relate to revenues earned.

2.3 Other operating income

Government grants
The Group receives certain government grants that support research efforts in defined projects. These grants generally provide for reimbursement of approved costs incurred as defined in various grants. Income associated with these grants is recognized when costs under each grant are incurred in accordance with the terms and conditions of the grant and the collectibility of the receivable is deemed probable and there is reasonable assurance that attaching conditions will be achieved. Where the grant relates to an expense item, it is recognized as income over the period necessary to match the grant on a systematic basis to the costs that it is intended to compensate.

Other income
Other income mainly consists of the reimbursement of development costs and funding by non-governmental agencies, but also includes non-core business transactions such as the sale of property, plant and equipment and income generated from training courses.

2.4 Research and Development expenses

Expenditure on research activities is recognized as an expense in the period in which it is incurred. Internally generated intangible assets arising from the Group's development activities are recognized if all of the recognition criteria for internally generated intangible assets are met, including:

- An asset is created that can be identified;
- It is probable that the asset created will generate future economic benefits; and
- The development cost of the asset can be measured reliably.

Product registration fees will, in principle, meet these recognition requirements. Where no internally generated intangible asset can be recognized, development expenditure is recognized as an expense in the period in which it is incurred. Research and development expenses consist of personnel expenses, laboratory expenses, technology purchases, patent related fees, technology license fees, depreciation and amortization of tangible and intangible assets related to research and development, and lease expenses for lab space and equipment leases. Research and development expenses also include fees paid to third parties who conduct research on behalf of the Group.

2.5 Taxes

Current tax
Current tax assets and liabilities for the current and prior periods are measured at the amount expected to be recovered from or paid to the tax authorities. The tax rates and tax laws used to compute the amount are those that are enacted, or substantially enacted, at the balance sheet date. Current income tax relating to items recognized directly in equity is recognized in equity and not in the income statement. Current tax assets and current tax liabilities are offset, if a legally enforceable right exists to offset the recognized amounts and the Group intends either to settle on a net basis, or to realize the asset and settle the liability simultaneously.

Deferred tax
Deferred income tax is calculated using the asset and liability method on temporary differences at the balance sheet date between the tax bases of assets and liabilities and their carrying amounts under IFRS. Deferred tax liabilities are recognized for all taxable temporary differences, except:

- Where the deferred tax liability arises from the initial recognition of goodwill or of an asset or liability in a transaction that is not a business combination and, at the time of the transaction, affects neither the accounting profit nor taxable profit or loss; and
- In respect of taxable temporary differences associated with investments in subsidiaries, associates and interests in joint ventures, where the timing of the reversal of the temporary differences can be controlled and it is probable that the temporary differences will not reverse in the foreseeable future.

Deferred income tax assets are recognized for all deductible temporary differences and carry-forwards of unused tax credits and unused tax losses, to the extent that it is probable that taxable profit will be available against which the deductible temporary differences, and the carry-forwards of unused tax credits and unused tax losses, can be utilized.

The unrecognized deferred income tax assets are reassessed at each balance sheet date and are recognized to the extent that it has become probable that future taxable profit will allow the deferred tax asset to be recovered. Deferred income tax assets and liabilities are measured at the tax rates that are expected to apply to the year when the asset is realized or the liability is settled, based on tax rates (and tax laws) that have been enacted at the balance sheet date.

Income tax relating to items recognized directly in equity is recognized in equity and not in the income statement. Deferred tax assets and deferred tax liabilities are offset, if a legally enforceable right exists to set off current tax assets against current tax liabilities and the deferred taxes relate to the same taxable entity and the same taxation authority.

2.6 Profit/ (loss) per share

Basic net profit/ (loss) per share is computed based on the weighted average number of ordinary shares outstanding during the period. Diluted net profit/ (loss) per share is computed based on the weighted average number of ordinary shares outstanding, including the dilutive effect of stock options, if any.

2.7 Cash and cash equivalents

Cash and cash equivalents include cash in hand and all highly liquid investments with maturities of three months or less that are convertible to a known amount of cash and bear an insignificant risk of change in value.

2.8 Financial assets

The Group classifies its financial assets in the following categories: at fair value through profit or loss, loans and receivables, and available for sale. The Group has no held-to-maturity investments. The classification depends on the purpose for which the financial assets were acquired. Management determines the classification of its financial assets at initial recognition.

Financial assets at fair value through profit or loss
Financial assets at fair value through profit or loss are financial assets held for trading. A financial asset is classified in this category if acquired principally for the purpose of selling in the short-term. Derivatives are also categorized as held for trading unless they are designated as formal hedges. Assets in this category are classified as current assets.

Loans and receivables
Loans and receivables are non-derivative financial assets with fixed or determinable payments that

are not quoted in an active market. They are included in current assets, except for maturities greater than 12 months after the balance sheet date. These are classified as non-current assets. The Group's loans and receivables comprise cash and cash equivalents, trade accounts receivable, other financial assets and other current assets in the balance sheet.

Trade accounts receivable, other current assets and other financial assets
Trade accounts receivable, other current assets and other financial assets are recognized initially at fair value and subsequently measured at amortized cost using the effective interest method, less provision for impairment. A provision for impairment of trade receivables is established when there is objective evidence that the group will not be able to collect all amounts due according to the original terms of the receivables.

Available-for-sale financial assets
Available-for-sale investments are those non-derivative financial assets that are designated as available-for-sale. After initial measurement, available-for-sale financial assets are measured at fair value with unrealized gains or losses being recognized directly in equity in the net unrealized gains reserve. When the investment is disposed of, the cumulative gain or loss previously recorded in equity is recognized in the income statement. Available-for-sale investments are included in non-current assets unless management intends to dispose of the investment within 12 months of the balance sheet date.

Derecognition of financial assets
A financial asset is derecognized when:

- The rights to receive cash flows from the asset have expired;
- The Group retains the right to receive cash flows from the asset, but has assumed an obligation to pay them in full without material delay to a third party under a 'pass through' arrangement; or
- The Group has transferred its rights to receive cash flows from the asset and either has transferred substantially all the risks and rewards of the asset, or has neither transferred nor retained substantially all the risks and rewards of the asset, but has transferred control of the asset.

2.9 Derivative financial instruments and hedging

Derivative financial instruments are initially recognized at fair value on the date a derivative contract is entered into and are subsequently remeasured at fair value. The fair value is based on the market prices of the instruments. Derivatives are carried as assets when the fair value is positive and as liabilities when the fair value is negative. To the extent that no formal hedge accounting is applied, any gains and losses arising from changes in the fair value of the instruments are recognized in the income statement during the period in which they arise.

The Group applies formal hedge accounting for specific forward derivative instruments that are designated as cash flow hedges. At the inception of derivative instruments, the relationship between the derivative and the underlying financial instrument, as well as the objective of the risk management and the strategy for undertaking transactions are documented. In the documentation it is also stated whether the hedge relationship is expected to be highly effective (prospective and retrospective) and how the effectiveness is tested.

Changes in the fair value of a highly effective derivative, that is designated and qualifies as a cash flow hedge, are recorded in equity for the effective part, until the profit or loss is affected by the variability in cash flows of the designated hedged item. The ineffective part of the cash flow hedge is recognized in the income statement.

2.10 Inventories

Inventories are stated at the lower of cost or net realizable value. The cost of inventories includes expenditures for materials acquired, directly attributable costs and related production overhead expenses. Net realizable value is determined using the estimated selling price in the ordinary course of business, less estimated costs of completion and the estimated costs necessary to make the sale. Allowances are made for obsolete inventory.

2.12 Property, plant and equipment

Property, plant and equipment is stated at cost, excluding the costs of day-to-day servicing, less accumulated depreciation and accumulated impairment in value. The cost of replacing a part of a plant or equipment is capitalized if the

recognition criteria are met. Where an item of property, plant and equipment comprises major components having different useful lives, they are accounted for as separate items of property, plant and equipment. Depreciation is charged to the income statement on a straight-line basis over the estimated useful life of the assets:

- Freehold land is not depreciated;
- Buildings: 20 to 50 years;
- Computer equipment: three years;
- Furniture and laboratory equipment: five years; and
- Leasehold improvements: the shorter of the lease term and ten years.

An item of property, plant and equipment is derecognized upon disposal or when no future economic benefits are expected from its use. Any gain or loss arising on derecognition of the asset is included in the income statement. The asset's residual values, useful lives and methods are reviewed, and adjusted if appropriate, at each financial year-end.

Borrowing costs
Borrowing costs directly attributable to the acquisition, construction or production of qualifying assets are added to the cost of these assets until they are substantially ready for their intended use. Qualifying assets are those assets that necessarily take a substantial period of time to be completed for their intended use. All other borrowing costs are recognized as an expense in the income statement when incurred.

2.13 Intangible assets

Intangible assets acquired are measured at cost on initial recognition. The cost of intangible assets acquired in a business combination is the fair value at the date of acquisition. Following initial recognition, intangible assets are carried at cost less any accumulated amortization and accumulated impairment losses. Internally generated intangible assets are not capitalized if the recognition requirements are not met, in which case the expenses associated with generating the intangible asset are recognized in the income statement. The useful lives of intangible assets are assessed to be either finite or indefinite. Intangible assets with finite lives are amortized over their useful lives. The amortization period and the amortization method are reviewed at least at each financial year-end. Changes in the expected useful life or the expected pattern of consumption of future economic benefits embodied in the asset are accounted for by changing the amortization period or method, and treated as changes in accounting estimates. The amortization expense on intangible assets with finite lives is recognized in the income statement consistent with the function of the intangible asset.

The estimated useful life of the assets is as follows:

- Patents and licenses: one year to 20 years;
- Customer lists: three years;
- Developed technology: five years to 20 years; and
- In-process R&D is not depreciated until completion of the asset.

2.14 Goodwill and business combinations

Business combinations are accounted for using the purchase method. This involves recognizing identifiable assets (including previously unrecognized intangible assets) and liabilities (including contingent liabilities, but excluding future restructuring) of the acquired business at fair value. Goodwill acquired in a business combination is initially measured at cost, which is the excess of the cost of the business combination over the Group's interest in the net fair value of the acquiree's identifiable assets, liabilities and contingent liabilities. Following initial recognition, goodwill is measured at cost less accumulated impairment losses.

Goodwill includes intangible assets that were identified in a business combination, but not valued separately because the assets were either not separable or could not be measured reliably. Assets identified and included as part of goodwill can be specific customer relationships or supply contracts not meeting the requirements for separate recognition and the workforce acquired.

Assigning fair values to the assets and liabilities acquired in a business combination inherently requires the use of estimates. Under IFRS 3 Business Combinations, these fair values can be adjusted up to one year after the acquisition date, which can affect the amount recognized as goodwill.

Goodwill acquired in a business combination is allocated from the acquisition date to each of the Group's cash-generating units that are expected to benefit from the synergies of the combination, irrespective of whether other assets or liabilities of the Group are assigned to those units or groups of units.

Goodwill and fair value adjustments arising on the acquisition of a foreign operation are treated as assets and liabilities of the foreign operation and, if necessary, translated into Euro at the rate of exchange ruling at the balance sheet date.

2.15 Impairment of non-financial assets

The Group assesses non-financial assets at each reporting date to determine whether there is an indication that an asset may be impaired. If any such indication exists, or when annual impairment testing for an asset is required, the Group estimates the asset's recoverable amount. An asset's recoverable amount is the higher of the asset's fair value less costs to sell and its value in use. The recoverable amount is determined for an individual asset, unless the asset does not generate cash inflows that are largely independent of those from other assets or groups of assets. Where the carrying amount of an asset exceeds its recoverable amount, the asset is considered impaired and is written down to its recoverable amount.

An impairment loss recognized in prior periods for an asset other than goodwill shall be reversed if, and only if, there has been a change in the estimates used to determine the asset's recoverable amount since the last impairment loss was recognized. If this is the case, the carrying amount of the asset shall be increased to its recoverable amount, but so that the increased carrying amount does exceed the carrying amount that would have been determined had no impairment loss been recognized for the asset in prior years.

Goodwill is reviewed for impairment annually or more frequently if events or changes in circumstances indicate that the carrying value may be impaired. Impairment is determined for goodwill by assessing the recoverable amount of the cash-generating unit to which the goodwill has been allocated. Where the recoverable amount of the cash-generating unit is less than the carrying amount of the cash-generating unit to which goodwill has been allocated, an impairment loss is recognized. Impairment losses relating to goodwill cannot be reversed in future periods.

2.16 Employee benefits

Pensions
The Group operates both defined benefit plans and defined contribution plans. For defined contribution plans, obligations for contributions are recognized as an expense when they are due. The Group has no obligation to pay further contributions into a defined contribution plan if the fund does not hold sufficient assets to pay all plan benefits.

Under defined benefit plans, the pension entitlements are calculated using the projected unit credit actuarial method. The pension liability recognized in the balance sheet is the present value of the defined benefit obligation at the balance sheet date, less the fair value of the plan assets after adding or subtracting unrecognized actuarial gains or losses and past-service costs.

The defined benefit obligation is calculated separately for each plan by estimating the amount of future benefit that employees have earned in return for their service in the current and prior periods. That benefit is discounted to determine its present value and any unrecognized past-service costs and the fair value of any plan assets are deducted. For each plan the recognized assets are limited to the net total of any cumulative unrecognized net actuarial losses and past-service costs and the present value of any future refunds from the plan or reductions in future contributions to the plan (the 'asset ceiling'). The economic benefit available as a reduction in future contributions is determined as the present value of the estimated future service cost in each year less the estimated minimum funding contributions required in respect of the future accrual of benefits in that year. Actuarial gains and losses in excess of a threshold of the higher of 10% of the pension liabilities and 10% of the fair value of the plan assets are charged or credited to the income statement over the employees' expected average remaining working lives.

Share-based payment transactions
Stock option plans
The Group operates a number of equity-settled, share-based compensation plans, under which the Group receives services from employees as consideration for equity instruments (options) of the Group. The cost of equity-settled transactions with employees is measured by reference to the fair value at the date on which the options are granted.

The maximum amount to be expensed is determined by reference to the fair value of the options granted, excluding the impact of any non-market service and performance vesting conditions. The impact of market conditions on the fair value of options under these plans is estimated on the date of grant using a lattice-based option valuation model. The model calculates the likelihood of achievement of the market-based measures at various levels.

Non-market vesting conditions are included in assumptions about the number of options that are expected to vest. The cost of equity-settled transactions is recognized, together with a corresponding increase in equity, over the period in which the performance and/or service conditions are fulfilled, ending on the date on which the relevant employees become fully entitled to the award ('the vesting date'). The cumulative expense recognized for equity-settled transactions at each reporting date until the vesting date reflects the extent to which the vesting period has expired and the Group's best estimate of the number of equity instruments that will ultimately vest. The income statement charge or credit for a period represents the movement in cumulative expense recognized as at the beginning and end of that period with the offsetting entry recorded in share premium in equity. Every option that is exercised results in the issuance of one ordinary share.

At each balance sheet date, the estimates of the number of options that are expected to vest based on the non-marketing vesting conditions are revised. The Group recognizes the impact of the revision to original estimates, if any, in the income statement, with a corresponding adjustment to equity.

Share based incentive plans
The fair value of share grants is estimated on the date of grant by multiplying the number of shares available to be granted by the fair value of the Company's shares on the grant date. Management assumes any performance goals required by the incentive plan will be achieved and the award will vest in full.

Options granted to non-employees
The cost of options granted to non-employees is recognized at the fair value of the goods or services received, together with a corresponding increase in equity, unless that fair value of the goods or services received cannot be estimated reliably, in which case the fair value is measured by reference to the fair value of the equity instruments granted.

2.17 Interest-bearing loans and borrowings

Short-term financial liabilities consist of all liabilities with maturities up to one year. Long-term financial liabilities are liabilities with maturities over one year. All loans and borrowings are initially recognized at the fair value of the consideration received less directly attributable transaction costs. After initial recognition, interest-bearing loans and borrowings are subsequently measured at amortized cost using the effective interest method. Gains and losses are recognized in the income statement when the liabilities are derecognized as well as through the amortization process. A financial liability is derecognized when the obligation underlying the liability is discharged, cancelled or expired.

2.18 Provisions

Provisions are recognized when there is a present obligation (legal or constructive) as a result of a past event, it is probable that an outflow of resources embodying economic benefits will be required to settle the obligation and a reliable estimate of the obligation can be made. The expense relating to any provision is presented in the income statement net of any reimbursement. If the effect of the time value of money is significant, provisions are discounted. Where discounting is used, the increase in the provision due to the passage of time is recognized as a financial expense.

2.19 Leases

Leases of property, plant and equipment where the Group assumes substantially all the risks and rewards of ownership of the leased asset are classified as finance leases. Finance leases are capitalized at the inception of the lease at the fair value of the leased property or, if lower, at the present value of the minimum lease payments. Lease payments are apportioned between the finance charges and reduction of the lease liability to achieve a constant rate of interest on the remaining balance of the liability. Finance charges are charged directly against income. Capitalized leased assets are depreciated over the shorter of the estimated useful life of the asset or, over the lease term, if there is no reasonable certainty that the Group will own the leased property by the end of the lease term.

Leases where the Group does not assume substantially all the risks and rewards of ownership are classified as operating leases, and are recognized as an expense in the income statement on a straight-line basis over the lease term.

The determination of whether an arrangement is, or contains, a lease is based on the substance of the arrangement and requires an assessment of whether the fulfilment of the arrangement is dependent on the use of a specific asset or assets and the arrangement conveys a right to use the asset.

3 Financial risk management

3.1 Risk management policies

Financial risk management
The Group's activities expose it to a variety of financial risks: market risk (including currency risk, interest rate risk and security price risk), credit risk and liquidity risk. The Group's overall financial risk management seeks to minimize potential adverse effects resulting from the unpredictability of financial markets on the Group's financial performance.

The Group has policies in place that describe the goals of the Group's financial risk management. The adherence to these policies is monitored by corporate treasury. The goals of the Group's corporate treasury function are to reduce the currency exposures in the income statement, optimize return on investments in cash deposits, provide financing services to the business and monitor the financial risks relating to the Group's operations.

The Group has specific operating procedures that prescribe the working practice on relevant specific financial risk management topics such as use of derivative financial instruments, investment of excess liquidity, centralization of cash, balance sheet position forecast procedures and authorization levels.

The Group uses derivative financial instruments to hedge certain foreign currency risk exposures. Corporate Treasury is responsible for using derivatives to mitigate foreign exchange risk arising from anticipated transactions and recognized monetary positions. Corporate treasury does this in close co-operation with the Group's subsidiaries. During the year 2008, the Group adopted a more proactive approach in hedging foreign currency exposures on monetary positions and forecasted transactions. In 2008, the Group applied for the first time formal hedge accounting to address specific economic exposures.

Capital risk management
The Group manages its capital to ensure that it will be able to continue as a going concern. The Group does not have a target debt-to-equity ratio. Although the Group entered into new finance leases and a new loan, the Group is committed to funding the majority of its operations with equity. The Group may choose to renew any loan that becomes payable.

As part of its overall working capital management efforts, the Group agreed with Novartis to extend payment terms on the supply of Quinvaxem antigens. These transactions are secured by identified assets of the Company. In specific cases, the Group makes use of factoring arrangements to manage the cash flow on outstanding trade accounts receivable.

The capital structure of the Group consists of financial liabilities, cash and cash equivalents and equity attributable to equity holders of the parent, comprising issued capital, reserves and retained earnings.

Significant accounting policies
Details of the significant accounting policies and methods adopted, including the criteria for recognition, the basis of measurement and the basis on which income and expenses are recognized, in respect of each class of financial asset, financial liability and equity instrument are disclosed in note 2.

3.2 Foreign currency risk

The Group divides the foreign currency risk into categories of transaction exposure, economic exposure and translation exposure.

The Group defines transaction exposure as the foreign currency exposure arising on monetary positions and forecasted transactions in the coming month that are denominated in a currency other than the functional currency of the group company. The Group has significant transactional currency exposures as the majority of the Group's sales are denominated in currencies other than the functional currency of the reporting subsidiaries.

Specifically, movements in the US Dollar/ Euro exchange rate affect the results of operations because a significant portion of sales are denominated in US Dollars. The Group's operating procedures require group companies to manage the foreign exchange risks against their functional currency. The target is to minimize foreign currency results on balance sheet items. Corporate treasury may hedge any remaining foreign exchange risk exposure on balance sheet positions.

The Group defines economic exposure as the foreign currency exposure to which the Group committed itself. This is the exposure associated with the time delay between entering into a contract, budget or forecast and the realization thereof. It is not the Group's policy to actively manage these exposures, but rather to hedge economic exposure on a selective basis by management's decision. The Group may apply formal hedge accounting in mitigating these risks.

The translation exposure is the exposure that arises on the translation of the financial statements of subsidiaries with different functional currencies into Euro. The Group has operations in Switzerland, Korea, Sweden and the US, which all have a different functional currency than the Euro. Consequently, movements in the currencies of these countries against the Euro will affect the results of operations because the balance sheet and the income statement of these subsidiaries are translated into Euro. The Group does not actively hedge its translation exposure.

Foreign currency risk sensitivity analysis
The Group is mainly exposed to US Dollar, Swiss Franc, Korean Won, Swedish Crown and Australian Dollar. The following table details the Group's sensitivity to a 10% strengthening of these currencies. The sensitivity analysis includes outstanding foreign currency denominated monetary items and adjusts their translation as at December 31, 2008 for a 10% change in foreign currency rates. A positive amount indicates an increase in income before income tax and equity.

For a 10% weakening of the foreign currencies against the Euro, there would be approximately an equal and opposite effect on the income before income tax and equity.

The sensitivities disclosed above are representative for the second half of 2008 as the Group applied in that period a more proactive approach on hedging of transaction exposures and also applied formal hedge accounting.

The revaluation effects of investments in foreign entities are recognized in equity. As we have significant operations denominated in other currencies than the Euro, the movements of currency exchange rates show a significant effect on equity. It is the Group's policy to limit the currency effects through the income statement. The Group does not proactively manage the currency exposure on the Group's equity.

3.3 Interest rate risk

The Group is exposed to interest rate risks as a result of changes in the market interest rates compared to loans with fixed rates. The Group has several loans with fixed interest rates, which total € 39,896 (2007: € 45,795). The Group has financial liabilities of € 20,855 with a variable interest rate as at December 31, 2008. Details on the interest rates and maturity of these loans are provided in note 5.19.

The Group has cash balances of € 183,865 of which € 12,896 is restricted. (2007: € 177,644 of which € 14,396 is restricted.) There are no other receivables that generate interest. The cash balances, including restricted cash, are either variable or fixed for a maximum period of 3 months.

	2008		2007		2006
	Impact on income statement	Impact on equity	Impact on income statement	Impact on equity	Impact on income statement
US Dollar	**229**	**482**	1,876	517	321
Swiss Franc	**(373)**	**17,980**	(4,950)	19,706	(1,180)
Korean Won	**(133)**	**8,414**	860	8,055	1,113
Swedish Crown	**(538)**	**2,924**	(486)	3,825	(33)
Australian dollar	**5**	**808**	882	—	—

Interest rate risk sensitivity analysis
The sensitivity analysis has been determined based on the exposure to interest rates at the balance sheet date and the stipulated change taking place at the beginning of the financial year and held constant throughout the reporting period. The effect of a 1% increase in interest rates on the Group's profit/ (loss) before tax would be a positive result of € 947 (2007: € 1,100; 2006: € 1,152). For a 1% decrease in interest rates there would be approximately an equal and opposite effect on the profit/ (loss) before tax. A change in the interest rate does not have an impact on the equity of the Group.

The positive effect of a 1% increase of interest on profit/ (loss) before tax is mainly attributable to the Group's interest income generating assets, which are higher than its interest bearing liabilities.

3.4 Credit risk

Credit risk represents the risk of financial loss caused by default of the counterparty. The Group's principal financial assets are cash and cash equivalents, short-term deposits and trade and other receivables. These represent the Group's maximum exposure to credit risk in relation to financial assets.

The Group's credit risk is primarily attributable to its trade accounts receivable and other receivables. The Group normally trades only with recognized, credit-worthy third parties. It is the Group's policy that all customers who wish to trade on credit terms are subject to credit verification procedures. Where considered appropriate, the Group requires issuance of letters of credit to mitigate credit risk.

Receivable balances are monitored on an ongoing basis and the Group tracks the payment history of its customers to identify any payment issues that have to be resolved before entering into any new transactions. Allowances are recognized for receivable balances deemed uncollectible upon identification. In determining the recoverability of a trade receivable, the Group considers changes in the credit quality of the trade receivable from the date credit was initially granted up to the reporting date. The customer base consists mainly of well-respected companies in the field of medicine and non-governmental organizations. In 2008, the Group has not encountered significant adverse events as a result of the weak global economy.

While the Group does have concentrations of trade accounts receivable outstanding to supranational organizations, management has determined the risk of default by these organizations to be limited and therefore considers the credit risk to be within acceptable boundaries. Management believes that no further credit provision is required in excess of the allowance for doubtful debts.

The credit risk on cash and cash equivalents, and short-term deposits is diversed as the counterparties are numerous major financial institutions. Furthermore the Group currently only invests in liquid securities and money market transactions. Management does not expect any counterparty to fail to meet its obligations.

The carrying value of these financial assets represents the Group's maximum exposure to credit risk. The maximum exposure at December 31, 2008 amounted to € 242,206 (2007: € 248,850).

3.5 Security price risk

The Group's security price risk is limited to its investment in Galapagos valued at € 4,922 (2007: € 10,009), which is classified as an available-for-sale investment. The fair value is based on the market quotation of Galapagos. The Group does not actively trade in available-for-sale investments.

Security price risk sensitivity analysis
The sensitivity analysis below has been determined based on the exposure to the security price risks at the reporting date. If the Galapagos share price had been 10% higher/lower:

- The profit for the year ended 31 December 2008 would have been unaffected as the investments are classified as available-for-sale and no investments were disposed of or impaired; and
- Net unrealized gains reserve would increase/ decrease by € 492 (2007: increase/decrease by € 1,001) for the Group as a result of the changes in the fair value of the available-for-sale investment.

The Group's sensitivity to security prices did not change significantly from the prior year.

3.6 Liquidity risk

Liquidity risk represents the risk that an entity will encounter difficulty in meeting obligations associated with its financial liabilities. Prudent liquidity risk management implies ensuring sufficient availability of cash resources for funding of the operations. The Group aims to maintain a solid cash base.

The current liquidity risk is considered to be limited because the Group has sufficient funding to meet its obligations in the foreseeable future. Reference is made to note 5.19 'Short and long-term financial liabilities' for an analysis of the most significant financial liabilities. The Group has a total cash balance of € 170,969 as at December 31, 2008 (2007: € 163,248).

3.7 Financial instruments by category

Financial assets

In thousands of Euro

	2008 Financial assets at fair value through profit and loss	Loans and receivables	Available-for-sale financial assets	2008 Total	2007 Financial assets at fair value through profit and loss	Loans and receivables	Available-for-sale financial assets	2007 Total
Derivative financial instruments	**1,761**	**—**	**—**	**1,761**	29	—	—	29
Investment Galapagos	**—**	**—**	**4,922**	**4,922**	—	—	10,009	10,009
Other financial assets	**—**	**14,920**	**—**	**14,920**	—	16,153	—	16,153
Cash and cash equivalents	**—**	**170,969**	**—**	**170,969**	—	163,248	—	163,248
Trade accounts receivable	**—**	**40,108**	**—**	**40,108**	—	47,563	—	47,563
Other current assets	**—**	**9,526**	**—**	**9,526**	—	11,848	—	11,848
Total	**1,761**	**235,523**	**4,922**	**242,206**	**29**	**238,812**	**10,009**	**248,850**

The carrying value of the financial assets approximates the fair value.

Financial liabilities

In thousands of Euro

	2008 Financial liabilities at fair value through profit and loss	Designated cash flow hedges	Financial liabilities at amortized cost	2008 Total	2007 Financial liabilities at fair value through profit and loss	Designated cash flow hedges	Financial liabilities at amortized cost	2007 Total
Derivative financial instruments	**194**	**685**	**—**	**879**	16	—	—	16
Financial liabilities	**—**	**—**	**60,751**	**60,751**	—	—	52,795	52,795
Other non-current liabilities	**—**	**—**	**591**	**591**	—	—	529	529
Accounts payable	**—**	**—**	**59,205**	**59,205**	—	—	50,970	50,970
Other current liabilities	**—**	**—**	**20,523**	**20,523**	—	—	29,960	29,960
Total	**194**	**685**	**141,070**	**141,949**	**16**	**—**	**134,254**	**134,270**

The fair values of the financial liabilities of the Group approximate the carrying amount of the Group's financial instruments.

The fair values of the loans have been calculated by discounting the face values with the interest rate of financial instruments with a similar risk profile and term. The fair values of the forward exchange contracts were calculated making use of the spot rate of the underlying exchange rates as at December 31, 2008.

3.8 Derivative financial instruments

The Group uses derivative financial instruments for the management of foreign currency risks.

	2008 Fair value assets	2008 Fair value liabilities	2008 Total fair value	2007 Fair value assets	2007 Fair value liabilities	2007 Total fair value
Foreign exchange contracts	1,761	(194)	1,567	29	(16)	13
Cash flow hedge	—w	(685)	(685)	—	—	—
Total derivative financial instruments	1,761	(879)	882	29	(16)	13

All derivative financial instruments mature within a year and are therefore presented as current assets or liabilities. The fair value of forward foreign exchange contracts is determined using forward foreign exchange rates.

All foreign exchange contracts, which are not designated as a qualifying hedge instrument, mature within 2 months after balance sheet date. The principal amount and fair value of foreign currency forwards that are not designated in a cash flow hedge are € 38,907 in 2008 (2007: € nil) and a positive unrealized result of € 1,567 in 2008 (2007: € 13). The Group enters in these derivative transactions to mitigate its foreign currency transaction exposure.

Cash flow hedging
The Group has designated certain qualifying derivative financial instruments as hedge instruments for cash flow hedge accounting to manage its currency risk resulting from specific contracts denominated in foreign currencies that differ from the functional currency of the Group company that engages in the contract. The principal amount and fair value of foreign currency forwards designated in a cash flow hedge are respectively € 7,535 (2007: € nil) and a negative unrealized result of € 685 (2007: € nil).

Cash flow hedges of foreign currency risks relate to forecasted transactions. These are expected to occur between 4 and 9 months after the balance sheet date. As at year-end 2008 the outstanding cash flow hedge was estimated to be 100% effective. No amounts were removed or reclassed from the hedge reserve during the period to non-financial balance sheet items or to the income statement. The Group did not engage in hedge accounting prior to 2008.

3.9 Off balance sheet transactions

The Group has the following off-balance sheet transactions, in addition to the guarantees given on assets as described in '5.6 property, plant and equipment' and '5.19 Short and long-term financial liabilities'.

Guarantees
The Group has a guarantee facility for an amount of € 10.0 million with a third-party bank.

As part of the overall working capital management efforts, the Group agreed with Novartis to extend payment terms on the supply of Quinvaxem antigens. We have provided Novartis with collateral on our Swiss premises for an amount up to € 22,847.

Total guarantees issued by the Group amount to € 3.1 million, which included a letter of credit issued by the Group for an amount of $ 1.6 million which will expire on April 14, 2013 for the benefit of the Percivia Development Center.

Covenants

Some of the Group's arrangements with financial institutions are subject to covenant clauses, whereby the Group is required to maintain certain cash thresholds. The Group did not breach any of these covenant clauses in 2008 nor does the Group foresee any breaches of these covenants in the foreseeable future.

4 Segment information

4.1 General

The Group operates in one reportable segment, which comprises the development, production and marketing of products that combat infectious diseases. The Group early adopted IFRS 8 'Operating Segments', which replaces IAS 14, 'Segment reporting', as of January 1, 2007. The Group identified the Management Board as the 'chief operating decision maker'. The Management Board reviews the consolidated operating results regularly to make decisions about resources and to assess overall performance.

In 2007, the Group's segmentation was based on the two segments that were reported to our Management Board:

- Vaccines: developing, producing and marketing vaccines worldwide to combat infectious diseases;
- Proteins: leverage Crucell's novel, proprietary technologies to develop monoclonal antibodies to combat infectious diseases.

In 2008, the Management Board decided to integrate both business units and reduce the complexity of our organization. In 2008, the separate segments were no longer reported to the Management Board.

4.2 Information about major products

The breakdown of the Group's revenues from its product sales was as follows:

In thousands of Euro

Year ended December 31,	2008	2007	2006
Paediatric vaccines	**111,039**	77,371	35,933
Respiratory vaccines	**32,474**	33,188	40,386
Travel vaccines	**55,572**	47,282	23,072
Other vaccines	**8,907**	10,705	2,998
Proteins and other business	**18,063**	9,023	1,529
	226,055	**177,569**	**103,918**

4.3 Information about major customers

In 2008, sales to our two largest customers, which are in the paediatric vaccines area, amounted to € 85,142 or 37.6% and € 18,390 or 8.1 % of net product sales. In 2007, sales to these customers accounted for € 45,480 or 25.6% and € 23,457 or 13.2% of net product sales, respectively.

4.4 Geographical segments

The Group operates principally in three geographical areas: Europe, North America and Asia. Segment revenue is based on the geographical location of the customers, which is the billing location of the customers. Segmentation of the assets is based on the geographical location of the assets.

In thousands of Euro

Year ended December 31,	2008	2007	2006
Revenues			
Europe	**209,473**	144,969	94,663
North America	**33,653**	33,346	13,868
Asia	**19,095**	18,589	16,506
Other	**4,936**	6,882	6,530
Total	**267,157**	**203,786**	**131,567**

	2008	2007
Investment in associates and joint ventures		
Europe	**—**	316
North America	**964**	549
Asia	**8,275**	8,205
Total	**9,239**	**9,070**

	2008	2007
Total assets		
Europe	**507,431**	472,557
North America	**7,472**	7,421
Asia	**121,394**	149,860
Total	**636,297**	**629,838**

	2008	2007
Capital expenditure property, plant and equipment		
Europe	**7,520**	26,472
North America	**14**	—
Asia	**8,253**	684
Total	**15,787**	**27,156**

5 Notes to the specific items of the consolidated financial statements

5.1 Personnel expenses

In thousands of Euro

	2008	2007	2006
Wages and salaries	**59,634**	58,493	48,841
Social security costs	**6,806**	6,734	4,469
Pension defined benefit plans	**(139)**	(1,592)	1,712
Pension defined contribution plans	**2,408**	2,436	1,770
Expenses for employee shares and option plans	**4,878**	7,349	4,296
Other personnel expenses	**6,436**	9,810	6,464
	80,023	**83,230**	**67,552**

As of December 31, 2008, we had 1,126 employees. The average number of employees in 2008 was 1,142. Personnel as at December 31, 2008 are employed in the following categories:

	2008	2007	2006
Research and Development	**303**	368	381
General and administrative	**147**	134	125
Operations	**527**	466	452
Marketing and sales	**149**	158	115
Total	**1,126**	**1,126**	**1,073**

The Group's personnel are located primarily in the Netherlands, Switzerland, Spain, Italy, South Korea, Sweden, the US and China.

The split per geographical area is as follows:

	2008	2007	2006
Europe	**861**	915	902
North America	**19**	19	17
Asia	**246**	192	154
Total	**1,126**	**1,126**	**1,073**

5.2 Financial income

In thousands of Euro

	2008	2007	2006
Currency gains	**1,914**	7,479	9,461
Interest income, third parties	**5,021**	5,711	3,718
Other financial income	**—**	—	274
	6,935	**13,190**	**13,453**

5.3 Financial expenses

	2008	2007	2006
Total interest expense	**(2,973)**	(3,053)	(2,481)
Less: amounts included in the cost of qualifying assets	**254**	772	744
	(2,719)	**(2,281)**	**(1,737)**
Currency losses	**(5,840)**	(8,785)	(9,625)
Other financial expenses	**(1,038)**	(746)	(344)
	(9,597)	**(11,812)**	**(11,706)**

5.4 Income tax

In thousands of Euro

Year ended December 31,	2008	2007	2006
Current income tax	**(3,200)**	(811)	(258)
Adjustments current income tax of previous years	**7**	(5)	(213)
Deferred taxation	**11,503**	3,024	10,922
Income tax	**8,310**	**2,208**	**10,451**

The reconciliation between the profit/ (loss) for the year multiplied by the applicable tax rate and the actual taxation is as follows:

In thousands of Euro

Year ended December 31,	2008	2007	2006
Profit/(loss) for the year before income tax	**6,276**	(45,118)	(97,649)
At gross weighted average income tax rate	**820**	12,197	21,337
Adjustments in respect of current income tax of previous years	**7**	(5)	(213)
Deferred tax assets not recognized	**(6,301)**	(380)	—
Recognition tax loss carry forwards	**9,284**	4,072	—
Effect of tax rate changes	**3,527**	(197)	3,894
Research and development tax credit	**2,916**	—	—
Other permanent differences	**(1,741)**	(3,488)	1,271
Effect of current tax losses not recognized as deferred tax assets	**(202)**	(9,991)	(15,838)
Income tax	**8,310**	2,208	10,451
Effective income tax rate	**(132.4%)**	4.9%	10.7%

The changes in deferred income tax assets and liabilities on a net basis were as follows in 2008 and 2007:

In thousands of Euro

	2008	2007
January 1,	**(29,267)**	(33,438)
Deferred tax through income statement	**11,503**	3,024
Deferred tax through goodwill	—	(697)
Effect of movements in exchange rates	**779**	1,844
December 31,	**(16,985)**	(29,267)

In 2007, a deferred tax asset of € 580 was recognized against goodwill as an adjustment to the provisional purchase price allocation on the acquisition of SBL. A deferred tax liability of € 1,277 was recognized against goodwill as an adjustment to the provisional purchase price allocation on the acquisition of Berna Products Corp.

The composition of the temporary differences and tax loss carry forwards in the balance sheet is as follows:

In thousands of Euro

Year ended December 31,	2008	2007
Deferred income tax liabilities		
Valuation differences attributable to:		
Inventories	**(2,171)**	(1,641)
Other assets	**(1,614)**	(521)
Net pension assets	**(1,852)**	(1,590)
Property, plant and equipment	**(7,316)**	(9,782)
Intangible assets	**(14,580)**	(21,269)
Liabilities	**(1,649)**	(105)
	(29,182)	(34,908)
Deferred income tax assets		
Losses available for offset against future taxable income	**9,060**	678
Valuation differences attributable to:		
Inventories	**469**	2,119
Other assets	**1,273**	595
Property, plant and equipment	**1,202**	1,910
Liabilities	**193**	339
	12,197	5,641
Offset of deferred tax balances	**12,197**	5,641
Reflected in the balance sheet as follows:		
Deferred tax assets	—	—
Deferred tax liability	**(29,182)**	(34,908)
Deferred tax liabilities, net	**(16,985)**	(29,267)

The Group has evaluated evidence impacting the recoverability of its deferred tax assets, which consist principally of tax loss carry forwards. In 2008, a deferred tax asset of € 8,585 was recognized for carry forward losses of Berna Biotech AG, which were previously unrecognized due to lack of evidence of future taxable income. At the end of the year the total deferred tax assets for carry forward losses amounted to € 9,060.

The Group has unrecognized tax carry forward losses of € 172,732 (2007: € 254,511; 2006: € 222,238) that are available, with certain restrictions in time, for offset against future taxable profits of the companies in which the losses arose.

The Group reached an agreement with the Dutch tax authorities to retroactively change the valuation of our intellectual property, to avoid the evaporation of unrecognized tax carry forward losses. This agreement allows the Group to recognize € 72,000 of our intellectual property as assets for tax purposes.

In the Netherlands anti-abuse laws may limit our ability to realize certain tax carry forward losses for an amount up to € 26,170.

The unrecognized carry forward losses expire as follows:

2011	17,502
2012	21,164
2013	19,153
After 2013	113,966
Unlimited	947
Total	172,732

Tax rate changes
In Korea, the tax holiday granted by the government is decreasing over time. In financial years 2008 and 2009, the applicable tax rate is 16.5%. As of 2010 the tax rate will be the regular statutory income tax rate of 22.0%. As of the year 2012 we will benefit from a tax holiday related to our investment in the Incheon, Free Economic Zone, which will significantly reduce the effective Korean income tax rate for a period of 5 years. The reduced expected realization rate for our deferred tax liabilities in Korea resulted in a taxation gain of € 3,384.

The Swedish domestic statutory corporate income tax rate amounted to 28.0% in 2008 and will decrease to 26.3% in 2009.

The Spanish domestic statutory corporate income tax rate amounted to 32.5% in 2007 and was decreased to 28.0% in 2008. The rate will also be 28.0% in 2009 and thereafter.

5.5 Profit/ (loss) per share

In thousands of Euro

	2008	2007	2006
Net profit/ (loss) attributable to ordinary shareholders	**14,586**	(42,910)	(86,946)
Weighted average number of ordinary shares for the year	**65,593,374**	65,102,801	57,064,034
Dilutive effect share options	**721,682**	—	—
Weighted average number of ordinary shares for diluted net profit/ (loss) for the year	**66,315,056**	65,102,801	57,064,034
Net profit/ (loss) per share — basic	**0.22**	(0.66)	(1.52)
Net profit/(loss) per share – diluted	**0.22**	(0.66)	(1.52)

5.6 Property, plant and equipment

Amounts in thousands of Euro

Cost	Freehold Land and buildings	Plant and equipment	Assets under construction	Total
At January 1, 2007	**69,747**	**75,090**	**34,298**	**179,135**
Additions	245	5,913	20,998	27,156
Disposals	(147)	(995)	—	(1,142)
Effect of movements in exchange rates	(4,238)	(5,299)	(412)	(9,949)
At December 31, 2007	**65,607**	**74,709**	**54,884**	**195,200**
Additions	66	7,917	7,804	15,787
Disposals	—	(1,620)	—	(1,620)
Transfer assets under construction	66	35,204	(35,270)	—
Effect of movements in exchange rates	5,456	2,450	1,886	9,792
At December 31, 2008	**71,195**	**118,660**	**29,304**	**219,159**
Depreciation and impairment				
At January 1, 2007	**(12,366)**	**(28,751)**	**—**	**(41,117)**
Depreciation charge for the year	(4,490)	(9,963)	—	(14,453)
Impairment	(171)	—	—	(171)
Disposals	144	935	—	1,079
Effect of movements in exchange rates	2,105	2,882	—	4,987
At December 31, 2007	**(14,778)**	**(34,897)**	**—**	**(49,675)**
Depreciation charge for the year	(6,715)	(9,914)	—	(16,629)
Impairment	(266)	(65)	—	(331)
Reversal of impairment	5,219	—	—	5,219
Disposals	—	1,498	—	1,498
Effect of movements in exchange rates	(3,526)	(4,509)	—	(8,035)
At December 31, 2008	**(20,066)**	**(47,887)**	**—**	**(67,953)**
Net book value				
At December 31, 2008	**51,129**	**70,773**	**29,304**	**151,206**
At December 31, 2007	**50,829**	**39,812**	**54,884**	**145,525**

Depreciation is included in the cost of goods sold for an amount of € 10,026 in 2008 (2007: € 11,176, 2006: € 8,995), research and development costs of € 4,157 in 2008 (2007: € 2,353, 2006: € 4,448) and selling, general and administrative costs of € 2,446 in 2008 (2007: € 924, 2006: 832).

Impairment
See '1 General information – 1.4 Use of estimates and judgments' in the financial statements for further details on any impairments or reversal thereof.

Lease and borrowing costs
At December 31, 2008 and 2007, the Group held equipment under finance leases with a cost of € 23,505, and €11,137, respectively and a net book value of € 21,936 and € 11,137. The equipment under finance leases includes the new Spanish filling line and laboratory equipment in Leiden, the Netherlands. These leases are secured by the value of the underlying assets.

At December 31, 2008 an amount of € 254 of borrowing costs related to the construction of a new production facility in Leiden, the Netherlands, has been capitalized (2007: € 772). The borrowing costs are capitalized at a capitalization rate of 4.55%,

Commitments
The remaining contractual commitments amount to € 20,380 (2007: € 4,696, 2006: € 11,693) for purchases of property, plant and equipment, mainly related to the new Korean production facility in the Incheon, Free Economic Zone, Korea.

5.7 Intangible assets

In thousands of Euro

Cost	Customer lists	Brands and licenses	Developed technologies	In process R&D	Total
At January 1, 2007	**11,209**	**23,142**	**87,214**	**6,962**	**128,527**
Effect of movements in exchange rates	(339)	(828)	(6,378)	(205)	(7,750)
At December 31, 2007	**10,870**	**22,314**	**80,836**	**6,757**	**120,777**
Effect of movements in exchange rates	1,172	2,480	(6,384)	770	(1,962)
At December 31, 2008	**12,042**	**24,794**	**74,452**	**7,527**	**118,815**
Amortization and impairment					
At January 1, 2007	**(979)**	**(3,254)**	**(11,217)**	**—**	**(15,450)**
Amortization	(3,032)	(3,655)	(5,207)	—	(11,894)
Effect of movements in exchange rates	54	226	332	—	612
At December 31, 2007	**(3,957)**	**(6,683)**	**(16,092)**	**—**	**(26,732)**
Amortization	(3,141)	(3,706)	(4,827)	—	(11,674)
Effect of movements in exchange rates	(640)	(1,299)	534	—	(1,405)
At December 31, 2008	**(7,738)**	**(11,688)**	**(20,385)**	**—**	**(39,811)**
Net book value					
At December 31, 2008	**4,304**	**13,106**	**54,067**	**7,527**	**79,004**
At December 31, 2007	**6,913**	**15,631**	**64,744**	**6,757**	**94,045**

Amortization of intangible assets is included in the cost of goods sold for an amount of € 127 in 2008 (2007: € 131, 2006: 0), research and development costs of € 8,635 in 2008 (2007: € 8,939, 2006: € 6,858) and selling, general and administrative costs of € 2,912 in 2008 (2007: € 2,824, 2006: 702).

Impairment
See '1 General information - 1.4 Use of estimates and judgments' in the financial statements for further details on impairments.

Material intangible assets
The following individual intangible assets are considered material to Crucell's financial statements:

In thousands of Euro

	Remaining amortization at December 31, 2008 (in years)	Carrying value December 31, 2008	Carrying value December 31, 2007
Developed technology Quinvaxem	17.7	**25,519**	34,778
Developed technology Epaxal	17.2	**10,959**	10,410
Manufacturing contract	2.2	**7,920**	10,391
Developed technology Inflexal	9.2	**7,084**	7,052
In-process R&D Flavimun	—	**7,526**	6,756
Developed Technology Vivotif	17.2	**5,595**	5,315
Brand name Berna Biotech	17.2	**4,153**	3,945

5.8 Goodwill

In thousands of Euro

	Goodwill
Cost	
At January 1, 2007	**47,419**
Additions	—
Adjustments to provisional values	697
Effect of movements in exchange rates	(3,739)
At December 31, 2007	**44,377**
Additions	—
Adjustment to cost of business combination	237
Effect of movements in exchange rates	1,462
At December 31, 2008	**46,076**
Net book value	
At December 31, 2008	**46,076**
At December 31, 2007	**44,377**

The goodwill was recognized on the following business combinations:

- In February 2006, the Company acquired approximately 97% of the outstanding common shares of Berna Biotech AG ('Berna Biotech') for € 348,852, excluding acquisition costs. During 2006 the remaining outstanding shares were also acquired. Berna Biotech was a fully integrated biotechnology company that marketed numerous vaccines on a global scale.
- In October 2006, the Company purchased, via its subsidiary Crucell Vaccines Inc. the assets and liabilities of the Florida-based Berna Products Corp. ('BPC') from Acambis plc for € 13,806. BPC was originally established in 1990 by Berna Biotech to market Vivotif, Berna's oral typhoid fever vaccine, in the US and Canada and was acquired by Acambis plc in 2003.
- In November 2006, the Group acquired the shares of Stockholm-based SBL Vaccin Holding AB (SBL) from 3i and SEB for a total consideration of € 39,341 in cash. SBL is a fully integrated independent Swedish biotechnology company employing 120 people. SBL's main product was Dukoral. In addition, SBL has a sales and distribution organization for vaccines in Scandinavia.

The selling shareholders of SBL Vaccin acquisition Holding AB are contractually entitled to earn-out payments based on contingent future events. In 2008, additional consideration resulting from the earn-out agreement with the former shareholders was treated as an adjustment to the cost of the business combination for an amount of € 237. This contingent consideration was not recognized in the prior year because the amount could not be measured reliably.

Goodwill allocation to cash-generating units
Goodwill acquired through business combinations has been allocated as follows:

In thousands of Euro

December 31,	2008	2007
Vaccines segment	—	44,377
2006 business acquisitions	46,076	—
Total goodwill	**46,076**	**44,377**

In 2008, the Group reorganized its reporting structure in a way that changed the composition of one or more cash-generating units to which goodwill has been allocated, as the Vaccines and the Proteins business units were integrated. In 2007, all goodwill was allocated to the Vaccines Unit. As a result of the change in composition of the reporting structure, all goodwill was allocated to the businesses acquired in 2006 on a combined basis.

Calculations of the recoverable amount show that there is no impairment as the recoverable amount of the 2006 business acquisitions exceeds the carrying amount by € 189 million.

Sensitivities to changes in assumptions
Management believes that any reasonable possible change in the key assumptions would not decrease the value in use to the extent that the related goodwill would exceed the recoverable amount. Several sensitivity analyses on key assumptions were performed and the outcome indicated that the carrying amount would not exceed the recoverable amount. Reference is made to the key assumptions below as these have a significant impact on the calculated recoverable amount:

- The recoverable goodwill amount was determined on the basis of a pre-tax weighted average cost of capital ('WACC') of 15.2%. A higher WACC percentage would reduce the recoverable amount;
- In the valuation model, future investments for enhancements/ improvements for which preparations are ongoing, have been included in the analysis; and

- The valuation is based on a discounted future cash flow model with a 5-year window and a terminal value after the last planning year in 2013. The terminal value has been set at 50%. The 50% reduction in the terminal value is to reflect that there are no new products available without significant investments for biotechnology companies.

5.9 Investments in associates and joint ventures

5.9.1 Associated companies

ADImmune Corp., Taiwan

The Group has an 11.8% stake in the share capital of Taiwan-based ADImmune Corp., (ADImmune) a company that develops, manufactures and distributes vaccines and other biological products. During 2008, our ownership of ADImmune Corp. was diluted from 20% to 11.8%. ADImmune will use Crucell's virosome technology to produce a virosomal adjuvanted influenza vaccine for the following specified markets: Taiwan, Japan and Macau. Additionally, ADImmune will produce influenza antigen in the future, which we may purchase to produce our influenza vaccine product, Inflexal V.

Summary financial information of ADImmune for the years ended December 31, 2008 and 2007, not adjusted for the percentage of ownership held by the Group is as follows:

In thousands of Euro

	2008	2007
Associate's balance sheet (ADImmune)		
Current assets	**21,781**	6,621
Non-current assets	**70,737**	38,447
Current liabilities	**(6,259)**	(4,918)
Non-current liabilities	**(16,821)**	(209)
Net assets	**69,438**	**39,941**
Associate revenues and expenses		
Revenues and other income	**5,844**	5,056
Expenses	**(6,548)**	(6,108)
Profit/ (loss) for the period	**(704)**	(1,052)

Kenta Biotech AG, Switzerland

On July 3, 2008, the Group sold all of the 2,625,000 shares it owned in Kenta Biotech AG to Ingro Finanz AG. Prior to this sale, our ownership interest had already been diluted from 37% in 2006 to 22% by the end of 2007. We realized an accounting gain of € 1,570 on the sale.

Pevion Biotech AG, Switzerland

Pevion Biotech AG develops vaccines based on its proprietary technology platforms. In November 2007, the Group sold all 2.9 million shares it owned in Pevion Biotech AG for € 6,081 to the other Pevion Biotech shareholders. The Group realized an accounting gain of € 2,186 on the sale.

5.9.2 Joint ventures

Percivia LLC, United States

In August 2006, DSM Pharmaceutical Products Inc, and the Group established a joint venture, Percivia LLC (Percivia) to operate the PERCIVIA PER.C6 Development Center in Cambridge, MA, US. Each company holds 50% of the shares. The initial contribution amounts to $ 500. The joint venture further develops the PER.C6 cell line and provides a unique solution for the production of pharmaceutical proteins to licensees utilizing the PER.C6 human cell line in the biotech industry. Percivia recharges the costs incurred to the venturers. No additional fundings are planned.

Summary financial information of this joint venture, not adjusted for the percentage ownership held by the Group is as follows:

In thousands of Euro

	2008	2007
Joint Venture' s balance sheet (Percivia)		
Current assets	**2,060**	1,131
Non-current assets	**1,360**	981
Current liabilities	**(1,440)**	(965)
Non-current liabilities	**—**	—
Net assets	**1,980**	1,147
Joint Venture's revenues and expenses		
Revenues	**8,721**	8,081
Expenses	**(7,972)**	(7,348)
Profit/ (loss) for the period	**749**	733

The tax charge for PERCIVIA PER.C6 Development Center is accounted for in the financial statements of the venturers. The tax charge recognized in the financial statements relating to the percentage owned by the Group amounts to € 151 in 2008 (2007: € 146).

5.10 Retirement benefit obligations

The Group provides employee benefit plans to most of its employees by means of various pension plans. These plans comply with local regulations and practices in the countries in which they operate and differ based on legal requirements, tax legislation, local customs and economic conditions in those countries. While the nature of the plans varies by country, in general, the benefits provided depend on remuneration and years of service. Most of these benefits are administrated by insurance companies or pension funds.

The Group adopted IFRIC 14, 'IAS 19 – The limit on a defined benefit asset, minimum funding requirements and their interactions' in 2008. The interpretation provides guidance on assessing the limit of the surplus in a defined benefit pension plan that can be recognized as an asset. It also explains how the pension asset or liability may be affected by a statutory or contractual minimum funding requirement. The pension fund in Switzerland has a minimum funding requirement and the application of the interpretation resulted in an increase in the assets recorded on the Group's balance sheet of € 7,853 (2007: € 4,918, 2006: € 746) and a corresponding increase in the Group's equity of € 6,165 (2007: € 3,861, 2006: € 586), which includes a net tax effect of € 1,688 (2007: € 1,057, 2006: € 160). The result for the year increased by € 2,101 (2007: € 3,037, 2006: € 367) as a result of the application of IFRIC 14. As required by IFRS, all comparative figures were adjusted retrospectively as if the interpretation had always been applied. Also see '1.5 Changes in accounting policies'.

Recognition of pension expenses in the income statement and balance sheet:

In thousands of Euro

Year ended December 31	2008	2007	2006
Income statement			
Defined benefit plans	**(139)**	(1,592)	1,712
Defined contribution plans	**2,408**	2,436	1,770
Total	**2,269**	**844**	**3,482**

Year ended December 31	2008	2007
Balance sheet		
Defined benefit plans		
Pension assets	**8,612**	7,397
Pension liability	**(2,710)**	(3,466)
Net pension asset	**5,902**	**3,931**

Prior to the acquisition of Berna Biotech and SBL, the Group did not operate any defined benefit plans. After the acquisitions in 2006, the Group operates defined benefit plans in Switzerland, Korea and Sweden. The pension asset of € 8,612 (2007: € 7,397) relates to the Swiss pension fund while the pension liability of € 2,710 (2008: € 3,466) relates to the Swedish and the Korean pension funds. In total, 97% (2007: 96%) of the plan assets and 91 % (2007: 90%) of the defined benefit obligation relate to the Swiss pension fund.

The weighted average of the principal assumptions used in determining the employee benefit obligations for the defined benefit plans of the Group are shown below:

In percent

	2008	2007	2006
Discount rate	**3.37%**	3.40%	3.32%
Expected return on plan assets	**4.53%**	4.53%	4.55%
Future salary increases	**1.19%**	1.22%	1.19%
Future pension increases	**0.71%**	0.78%	0.66%

Changes in these key assumptions can have a significant impact on the defined benefit obligations, funding requirements and periodic costs incurred. The Group consults at least annually with external actuaries regarding these assumptions.

Changes in the present value of the defined benefit obligation are as follows:

In thousands of Euro

Year ended December 31,	2008	2007
Opening defined benefit obligation, January 1,	**(74,506)**	**(72,679)**
Interest cost	(2,165)	(2,363)
Current service cost	(3,748)	(3,369)
Benefits paid	4,418	2,450
Actuarial gains/(losses)	(3,038)	(934)
Exchange differences	(6,446)	2,389
Closing defined benefit obligation	**(85,485)**	**(74,506)**

Changes in the fair value of plan assets are as follows:

In thousands of Euro

	2008	2007
Opening fair value of plan assets	**99,032**	**102,306**
Expected return on plan assets	4,606	4,528
Contributions by employer	597	2,338
Contributions by participants	1,053	984
Benefits paid	(4,062)	(2,208)
Actuarial gains/(losses)	(9,213)	(5,727)
Exchange differences	9,555	(3,189)
Fair value of plan assets, December 31	**101,568**	**99,032**

In 2009, the Group expects to contribute an amount similar to the amount contributed in 2007 to its defined benefit pension plans. The amount in 2008 was lower due to partial usage of an employer contribution reserve in Switzerland. The actual return on plan assets for the year ended December 31, 2008 amounted to a loss of € 4,639 (2007: loss of € 1,199).

The costs for defined benefit plans are as follows:

In thousands of Euro

Year ended December 31,	2008	2007	2006
Current service cost	**3,748**	3,369	3,105
Interest cost	**2,166**	2,363	2,012
Expected return on plan assets	**(4,606)**	(4,528)	(3,758)
Actuarial gains and losses	**11,014**	6,651	(862)
The effect of changes due to the asset ceiling	**(11,408)**	(8,463)	2,260
Employee contributions	**(1,053)**	(984)	(981)
Other	**—**	—	(64)
	(139)	**(1,592)**	**1,712**

The amounts in the balance sheet are determined as follows:

In thousands of Euro

Year ended December 31,	2008	2007
Defined benefit obligation	**(85,485)**	(74,506)
Fair value of plan assets	**101,568**	99,032
Funded status	**16,083**	**24,526**
Unrecognized net actuarial losses	**1,261**	233
Amount not recognized as asset due to asset ceiling	**(11,442)**	(20,828)
Net pension asset	**5,902**	**3,931**

In thousands of Euro

Year ended December 31,	2008	2007	2006
Defined benefit obligation	**(85,485)**	(74,506)	(72,679)
Plan assets	**101,568**	99,032	102,306
Surplus	**16,083**	24,526	29,627
Experience adjustments on plan liabilities – loss	**(3,038)**	(934)	834
Experience adjustments on plan assets – loss	**(9,213)**	(5,727)	(211)

The major categories of plan assets as a percentage of the fair value of total plan assets are as follows:

	2008	2007
Bonds	**44.9%**	41.7%
Equity	**22.0%**	26.1%
Property	**28.4%**	28.6%
Other	**4.7%**	3.6%
	100.0%	**100.0%**

The overall expected rate of return on assets is determined based on the market prices expected to be applicable to the period over which the obligation is to be settled and the relative weight of the separate categories of plan assets.

5.11 Other financial assets (non-current)

In thousands of Euro

Year ended December 31,	2008	2007
Long-term restricted cash	**12,896**	14,396
Long-term deposits and guarantees	**1,645**	1,388
Other long-term receivables	**379**	369
	14,920	**16,153**

5.12 Cash and cash equivalents

In thousands of Euro

Year ended December 31,	2008	2007
Cash at banks and in hand	**91,853**	108,273
Call deposits	**79,116**	54,975
	170,969	**163,248**

Cash and cash equivalents are denominated in the following currencies (translated into Euros):

In thousands of Euro

Year ended December 31,	2008	2007
Euro (€)	**111,909**	99,304
US Dollar ($)	**37,975**	41,954
Swiss Franc (CHF)	**4,144**	8,426
Swedish Crown (SEK)	**7,746**	9,997
Korean Won (KRW)	**7,360**	2,331
Other currencies	**1,835**	1,236
	170,969	**163,248**

5.13 Trade accounts receivable

In thousands of Euro

Year ended December 31,	2008	2007
Trade receivables from third-party customers	**39,343**	47,553
Trade receivables from associates and joint ventures	**765**	10
	40,108	**47,563**

At December 31, 2008, trade receivables are shown net of an allowance for doubtful debts for an amount of € 2,289 (2007: € 2,763). The Group's normal credit period is 30 days, although in some jurisdictions, including Italy, Korea and Spain, a credit period of 60 days is maintained in line with local customs. Receivables are denominated in several currencies and can be specified as follows:

Year ended December 31,	2008	2007
Euro (€)	**20,569**	28,343
US Dollar ($)	**8,985**	6,056
Swiss Franc (CHF)	**5,058**	4,077
Swedish Crown (SEK)	**2,810**	7,264
Korean Won (KRW)	**1,334**	985
Other currencies	**1,352**	838
	40,108	**47,563**

Aging of past due but not impaired
Included in the Group's trade receivables balance are debtors with a carrying amount of € 11,678 (2007: € 9,051) which are past due at the reporting date for which the Group has not provided because there has not been a significant change in credit quality and the amounts are considered recoverable. The Group does not hold any collateral over these balances.

In thousands of Euro

Year ended December 31,	2008	2007
0-60 days	**7,810**	5,083
60-90 days	**1,407**	479
90-120 days	**340**	1,411
Over 120 days	**2,121**	2,078
	11,678	**9,051**

Movement in the allowance for doubtful debts:

In thousands of Euro

	2008	2007
Balance at beginning of the year	**2,763**	**4,069**
Additions to provisions	1,429	535
Amounts written off as uncollectible	(1,379)	(968)
Unused amounts reversed	(289)	(601)
Effect of movements in exchange rates	(235)	(272)
	2,289	**2,763**

The amount written off in 2008 as uncollectible relates to customers of our Korean subsidiary and was already provided for in the purchase price allocation of the Berna Biotech Group.

The amount written off in 2007 as uncollectible relates to customers of our Swedish subsidiary and was already provided for in the purchase price allocation of SBL Vaccin Holding AB.

5.14 Inventories

In thousands of Euro

	2008	2007
Raw materials and consumables	**13,286**	15,162
Work in progress	**61,980**	46,157
Finished products	**16,581**	5,914
	91,847	**67,233**

In order to be able to meet the demand from the market (e.g. in case of outbreak of a disease) the Group stocks certain inventories to a level such that they may not be utilized in one year. Provisions are recognized for obsolete inventory. The amount of write-down of inventories recognized as an expense is € 3,218 (2007: € 6,428).

The amount of inventories recognized as an expense in cost of product sales is € 128,632 (2007: € 113,250, 2006: € 74,523).

5.15 Other current assets

In thousands of Euro

Year ended December 31,	2008	2007
Accrued income	4,495	10,164
Prepaid expenses	3,612	3,177
Other short-term receivables	6,658	10,826
Director's loan	134	134
Income tax receivables	2,734	888
Derivative financial instruments	1,761	29
	19,394	25,218

5.16 Issued share capital and reserves

Crucell's authorized share capital amounts to 85,000,000 ordinary shares and 85,000,000 preference shares, each with a par value of € 0.24. As of December 31, 2008, there were 65,833,242 ordinary shares issued and outstanding (2007: 65,348,796). No preference shares are issued and outstanding as of December 31, 2008.

On October 25, 2000, the Company established a foundation called Stichting Preferente Aandelen Crucell, also referred to as the Preferred Foundation. The Preferred Foundation's object is to safeguard the interests of Crucell, its business and parties connected therewith by blocking any influences that may threaten these interests, which interests may include the continuity, independence or identity of Crucell, its business and parties connected therewith. The Preferred Foundation can safeguard these interests through acquiring and managing the preference shares and by exercising the rights attaching to these shares, in particular, the voting rights.

The agreement between the Company and the Preferred Foundation grants an option to the Preferred Foundation to acquire preference shares up to 100% of the number of our outstanding shares as necessary to match the total number of statutory votes on all of the ordinary shares outstanding at the time of an acquisition. The Preferred Foundation must pay at least 25% of the nominal value of the preference shares it acquires from the Company. If the Company has previously acquired any preference shares, they may be cancelled.

A board of governors of up to five persons directs the Preferred Foundation. Mr. J.P. Oosterveld, in his capacity as chairman of our Supervisory Board, and Mr. P. Bouw, Mr. M.W. den Boogert, Mr. S. van Wijnbergen and Mr. G.P. Krans, have been appointed to the board of governors. A majority of these members may not be members or former members of the Management or Supervisory Board of the Company, or an employee of any of our advisers, any of our banks or us. The board of governors appoints these independent members. The Supervisory Board appoints the non-independent members after consultation with the Management Board.

Ordinary shares issued and fully paid	Shares 000	Issued capital € 000
At January 1, 2006	41,441	9,946
Issued in February 2006 in exchange for issued share capital of Berna Biotech	16,931	4,064
Shares issued in relating to private placement and acquisition of minority interests	5,022	1,205
Shares issued relating to share-based payments	1,408	338
At December 31, 2006	64,802	15,553
Shares issued relating to share-based payments	547	132
At December 31, 2007	65,349	15,685
Shares issued relating to share-based payments	484	115
At December 31, 2008	65,833	15,800

5.17 Share-based payment plans

Stock-based compensation
Employee stock option plans
The Group maintains stock option plans whereby the Remuneration committee of the Supervisory Board may grant options to employees, directors and members of the Supervisory Board. The compensation expenses included in operating expenses for those plans were € 5,053, € 6,524 and € 4,000 in 2008, 2007 and 2006, respectively.

In December 2004, the Supervisory Board approved a new option plan (the '2005 Plan') providing for the grant of stock options to non-Management Committee members. Options granted under this stock option plan are exercisable once vested. Granted options vest straight line over a period of four years. Compensation costs are recognized in accordance with the accelerated method.

The options expire five years after date of grant. Upon termination of employment with Crucell, options must be exercised within 90 days. Options granted under the stock option plan are granted at exercise prices, which equal the fair value of the ordinary shares of the Company at the date of grant.

All options granted under previous stock option plans (the 'Prior Plans') are exercisable immediately upon grant. The options expire four to eight years from the date of grant, or earlier upon termination of employment with the Group. Upon termination of employment, options must be exercised within 90 days. No further grants are to be made under the Prior Plans.

At the annual General Meeting of Shareholders in 2008, the shareholders of the Company approved the revised long-term incentive (LTI) plan for the Management Board. Under the terms of the LTI plan, options are conditionally granted and vest at the end of a four-year performance period. The conditionally granted options include a market condition that is taken into account when estimating the fair value of the equity instruments granted. The number of LTI options that vest are based on the fulfilment of the LTI performance condition. On the vesting date, Crucell's Total Shareholder Return ('TSR') performance is measured against the performance of the NASDAQ Biotechnology Index during the performance period. The positive difference in percentages, if any, between Crucell's TSR compared to the performance of the NASDAQ Biotechnology Index, determines the number of LTI options that vest on the vesting date. Depending on the level of achievement of these market measures, at the end of three years, the number of shares vesting could be 0%-200% of the number of options originally granted. The new LTI plan will impact the Group's results for the first time in 2009.

At the annual General Meeting of Shareholders in 2008, the shareholders of the Company approved an additional option grant to the Management Board of 800.000 options. The options are conditionally granted and vest at the end of a three-year performance period starting June 2, 2008. The conditionally granted options include a market condition that is taken into account when estimating the fair value of the equity instruments granted. The market condition is an absolute total shareholder return of plus 50% share value measured three years after the grant.

The Group accounts for its employee stock options under the fair value method. The fair value of options is estimated at the date of grant using the Black-Scholes option-pricing model, with the following weighted average assumptions:

In percent

Year ended December 31,	2008	2007	2006
Risk-free interest rate	**4.3%**	4.1%	3.6%
Expected dividend yield	**—**	—	—
Expected volatility	**36.7%**	33.3%	41.8%
Expected life (years)	**4.76**	4.25	4.25

The risk-free interest rate is based on Dutch treasury securities in effect at the time of grant. In determining the expected volatility, we take into account the historical volatility of the Company's stock over a period commensurate with the expected term of the employee stock options. When establishing the expected life, we take into account the contractual term of the options and historical employee exercise behavior. The weighted average fair value of options granted during the years ended December 31, 2008, 2007 and 2006 was € 4.03, € 5.34 and € 6.96, respectively.

A summary of the stock option activity for the outstanding plans is as follows:

	Number of options	Weighted average exercise price
Balance at January 1, 2006	**4,029,504**	**6.43**
Granted	953,466	18.76
Exercised	(1,284,655)	4.16
Forfeited	(12,875)	19.40
Balance at December 31, 2006	**3,685,440**	**10.36**
Granted	1,514,165	16.97
Exercised	(301,475)	6.45
Forfeited	(237,447)	19.15
Balance at December 31, 2007	**4,660,683**	**12.31**
Granted	2,639,640	11.59
Exercised	(420,270)	7.58
Forfeited	(592,175)	16.55
Balance at December 31, 2008	**6,287,878**	**11.92**

Included in the options outstanding as of December 31, 2008 are also options to acquire ordinary shares held by certain former employees and consultants. These individuals have been permitted to continue vesting in these options for services rendered.

The following table summarizes information about the company's stock options outstanding at December 31, 2008:

Exercise price	Outstanding options at December 31, 2008	Weighted average exercise price	Weighted average remaining contractual life (years)	Excercisable options	Weighted average exercise price-exercisable options
€ 2.35 – € 5.00	516,125	3.34	2.12	516,125	3.34
€ 5.00 – € 9.99	1,689,724	8.19	2.22	1,223,104	7.74
€ 10.00 – € 14.99	2,677,125	12.45	4.34	247,625	12.74
€ 15.00 – € 19.99	1,193,031	18.20	2.92	452,483	17.91
€ 20.00 – € 22.22	211,873	20.42	2.19	113,970	20.50
Total	**6,287,878**	**11.92**	**3.24**	**2,553,307**	**9.71**

As of December 31, 2008, a total of 9,874,986 ordinary shares, representing 15% (2007: 15%) of the issued share capital, has been reserved for issuance under the option plan, of which 6,287,878 (2007: 4,660,683) were subject to outstanding options.

Share-based incentive plans
In addition to the employee stock option plans for executives as described in the previous paragraph, the Company operated incentive plans for executives up to 2008 that involved the issuance of share awards.

Up to 2008, the Group operated the 2005 Short-term Incentive Plan (the 'STI Plan'). Crucell granted executives share awards with vesting contingent upon meeting various company-wide, departmental and individual performance goals. The employees granted shares under the STI Plan were allowed to elect to receive either cash (at a 25% discount from the total award) or shares if certain performance criteria were met.

Grants under the STI Plan were accounted for as liabilities and included in accrued compensation and related benefits in the accompanying balance sheets. In 2007, executives were entitled to a total of 15,544 STI Plan shares, after deduction of income tax. Shares granted under the STI Plan were issued to the executives in the first quarter of 2008. No more issuances under this STI plan can take place. At the annual General Meeting of Shareholders in 2008, the shareholders approved the 2008, STI cash-based payment plan and this supersedes the 2005 STI share-based payment plan.

Up to 2008, the Group operated the 2005 Long-term Incentive Plan (the 'LTI Plan'), which allowed for the issuance of up to 36,842 shares of common stock to be granted to executives with vesting contingent upon meeting various performance conditions. Depending on the level of achievement of these market measures, at the end of three years, the number of shares vesting could be 0%-200% of the number of shares originally allowed for issuance. In 2008, a total of 20,104 shares was granted under the terms of the 2005 LTI plan. No more issuances under this LTI plan can take place. At the annual General Meeting of Shareholders in 2008, the shareholders approved the 2008 LTI option-based payment plan as described above and this supersedes the 2005 LTI share-based payment plan.

Stock option grants to non-employees
Crucell has a total number of 67,604 (2007: 67,604) stock options to various non-employees outstanding in connection with consulting agreements over the years. The exercise prices range from € 5.38 to € 18.22 per share and the stock options expire on dates ranging from May 2010 through August 2012. During 2008, the Company issued no stock options to non-employees.

The Company recorded compensation expense associated with these stock options of € 24, € 11 and € 295 for the years ended December 31, 2008, 2007 and 2006, respectively.

Stock option grants to non-employees are made pursuant to approved stock option plans and activity related thereto is included in the tables above with the employee grants of the approved plans.

5.18 Provisions, commitments and contingencies

In thousands of Euro

	Restructuring	Litigation	Employee benefits	Other	Total
At January 1, 2007	**1,646**	**1,000**	**3,919**	**1,441**	**8,006**
Arising during the year	—	—	—	657	657
Utilized	(1,364)	(77)	—	(752)	(2,193)
Unused amounts reversed	(276)	(50)	—	(290)	(616)
Movement defined benefit liability	—	—	(267)	—	(267)
Exchange adjustment	(6)	(18)	(186)	(43)	(253)
At December 31, 2007	**—**	**855**	**3,466**	**1,013**	**5,334**
Current 2007	—	—	—	761	761
Non-current 2007	—	855	3,466	252	4,573
At January 1, 2008	**—**	**855**	**3,466**	**1,013**	**5,334**
Arising during the year	684	705	—	626	2,015
Utilized	(74)	(2)	—	(491)	(567)
Unused amounts reversed	—	—	—	(33)	(33)
Movement defined benefit liability	—	—	(204)	—	(204)
Exchange adjustment	—	90	(552)	75	(387)
At December 31, 2008	**610**	**1,648**	**2,710**	**1,190**	**6,158**
Current 2008	610	—	—	971	1,581
Non-current 2008	—	1,648	2,710	219	4,577

Provisions

Restructuring

In 2008, a restructuring program in our Italian subsidiary Berna Biotech Italia Srl. was executed. A total provision of € 684 was recognized of which € 610 was outstanding as per year-end 2008.

In 2006, a restructuring charge was recognized in relation to centralization of R&D functions in Leiden and phasing out R&D projects in Switzerland. The decision to concentrate R&D in Leiden was made to increase efficiency in R&D spending and resulted in a reduction in the number of staff employed, which was effectuated in the first quarter of 2007.

Legal proceedings

The Group is subject to certain lawsuits and other legal proceedings. The current status of any pending proceedings has been reviewed with legal counsel. Upon consideration of known relevant facts and circumstances, provisions are recognized for losses that are considered to be probable and that can be reasonably estimated at balance sheet date.

Complaint filed by Korean landlord

At the end of 2007, our Korean landlord advised us it would stop providing utilities to us in the near future and also filed a complaint against us seeking the removal of two additional buildings at the Korean facility and delivery to the landlord of the land on which those buildings are located. In October 2008, we reached an agreement to relocate our Korean production facility from the Shingal site in Yongin City to the Incheon, Free Economic Zone. All parties involved, including our current landlord, have agreed on the time line and conditions of this relocation, enabling a smooth transition to the new production facility. All litigation surrounding our existing Korean production facility has been settled.

Deductibility of research and development costs

In Italy, Berna Biotech Italia Srl. was subject to a tax audit for fiscal years 2001 and 2002. For the year 2001, a settlement was reached with the Italian tax authorities in 2007. For the year 2002, no settlement has been reached. The tax authorities issued an assessment that deviates from the amount that was filed in the tax return. We have challenged this assessment in court. We made a provision for the costs of additional taxes, penalties

and interest, as well as lawyers' fees, which we expect we would have to pay as a result. One of the items in dispute is the deductibility of the research and development costs we make in Italy. The Group won the initial court case with respect to the deductibility of the research and development costs. The Italian tax authorities appealed this decision.

In 2008, the Italian tax authorities also challenged the deductibility of research and development costs for the year 2003 and issued an assessment. We will challenge this assessment in court. The Italian tax authorities may also challenge the deductibility of research and development costs for the years 2004 to 2008. As the Group considers it more likely than not that the research and development cost will be tax deductible, no additional provision was recognized for the deductibility of research and development costs.

Complaint against government grant awarded
In 2008, a competitor of Crucell filed a protest against the award of a government grant to Crucell for the development and manufacture of a vaccine against the Ebola and Marburg virus. The complaint was filed against the US. Government but Crucell voluntarily joined the proceedings to defend the award. Following a dismissal of the protest by the US Government Accountability Office (GAO), the competitor filed an appeal which is currently pending before the Court of Appeal of the Federal Circuit (CAFC).

Employee benefits
Further reference is made to retirement benefit obligations. See note 5.10.

Other
Other provisions mainly relate to asset retirement obligations and warranties.

Commitments and contingencies
Contingent liability STAR technology
The Group acquired STAR technology in 2004 through the purchase of ChromaGenics B.V., a privately held biotechnology company based in Amsterdam. In connection with the purchase, we also entered in a contingent payment agreement that could result in additional payments of up to € 7.0 million to former ChromaGenics shareholders upon receipt of revenues and royalties generated from the STAR technology. In connection with this agreement, we paid € 2.0 million in 2007. The expense was recognized in the cost of goods sold. No payments were made in 2008.

5.19 Short and long-term financial liabilities

This note provides information about the contractual terms of the Group's loans and borrowings. For more information about the Group's exposure to financial market risks, see note 3.

Debt repayment schedule at December 31, 2008:

In thousands of Euro

	Total 2008	2009	2010	2011	2012	2013	More than 5 years	Total 2007
Mortgage loan*	**16,461**	367	384	401	420	441	14,448	16,811
Equipment lease	**20,526**	2,777	3,010	3,371	6,135	1,776	3,457	10,080
Comprehensive credit limit Berna Biotech Korea Corp.	**20,855**	20,855	—	—	—	—	—	—
Privately placed bond Korea Corp.	**—**	—	—	—	—	—	—	14,540
Loan Berna Biotech Korea Corp.	**2,909**	1,455	1,454	—	—	—	—	4,364
Factoring liabilities	**—**	—	—	—	—	—	—	5,653
Other short-term bank loans	**—**	—	—	—	—	—	—	1,347
	60,751	**25,454**	**4,848**	**3,772**	**6,555**	**2,217**	**17,905**	**52,795**

* Calculated at the interest rate applicable until December 31, 2010.

Mortgage loan
In December 2005, the Group entered into a Euro mortgage loan of up to € 17,091 and as of December 31, 2006 the Group has drawn the maximum amount. In 2006, interest was accrued to the loan and no payments of principal or interest were required. Beginning January 1, 2007, the loan is being repaid through monthly payments over 15 years. A balloon repayment of € 10,000 will be made at the end of the 15 years. The loan matures on December 31, 2021. The loan bears interest at 4.55% for the first five years. After this period the rates will be renegotiated. The land, building, part of the equipment and a compensating cash balance arrangement with a bank in the amount of € 10,000 secure the loan. The carrying amount of the underlying secured assets was at the year-end € 24,015 (2007: € 26,946).

Finance lease liabilities
Finance leases mainly relate to equipment for the new production facility in Leiden. The vast majority of the finance lease liabilities are denominated in Euro. All leases are on a fixed repayment basis and interest rates are fixed at the contract date. For further information see note 5.22.

Comprehensive credit limit Berna Biotech Korea Corp.
On June 12, 2008 Berna Biotech Korea Corp. entered into a comprehensive credit limit transaction agreement. Under the terms of the agreement Berna Biotech Korea Corp. may freely borrow and repay money for an amount of KRW 30 billion during the period ending on May 31, 2009. In December 2008, Berna Biotech Korea Corp. agreed on an additional facility for KRW 10 billion. The loan has a variable interest rate that is based on a Korean interest index plus a mark-up. As per year-end the interest percentage was 6.79% and an amount of KRW 37 billion (€ 20,855) was drawn under the agreement.

Loan Berna Biotech Korea Corp.
Berna Biotech Korea Corp. had an unsecured Euro loan that bears interest at 5.45% which is outstanding as per December 31, 2008. The original maturity date of the loan was August 1, 2010, but the loan was repaid in full on February 2, 2009.

Privately placed bond Berna Biotech Korea Corp.
Berna Biotech Korea Corp ('Berna Biotech Korea') issued a Korean Won denominated bond with an interest rate of 6.73%. The privately placed bond by Berna Biotech Korea Corp. was repaid on June 13, 2008.

Factoring liabilities
In December 2007, the Group factored trade accounts receivable for a total amount of € 5,653 with an external party in Italy. The Group did not transfer substantially all the risks and rewards associated with ownership of the transferred trade accounts receivable, specifically the credit risk, and consequently the cash payments received are accounted for as a financial liability. No interest is charged on the factoring liabilities.

5.20 Other liabilities and deferred income – current and non-current

In thousands of Euro

	2008			2007		
	Current	Non-current	Total	Current	Non-current	Total
Deferred income	7,882	7,054	14,936	7,921	11,594	19,515
Accrued salary expenses and payroll taxes	9,817	—	9,817	10,318	—	10,318
Accrued expenses	8,540	—	8,540	14,684	—	14,684
Derivative financial instruments	879	—	879	16	—	16
Other liabilities	2,166	591	2,757	4,958	529	5,487
	29,284	7,645	36,929	37,897	12,123	50,020

5.21 Trade accounts payables

In thousands of Euro

Year ended December 31,	2008	2007
Trade accounts payables to third parties	58,182	50,638
Trade accounts payables to joint ventures	1,023	332
	59,205	50,970

Trade accounts payables are generally paid under the payment terms, which vary by company and region. The Group's general payment terms are typically 30 days.

5.22 Operating and finance leases

Operating lease commitments

The Group leases certain research and corporate facilities, motor vehicles and items of machinery and equipment. No restrictions are placed upon the lessee by entering into these leases. Future minimum lease payments under operating leases as at December 31, 2008 and 2007 are as follows:

In thousands of Euro

Year ended December 31,	2008	2007
Within one year	3,830	4,798
After one year but not more than five years	10,073	15,308
More than five years	10,759	14,155
	24,662	34,261

Most operating leases are increased by a general price index on an annual basis.

Finance lease commitments

Certain of the Group's fixtures and equipment are subject to finance leases. These leases mainly relate to equipment for the new production facility in Leiden. Interest rates are fixed at the contract date. All leases are on a fixed repayment basis and no arrangements have been entered into for contingent rental payments. The fair value of the Group's lease obligations approximates their carrying amount. The Group's obligations under finance leases are secured by the value of the underlying assets. The average term of finance leases entered into is 5.5 years.

Future minimum lease payments under finance leases as at December 31, 2008 and 2007 are as follows:

In thousands of Euro

	2008		2007	
	Minimum payments	Present value of minimum payments	Minimum payments	Present value of minimum payments
Within one year	4,134	2,777	2,038	1,420
After one year but not more than five years	17,284	14,292	10,937	8,660
More than five years	3,580	3,457	—	—
	24,998	20,526	12,975	1 0,080

5.23 Related parties

Related party transactions within the group

The Group has related party transactions and balances with joint venture partners, associates and directors and executive officers. All transactions with related parties were carried out under normal market conditions (arm's length principle). There are no related party transactions outside the normal course of business.

The following table provides the total value of transactions which have been entered into with related parties, excluding directors and executive officers, for the relevant financial year.

In thousands of Euro

	Income and expenses for the year ended December 31,			Balance outstanding as at December 31,	
Related party	2008	2007	2006	2008	2007
Sales of goods and services					
Pevion Biotech AG	—	364	251	—	—
Kenta Biotech AG	130	223	168	—	—
ADImmune Corp.	3,262	2,271	—	4,495	6,724
Expenses					
Percivia	(4,081)	(4,247)	(1,227)	(1,023)	(332)
Avv Falaguerra	(34)	(17)	(12)	(43)	(6)
Kenta Biotech AG	—	—	(60)	—	—

Mr. Falaguerra, the chairman of the Board of Directors of the Italian subsidiary, is related to Avv. Falaguerra, an Italian firm that provides taxation services to the Italian subsidiary.

Terms and conditions of transactions with related parties

The sales to and purchases from related parties are made at normal market prices. Outstanding balances at the year-end are unsecured, interest free and settlement occurs in cash. There have been no guarantees provided by the Group or received in respect of any related party receivables or payables. For the year ended December 31, 2008, the Group has not made any provision for doubtful debts relating to amounts owed by related parties (2007: nil). This assessment is undertaken each financial year through examining the financial position of the related party and the market in which the related party operates.

Transactions between the Company and its subsidiaries, which are related parties, have been eliminated on consolidation and are not disclosed in this note.

Management Board

The total remuneration and related costs (excluding share-based payments – see information below on stock options and performance stock) of the members of the Management Board over the past three years, is as follows:

In thousands of Euro

	2008	2007	2006
Salaries	1,259	1,035	1,005
Bonuses	782	647	893
Pension costs	260	202	205
Other	39	37	37
	2,340	1,921	2,140

The remuneration of the individual members of our Management Board during 2008, excluding stock options, was as follows:

Name	Salaries	Bonuses[1]	Pension costs[2]	Other costs[3]	Total
R.H.P. Brus	433	373	77	—	883
L. Kruimer	292	168	62	13	535
C. de Jong (as of May 31, 2008) [4]	184	119	27	7	337
J. Goudsmit	350	122	94	19	585
Totals	**1,259**	**782**	**260**	**39**	**2,340**

[1] Bonus expense includes the incentive plans to which the Management Board is entitled as at December 31, 2008. The bonus expense excludes option exercises.

[2] 'Pension Costs' include pensions, social security costs and disability insurance.

[3] 'Other costs' include company cars.

[4] Cees de Jong's remuneration for the year 2008 is included pro rata as of May 31, 2008.

Pension, retirement and similar arrangements for our Management Board members consist of the defined contribution plan, and we do not have further pension obligations beyond the annual premium contribution.

The Company's Management Board members held the following options for the period ended December 31, 2008:

Name of Holder	Options held at December 31, 2007[1]	Year of expiration	Exercise Price	Granted 2008	Exercised 2008	Forfeited 2008	Options held at December 31, 2008
R.H.P. Brus	250,000	2009	9.40	—	—	—	**250,000**
	200,000	2011	3.49	—	—	—	**200,000**
	90,000	2011	2.64	—	—	—	**90,000**
	125,000	2011	5.94	—	—	—	**125,000**
	—	2013	12.23	300,000	—	—	**300,000**
L. Kruimer	85,000	2009	9.40	—	(85,000)	—	**—**
	30,000	2011	3.49	—	—	—	**30,000**
	125,000	2011	5.94	—	—	—	**125,000**
	—	2013	12.23	150,000	—	—	**150,000**
C. de Jong	185,000	2012	14.58	—	—	—	**185,000**
	—	2013	12.23	200,000	—	—	**200,000**
J. Goudsmit	85,000	2009	9.40	—	—	—	**85,000**
	60,000	2011	2.64	—	(60,000)	—	**—**
	125,000	2011	5.94	—	—	—	**125,000**
	—	2013	12.23	150,000	—		**150,000**
Totals	**1,360,000**			**800,000**	**(145,000)**	**—**	**2,015,000**

[1] The options held at December 31, 2007 include 185,000 options of Cees de Jong who was not a member of the Management Board until May 30, 2008.

In April 2008, Jaap Goudsmit exercised 60,000 options with an exercise price of € 2.64 and a total value of € 431. In May 2008, Leon Kruimer exercised 85,000 options with an exercise price of € 9.40 and a total value of € 258.

The Company's Management Board members held the following shares in the Company at December 31, 2008:

Name of holder	Ordinary shares held at December 31, 2008	% of total ordinary shares
R.H.P Brus	**154,202**	0.23%
L. Kruimer	**28,195**	0.04%
C. de Jong	**2,406**	0.01%
J. Goudsmit	**159,276**	0.24%
	344,079	**0.52%**

The following table describes loans granted to the members of Crucell's Management Board and senior management since January 1, 2001. Crucell has not granted any loans to any Supervisory Board members. The Company sets interest rates on these loans in relation to Dutch income tax law. The loans were granted to the persons listed below in connection with options granted to them on Crucell's ordinary shares. These loans become payable at the time shares received on exercise of the related options are sold or immediately in case the employee ceases to work for Crucell before this time. Crucell funds payments due under the loans prior to July 30, 2002, the date legislation was passed in the US prohibiting the granting of additional loans to company officers.

Name	Largest amount of loan outstanding since January 1, 2001	Amount of loan outstanding at December 31, 2008	2008 interest rate in %
R.H.P. Brus	132	87	3.5%
J. Goudsmit	25	—	3.5%
Other personnel	61	47	3.5%
		134	

The Group is not a party to any material transactions, or proposed transactions, in which any director, any executive officer, any spouse or relative of any of the foregoing, or any relative of any such spouse had, or was to have, a direct or indirect material interest other than those transactions disclosed in these financial statements.

Supervisory Board

Due to the fact that Crucell operates on a global scale with many of its supervisory directors used to the international arena, Crucell offers compensation to its supervisory directors in accordance with customary practice in the biotechnology sector.

From 2008 and onwards, compensation for all Supervisory Board members consists of a fixed fee in cash and an annual share grant. The fixed fee in cash ranges from € 34 to € 44 per Supervisory Board member. In addition, the chairman of the Supervisory Board is awarded annually a net allowance of € 5 that is grossed up for taxation purposes. The annual share grant awarded to each member of the Supervisory Board shall equal 2,500 ordinary shares. The amounts will be revised on a triennial basis. The shares should be held for as long as an individual is a member of the Supervisory Board. Instead of the share grant, a Supervisory Board member may also choose to receive a cash amount equalling the value of 2,500 shares at the date of grant minus 25%.

During 2008, 2007 and 2006, the individual members of the Supervisory Board were entitled to receive the following remuneration (excluding share-based payments – see information below on stock options and performance stock):

Year ended December 31,	2008	2007	2006
P. Strijkert[1]	—	—	16.7
J.P. Oosterveld[2]	54.2	60.8	38.7
A. Hoevenaars	35.0	25	25
S.P. Lance	34.0	25	25
P.M. Satow	35.0	25	25
C.E. Wilhelmsson	35.0	25	25
S. Davis	34.0	—	—
D.S. Koechlin[3]	12.5	25	25
J. Witmer[4]	—	10.4	25
C.E. Thomann[4]	—	10.4	25
Totals	239.7	206.6	230.4

[1] Mr. P. Strijkert resigned from the Supervisory Board on June 2, 2006.

[2] Mr. J.P. Oosterveld was appointed Chairman on June 2, 2006.

[3] Mr. D.S. Koechlin was appointed member of the Supervisory Board on June 2, 2006, but has attended meetings since January 2006. Mr. D.S. Koechlin resigned from the Supervisory Board on May 30, 2008.

[4] Mr. J. Witmer and Mr. C.E. Thomann were appointed member of the Supervisory Board on June 2, 2006, but have attended meetings since January 2006. Mr. J. Witmer and Mr. C.E. Thomann resigned from the Supervisory Board on June 1, 2007.

The Company's Supervisory Board members held the following options for the period ended December 31, 2008:

Name of Holder	Options held per December 31, 2007	Year of expiration	Exercise price €	Granted 2008	Exercised 2008	Forfeited 2008	Options held per December 31, 2008
J.P. Oosterveld	**10,000**	2009	8.81	—	—	—	**10,000**
	10,000	2009	11.55	—	—	—	**10,000**
S.P. Lance	**10,000**	2011	7.86	—	—	—	**10,000**
	10,000	2009	11.55	—	—	—	**10,000**
P.M. Satow	**10,000**	2009	11.55	—	—	—	**10,000**
	22,000	2011	3.49	—	—	—	**22,000**
	10,000	2011	6.48	—	—	—	**10,000**
C.E. Wilhelmsson	**10,000**	2009	11.55	—	—	—	**10,000**
	10,000	2011	6.48	—	—	—	**10,000**
A.Hoevenaars	**5,000**	2009	8.81	—	—	—	**5,000**
	10,000	2009	11.55	—	—	—	**10,000**
Totals	**117,000**			—	—	—	**117,000**

Crucell's Supervisory Board members held the following shares in the Company per December 31, 2008:

Name of holder	Ordinary shares held per December 31, 2008	% of total ordinary shares
J.P. Oosterveld	**9,500**	0.01%
A. Hoevenaars	**7,500**	0.01%
S.P. Lance	**—**	—
P.M. Satow	**63,800**	0.10%
C.E. Wilhelmsson	**7,500**	0.01%
S. Davis	**—**	—
	88,300	**0.13%**

Pursuant to Dutch law, each member of Crucell's Supervisory Board and Management Board is responsible to the Company for the proper performance of his or her assigned duties. They are also responsible for taking measures to prevent the consequences of any improper performance of duties by another member of Crucell's Supervisory Board or Crucell's Management Board. The Company's articles of association provide that Crucell's Management Board members and Crucell's Supervisory Board members are discharged from liability for their actions as board members, if Crucell's General Meeting of Shareholders adopts a resolution to that effect.

This discharge extends only to actions or omissions disclosed in or apparent from the adopted annual accounts or otherwise communicated to the Company's General Meeting of Shareholders.

Mandatory provisions of Dutch law may limit this discharge of liability, for example in the case of bankruptcy. Under Dutch law, the Company's Supervisory Board members and members of the Company's Management Board generally cannot be held personally liable for decisions made exercising their reasonable business judgment.

The Company's articles of association provide that the Company shall generally indemnify any person who is or was a member of the Company's Supervisory Board or of the Company's Management Board or one of the Company's employees, officers or agents, and suffers any loss as a result of any action in connection with their service to the Company, provided they acted in good faith in carrying out their duties.

This indemnification generally will not be available if the person seeking indemnification acted with gross negligence or wilful misconduct in the performance of his or her duties to the Company. A court in which an action is brought, may however determine that indemnification is appropriate nonetheless.

Company Financial Statements

6 Balance sheet (After appropriation of result)

(Amounts in thousands of Euro)

	Notes	2008	2007
Assets			
Non-current assets			
Investments in subsidiaries	9.1	**305,572**	307,355
Other long-term receivables	9.2	**49,272**	87,680
		354,844	**395,035**
Current assets			
Short-term receivables		**1,015**	2,175
Cash and cash equivalents		**79,295**	54,997
Short term receivables related parties		**18,614**	—
		98,924	57,172
Total assets		**453,768**	**452,207**
Liabilities and shareholders' equity			
Shareholders' equity			
Issued capital		**15,800**	15,685
Share premium		**743,746**	735,578
Translation reserve (legal reserve)		**(33,026)**	(28,317)
Hedge reserve		**(685)**	—
Available-for-sale reserve		**3,254**	8,340
Accumulated deficit		**(275,597)**	(290,183)
	9.3	**453,492**	**441,103**
Non-current liabilities			
Liabilities to related parties		**149**	142
		149	**142**
Current liabilities			
Accrued compensation and related benefits		**122**	927
Liability to related parties		**5**	10,035
		127	**10,962**
Total liabilities and shareholders' equity		**453,768**	**452,207**

7 Income statement

In thousands of Euro

For the year ended December 31,	2008	2007	2006
Result from subsidiaries	**4,019**	(46,944)	(89,598)
Other income	**10,567**	4,034	2,652
Profit/(loss) for the year	**14,586**	**(42,910)**	**(86,946)**

Notes to the Company Financial Statements

8 General

The description of the Group's activities and the Group structure as included in the notes to the consolidated financial statements also apply to the Company financial statements (see note 1.1).

In accordance with article 2:362 section 8 of Book 2 Title 9 of the Dutch Civil Code, the accounting policies used in the preparation of the Company financial statements are the same as those used in the preparation of the consolidated financial statements. Investments in subsidiaries are stated at net asset value as the Company effectively exercises significant influence over the operational and financial activities of these investments. The net asset value is determined on the basis of the IFRS accounting principles applied by the Group in its consolidated financial statements.

In accordance with article 402, Book 2 Title 9 of the Dutch Civil Code, the Company income statement is presented in abbreviated form.

9 Notes to the Company financial statements

9.1 Investments in subsidiaries

Investments in subsidiary companies are stated at net asset value as the Company effectively exercises significant influence over the operational and financial activities of these investments.

In thousands of Euro

	2008	2007
Book value as of January 1,	**307,355**	**318,979**
Share in result of subsidiaries	4,019	(46,944)
Net unrealized result on available-for-sale reserve	(5,086)	(2,330)
Effect of movements in exchange rates	(4,709)	(20,384)
Dividends received from Berna Biotech AG	(43,069)	(80,907)
Acquisition shares Berna Rhein B.V.	—	80,907
Provisions reversed during the year	—	(1,341)
Offset of receivables	47,062	59,375
Book value at December 31,	**305,572**	**307,355**

On June 12, 2008 Berna Biotech AG distributed a dividend equivalent to € 43,069 to the Company.

Beginning 2007, Crucell owned 7.3% of the shares of Berna Rhein B.V., the remaining 92.7% of the shares were owned by Crucell's subsidiary Berna Biotech AG. On November 3, 2007 Crucell acquired the remaining 92.7% shares for € 80,907. Berna Biotech AG subsequently distributed a dividend equivalent to € 80,907 to the Company.

9.2 Other long-term receivables

In thousands of Euro

	2008	2007
Long-term receivables on related parties	**36,376**	73,284
Other long-term receivables	**12,896**	14,396
	49,272	**87,680**

9.3 Shareholders' equity

Reference is made to the Consolidated Statement of Changes in Equity and to note 5.16 'Issued share capital and reserves' of the notes to the consolidated financial statements as of, and for the year ended December 31, 2008.

9.4 Taxes

The Company constitutes a fiscal unity with the Dutch wholly owned subsidiaries Crucell Holland B.V., U-BiSys B.V. and ChromaGenics B.V. and is for that reason jointly and severally liable for the tax liabilities of the whole fiscal unity. As of the financial year 2008, Berna Rhein B.V. was included in that fiscal unity.

9.5 Employee information

The Company had no employees in 2008 and 2007.

9.6 Auditor's fees

	2008			2007		
	Deloitte Accountants B.V.	Network Deloitte Accountants B.V.	Total	Deloitte Accountants B.V.	Network Deloitte Accountants B.V.	Total
Audit fees	481	359	840	491	413	904
Audit related fees	75	—	75	54	10	64
Tax fees for services provided related to consultation on tax matters	—	—	—	—	—	—
Total fees	556	359	915	545	423	968

9.7 Joint and several liability

In accordance with Section 403 of Book 2 Title 9 or the Netherlands Civil Code, the Company has assumed joint and several liability for all legal transactions carried out by the following subsidiaries:

Crucell Holland B.V., Leiden
U-BiSys B.V., Utrecht
ChromaGenics B.V., Amsterdam

Signing of the financial statements

The financial statements were approved by the Management Board and Supervisory Board and authorized for issue on April 17, 2009.

Management Board
R.H.P. Brus
L. Kruimer
C. de Jong
J. Goudsmit

Supervisory Board
J.P. Oosterveld
A. Hoevenaars
S.P. Lance
P.M. Satow
C.E. Wilhelmsson
S. Davis

Other Information

Appropriation of result

Annual dividends may only be paid out of profits as shown in the adopted annual financial statements. We may not make distributions if the distribution would reduce our shareholders' equity below certain reserves required by Dutch law or our articles of association. The profits must first be used to set up and maintain reserves required by Dutch law and must then be set off against certain financial losses. The preference shares will be paid their dividends first, which will be a certain percentage of their nominal value. With Supervisory Board approval, our Management Board then decides whether and how much of the remaining profit will be reserved. Any profits remaining shall be paid as a dividend on the ordinary shares. If the retained earnings are negative or are to be used to form a statutory reserve no dividend will be paid out. The profit for the year 2008 was added to the accumulated deficit.

Preference shares

On October 25, 2000, the Company established a foundation called Stichting Preferente Aandelen Crucell, also referred to as the Preferred Foundation. The Preferred Foundation's object is to safeguard the interests of Crucell, its business and parties connected therewith by blocking any influences that may threaten these interests, which interests may include the continuity, independence or identity of Crucell, its business and parties connected therewith. The Preferred Foundation can safeguard the interests through acquiring and managing the preference shares and by exercising the rights attaching to these shares, in particular, the voting rights.

The Preferred Foundation has an option to acquire preference shares up to 100% of the number of our outstanding shares, necessary to match the total number of statutory votes on all of the ordinary shares outstanding at the time of an acquisition. The Preferred Foundation must pay at least 25% of the nominal value of the preference shares it acquires from us. If we acquire any preference shares, they may be cancelled.

A board of governors of up to five persons directs the Preferred Foundation. Mr. J.P. Oosterveld, in his capacity as chairman of our Supervisory Board, and Mr. P. Bouw, Mr. M.W. den Boogert, Mr. S. van Wijnbergen and Mr. G.P. Krans, have been appointed to the board of governors. A majority of these members may not be members or former members of our Management or Supervisory Board, or an employee of any of our advisers, any of our banks or us. The board of governors appoints these independent members. Our Supervisory Board appoints the non-independent members after consultation with our Management Board.

Auditor's Report

To the Supervisory Board and Shareholders of Crucell N.V., Leiden, The Netherlands

Report on the financial statements

We have audited the accompanying financial statements 2008 as set out on pages 125 to 174 of Crucell N.V., Leiden. The financial statements consist of the consolidated financial statements and the company financial statements. The consolidated financial statements comprise the consolidated balance sheet as at December 31, 2008, profit and loss account, statement of changes in equity and cash flow statement for the year then ended, and a summary of significant accounting policies and other explanatory notes. The company financial statements comprise the company balance sheet as at December 31, 2008, the company profit and loss account for the year then ended and the explanatory notes.

Management's responsibility

Management is responsible for the preparation and fair presentation of the financial statements in accordance with International Financial Reporting Standards as adopted by the European Union and with Part 9 of Book 2 of the Netherlands Civil Code, and for the preparation of the management board report in accordance with Part 9 of Book 2 of the Netherlands Civil Code. This responsibility includes: designing, implementing and maintaining internal control relevant to the preparation and fair presentation of the financial statements that are free from material misstatement, whether due to fraud or error; selecting and applying appropriate accounting policies; and making accounting estimates that are reasonable in the circumstances.

Auditor's responsibility

Our responsibility is to express an opinion on the financial statements based on our audit. We conducted our audit in accordance with Dutch law. This law requires that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance whether the financial statements are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers internal control relevant to the entity's preparation and fair presentation of the financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the entity's internal control. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made by management, as well as evaluating the overall presentation of the financial statements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Opinion with respect to the consolidated financial statements

In our opinion, the consolidated financial statements give a true and fair view of the financial position of Crucell N.V.as at December 31, 2008, and of its result and its cash flow for the year then ended in accordance with International Financial Reporting Standards as adopted by the European Union and with Part 9 of Book 2 of the Netherlands Civil Code.

Opinion with respect to the company financial statements

In our opinion, the company financial statements give a true and fair view of the financial position of Crucell N.V. as at December 31, 2008 and of its result for the year then ended in accordance with Part 9 of Book 2 of the Netherlands Civil Code.

Report on other legal and regulatory requirements

Pursuant to the legal requirement under 2:393 sub 5 part f of the Netherlands Civil Code, we report, to the extent of our competence, that the management board report is consistent with the financial statements as required by 2:391 sub 4 of the Netherlands Civil Code.

Signed by:

Deloitte Accountants B.V.
P.J.M.A van de Goor
Amsterdam, the Netherlands
April 21, 2009

Information for Shareholders and Investors

Investor relations approach

Crucell maintains an active and transparent approach to relations with shareholders and investors. We inform the financial markets regularly about the Company's strategy and developments. Quarterly results releases, presentations and press releases on important business developments are disseminated on a regular basis and reinforced with briefings by phone and in person. Since August 2007, we have strengthened our Investor Relations activities with the addition of two dedicated Investor Relations Officers whose mission it is to ensure the investor community understands clearly the Company's prospects and performance. This reflects our ambition to widen our investor base as well as to deepen existing investors' understanding of Crucell.

Activities in 2008 for shareholders and investors comprised:

- A full presentation of quarterly results to financial journalists and analysts at each quarter, consisting of an online slide show and audio commentary, question and answer sessions and archiving for subsequent retrieval;
- An investor and analyst day in London in March 2008 with presentations on our strategy, business and pipeline. This event was supported by online slide shows and was video webcasted via our website with question and answer sessions and archiving for subsequent retrieval;
- Various additional telephone conference calls with management for analysts and investors;
- Regular road show meetings with potential and existing shareholders and sell-side analysts who cover the Company;
- Timely updates in the Investor Relations section of the website www.crucell.com;
- Periodic website updates of more comprehensive financial Company data, including filings with the United States Securities and Exchange Commission; and
- Online publication of relevant scientific company presentations.

Crucell Shares

- Crucell's ordinary shares are listed on:
- NYSE Euronext Amsterdam N.V. (symbol: CRXL) since 2000;
- NASDAQ in the US (symbol: CRXL) in the form of ADS's since 2000;
- SWX Swiss Exchange in Zurich (symbol: CRXL) since 2005;
- The Company's primary listing is Amsterdam where trading turnover reached € 1.24 billion in 2008; Crucell's shares are included in the AMX mid-cap index (since 2005);

Share data

	2008	2007
Earnings per share	**0.22**	(0.66)
Shares outstanding (million) at year-end	**65.8**	65.3
Dividend	**–**	–
Highest price	**14.10**	22.45
Lowest price	**7.40**	10.26
Price at December 31,	**10.89**	11.40
Average daily trading volume on Euronext Amsterdam (X 1000)	**465**	470

Shareholders with holdings of Crucell shares exceeding 5%

Percentage of beneficial ownership is based on an aggregate of 66,544,577 ordinary shares outstanding at April 17, 2009 except as otherwise noted:

	Ordinary Shares Beneficially Owned[1]	
Beneficial Owner	Number of Ordinary Shares	Holding (%)
A. van Herk B.V.	6,697,411	10.06[2]
Aviva plc	3,514,230	5.28[3]
Ordinary shares held by our Management Board members	439,079	0.66
Ordinary shares held by our Supervisory Board members	115,800	0.17

[1] Under Rule 13d 3 of the Exchange Act, more than one person may be deemed to beneficially own certain ordinary shares (if, for example, persons share the power to vote or the power to dispose of the ordinary shares). In addition, a person is deemed to beneficially own ordinary shares if the person has the right to acquire the ordinary shares (for example, upon exercise of an option) within 60 days of the date as of which the information is provided. As a result, the percentage of outstanding ordinary shares of any person as shown in this table does not necessarily reflect the person's actual ownership or voting power with respect to the number of ordinary shares actually outstanding. In addition, filings with the Netherlands Authority for the Financial Markets (Autoriteit Financiële Markten or AFM) with respect to shareholdings in public companies do not specify the number of shares held by the filing party.

(2) Percentage holding is derived from a filing made by A. van Herk B.V. with the Netherlands AFM.

(3) Percentage holding is derived from a filing made by Aviva plc. with the Netherlands AFM.

As of April 17, 2009 there were 13,045,583 ADSs, each representing one ordinary share, all of which were held of record by nine registered holders in the US (including The Depository Trust Company). The number of ADSs at April 17, 2009 represent 19.6% of our ordinary shares that were issued and outstanding on that date.

To the best of our knowledge, we are not directly or indirectly owned or controlled by any other corporation, foreign government or other person or entity.

Share information

Crucell shares are included in the NYSE Euronext Amsterdam Dutch mid-cap index (AMX), and in the NASDAQ Composite Index. They are also included in the FTSE NASDAQ Small Cap index since 2005 and in the NYSE Euronext NEXT Biotech Index as of April 2008.

	2008	2007
Market Capitalization at December 31, (€ million)	**716.6**	744.4
Market Capitalization at December 31, ($ million)	**1,000.2**	1,080.1
Closing share price at December 31, (€)	**10.89**	11.40
Closing share price at December 31, ($)	**15.20**	16.54
Shares outstanding at December 31, (million)	**65.8**	65.3

Shareholder information

At December 31, 2008, institutional investors held 42% of the outstanding shares in Crucell, private investors held 57% of shares and holdings of affiliates were approximately 1%.

Geographical spreads of shareholders in approximate percentages on December 31, 2008, compared to the previous year are as follows:

	2008	2007
The Netherlands	**68%**	66%
United States	**22%**	22%
Germany	**4%**	8%
United Kingdom	**3%**	1%
Scandinavia	**2%**	1%
Other	**1%**	2%
Total	**100%**	**100%**

Outlook for 2009

In constant currencies; weighted average €/$ rate of 1.35 in 2008:

Total revenue & other operating income	20% growth
Operating profit	Significant improvement compared to 2008
Cash flow	Solid, despite significant investments in the new facility being built in Korea

General information

Auditors
Deloitte Accountants B.V.

Legal Counsel
Allen & Overy LLP
Cleary Gottlieb Steen & Hamilton LLP

Tax Advisors
Ernst & Young

ADS Depository
Bank of New York Mellon

Investor Relations
Oya Yavuz, Director of Corporate Communications and Investor Relations
Frauke Groenevelt, Coordinator Investor Relations
Tel: +31 71 5197064
Email: ir@crucell.com

Our ordinary shares and ADSs

Our ordinary shares are traded in the US solely in the form of ADSs, each ADS representing one ordinary share. Each ADS is evidenced by an American Depositary Receipt issued by The Bank of New York Mellon acting as depositary in respect thereof.

The following table sets forth the range of high and low closing prices, in US dollars, for our ADSs on the NASDAQ National Market for the periods indicated.

	ADSs	
	High	Low
Annual information for the past five years		
2004	13.77	6.38
2005	29.95	12.30
2006	28.82	17.27
2007	28.96	16.08
2008	19.88	9.60
Quarterly information for the past two years		
2007		
First Quarter	28.96	23.85
Second Quarter	26.01	21.48
Third Quarter	23.81	19.11
Fourth Quarter	20.85	16.08
2008		
First Quarter	19.39	13.15
Second Quarter	19.88	15.47
Third Quarter	18.18	13.27
Fourth Quarter	15.86	9.60
2009		
First Quarter	23.29	15.65
Monthly information for the most recent six months		
November 2008	14.69	11.60
December 2008	15.86	12.42
January 2009	23.29	15.65
February 2009	21.01	18.66
March 2009	20.78	17.58
April 2009 (Until April 17, 2009)	21.12	19.09

Our ordinary shares trade on Eurolist by NYSE Euronext Amsterdam N.V. through the book-entry facilities of NEGICEF, Euroclear and Clearstream Luxembourg. For the ordinary shares the International Securities Identification Number (ISIN) code is NL0000358562, the Amsterdam Security Number is 35856 and the Common Code is 11907164.

The following table sets forth the range of high and low closing prices, in Euro, for our ordinary shares in the Netherlands for the periods indicated.`

	Ordinary shares	
	High	Low
Annual information for the past five years		
2004	10.10	4.83
2005	24.77	9.50
2006	23.49	14.04
2007	22.27	10.96
2008	13.26	7.77
Quarterly information for the past two years		
2007		
First Quarter	22.27	18.30
Second Quarter	19.35	14.29
Third Quarter	17.33	13.53
Fourth Quarter	14.96	10.96
2008		
First Quarter	13.26	8.55
Second Quarter	12.85	9.86
Third Quarter	12.10	9.15
Fourth Quarter	11.35	7.77
2009		
First Quarter	17.15	11.33
Monthly information for the most recent six months		
November 2008	11.20	9.31
December 2008	11.35	10.05
January 2009	17.15	11.33
February 2009	16.40	14.65
March 2009	15.71	14.17
April 2009 (Until April 17, 2009)	15.80	14.48

Exchange rate information

The following table sets forth, for the years indicated, the high, low, average and year-end noon buying rates in New York City for cable transfers as certified for customs purposes by the Federal Reserve Bank of New York ('Noon Buying Rates') expressed in Euro per USD 1.00.

In Euro Year ended December 31,	High	Low	Average[1]	End of period
2004	0.85	0.73	0.81	0.73
2005	0.86	0.73	0.80	0.84
2006	0.84	0.75	0.80	0.76
2007	0.77	0.67	0.73	0.68
2008	0.80	0.62	0.68	0.72

[1] The average of the Noon Buying Rates on the last business day of each month during the period indicated.

The following table sets forth, for the previous six months, the high and low Noon Buying Rates expressed in Euro per USD 1.00.

	High €	Low €
November 2008	0.80	0.77
December 2008	0.79	0.70
January 2009	0.78	0.72
February 2009	0.80	0.77
March 2009	0.80	0.73
April 2009 (Until April 17, 2009)	0.77	0.74

On April 17, 2009 the Noon Buying Rate was $ 1.00 = € 0.77. These rates may differ from the actual rates used in the preparation of our financial statements and other financial information appearing in this Annual Report.

Taxation

The following is a summary of the material Dutch and US tax consequences of an investment in ordinary shares or ADSs. This summary does not discuss every aspect of taxation that may be relevant to a particular investor who is subject to special treatment under any applicable law, and is not intended to be applicable in all respects to all categories of investors. This summary also assumes that our business will be conducted in the manner outlined in this document. Changes in our organizational structure or the manner in which we conduct our business may invalidate this summary. The laws upon which this summary is based are subject to change, perhaps with retroactive effect. A change to these laws may invalidate the contents of this summary, which will not be updated to reflect changes in the laws. Prospective investors should consult their professional tax advisors regarding their particular personal tax consequences of acquiring, owning and disposing of our ordinary shares or ADSs.

Certain Dutch tax consequences for holders of ordinary shares or ADSs

This summary describes the principal tax consequences that will generally apply in the case of an investment in the ordinary shares or ADSs under Dutch tax laws in force and in effect as of the date hereof, and is subject to changes in Dutch law, including changes that could have retroactive effect. Not every potential tax consequence of such investment under the laws of the Netherlands will be addressed.

Dutch taxation of resident shareholders

The summary of certain Dutch taxes set out in this section 'Dutch Taxation of Resident Shareholders' is only intended for the following investors:

- Individuals who are resident or deemed to be resident or who have opted to be resident in the Netherlands for purposes of Dutch taxation and who invest in the ordinary shares or ADSs, excluding individuals who invest in the ordinary shares or ADSs that form part of a substantial interest (as described below) or deemed substantial interest in us and excluding individuals who are our employees or who are deemed to be our employees or employees of any entity related to us (the 'Dutch Individuals'); and
- Corporate entities (including associations which are taxable as corporate entities) that are resident or deemed to be resident in the Netherlands for purposes of Dutch taxation and who invest in the ordinary shares or ADSs, excluding:
- Corporate entities that are not subject to Dutch corporate income tax;
- Pension funds (pensioenfondsen) and other entities that are wholly or partly exempt from Dutch corporate income tax;

- Corporate entities that hold ordinary shares or ADSs that qualify for application of the participation exemption (as laid down in the Dutch Corporate Income Tax Act 1969); and
- Investment institutions (beleggingsinstellingen) and tax exempt investment institutions (vrijgestelde beleggingsinstellingen) as defined in the Dutch Corporate Income Tax Act 1969; (the 'Dutch Corporate Entities').

Generally, a holder of ordinary shares or ADSs will not have a substantial interest if he, his spouse, certain other relatives (including foster children) or certain persons sharing his household, do not hold, alone or together, whether directly or indirectly, the ownership of, or certain other rights over, ordinary shares representing 5% or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of shares), or rights to acquire ordinary shares, whether or not already issued, that represent at any time 5% or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of shares) or the ownership of certain profit participating certificates that relate to 5% or more of our annual profit and/or to 5% or more of our liquidation proceeds.

Individual and corporate income tax
For Dutch Individuals not engaged or deemed to be engaged in an enterprise and Dutch individuals for whom the benefits derived from the ordinary shares or ADSs are not treated as 'result from other activities', the following applies:

The taxable benefit from a Dutch Individual's 'savings and investments' (sparen en beleggen) is set annually at 4% of the average of the so-called 'yield basis' (rendementsgrondslag) at the beginning and at the end of a year, insofar as the average exceeds the 'exempt net asset amount' (heffingvrij vermogen). Such taxable benefit is reduced by such portion of the personal allowance as has not been taken into account in respect of certain other types of income. This benefit is taxed at the rate of 30%. For Dutch Individuals who invest in the ordinary shares or ADSs, the ordinary shares or ADSs will form part of the yield basis. The ordinary shares or ADSs will be taken into account in the yield basis at their fair market value. The actual benefits from the ordinary shares or ADSs do not influence the taxable benefit, even if they exceed, or are lower than, 4% of the yield basis.

For Dutch Individuals engaged or deemed to be engaged in an enterprise, Dutch Individuals for whom the benefits derived from the ordinary shares or ADSs are treated as result from other activities, and Dutch Corporate Entities, the following applies:

Any benefits derived or deemed to be derived from the ordinary shares or ADSs (including any capital gains realized on the disposal thereof) that are attributable to an enterprise carried on in the Netherlands by a Dutch Individual or to an enterprise effectively managed in the Netherlands in which he has an interest, are generally subject to income tax charged at progressive rates. The same applies to a Dutch Individual for whom the benefits derived from the ordinary shares or ADSs are treated as result from other activities. Any benefits derived or deemed to be derived from the ordinary shares or ADSs (including any capital gains realized on the disposal thereof) that are held by a Dutch Corporate Entity are generally subject to corporate income tax.

Withholding tax
Dividends we distribute are generally subject to a withholding tax imposed by the Netherlands at a rate of 15%. The concept 'dividends we distribute' used in this section includes, but is not limited to:

- Distributions in cash or in kind, deemed and constructive distributions and repayments of paid-in capital not recognized for Dutch dividend withholding tax purposes;
- Liquidation proceeds, proceeds of redemption of the ordinary shares or ADSs or, as a rule, consideration for the repurchase of the ordinary shares or ADSs by us in excess of the average paid-in capital recognized for Dutch dividend withholding tax purposes;
- The par value of the ordinary shares or ADSs issued to a holder of the ordinary shares or ADSs or an increase of the par value of the ordinary shares or ADSs, as the case may be, to the extent that it does not appear that a contribution, recognized for Dutch dividend withholding tax purposes, has been made or will be made; and
- Partial repayment of paid-in capital, recognized for Dutch dividend withholding tax purposes, if and to the extent that there are net profits (zuivere winst), unless:
  - The general meeting of our shareholders has resolved in advance to make such repayment; and
  - The par value of the ordinary shares or ADSs concerned has been reduced by an equal amount by way of an amendment of the articles of association.

- Dutch Individuals and Dutch Corporate Entities generally can credit the dividend withholding tax against their income tax or corporate income tax liability and will be entitled to a refund of dividend withholding tax insofar as such tax, together with any other creditable domestic and/or foreign taxes, exceeds their aggregate income tax or corporate income tax liability. A condition to avoid 'dividend stripping' is that the recipient of proceeds from the ordinary shares or ADSs qualifies as the beneficial owner thereof. A recipient of proceeds from the ordinary shares or ADSs is not considered to be the beneficial owner thereof if the amount of dividend, following a set of transactions, is ultimately wholly or partly received by another person, if this other person also retains, directly or indirectly, an interest in the ordinary shares or ADSs and the recipient is entitled to a (partial) refund or exemption to which the other person is not entitled.

Gift and inheritance taxes

A gift tax liability will arise in the Netherlands with respect to an acquisition of the ordinary shares or ADSs by way of a gift made by a Dutch individual or a Dutch corporate entity. An inheritance tax liability will arise in the Netherlands with respect to an acquisition or deemed acquisition of the ordinary shares or ADSs on the death of a Dutch individual.

For purposes of Dutch gift and inheritance taxes, an individual of Dutch nationality will be deemed to be resident in the Netherlands if he has been resident in the Netherlands at any time during the ten years preceding the date of the gift or his death. For purposes of the Dutch gift tax, an individual not holding Dutch nationality will be deemed to be resident in the Netherlands if he has been resident in the Netherlands at any time during the 12 months preceding the date of the gift.

Taxation of US investors

The following is a summary of the material US federal income tax considerations regarding the purchase, ownership and disposition of ordinary shares or ADSs to you if you are an "eligible US holder" (as defined below) but it does not purport to be a comprehensive description of all of the tax considerations that may be relevant to you or your situation, including tax considerations that arise from rules of general application to all taxpayers or to certain classes of investors or that are generally assumed to be known by you. In particular, the summary does not address considerations that may be applicable to you if you will not hold ordinary shares or ADSs as capital assets, if you are not an eligible US holder, or if you are a taxpayer subject to special tax rules, such as a bank, tax-exempt entity, insurance company, a regulated investment company, a pension fund, a real estate investment trust, a dealer in securities or currencies, a person that holds ordinary shares or ADSs as part of an integrated investment (including a 'straddle') comprised of ordinary shares or ADSs and one or more other positions, a person that holds ordinary shares or ADSs as a position in a synthetic security, hedging transaction or conversion transaction, a person liable for the alternative minimum tax and a person who owns or is deemed to own 10% or more of any class of our stock. The summary is based on laws, treaties and regulatory interpretations in effect on the date of this document, all of which are subject to change.

You should consult your own advisers regarding the tax consequences of an investment in the ordinary shares or ADSs in light of your particular circumstances, including the US tax considerations discussed below and the effect of any state, local or other national laws.

You are an eligible US holder if you are a resident of the US for purposes of the tax treaty between the Netherlands and the US (the 'tax treaty') and are fully eligible for benefits under the tax treaty. You generally will be entitled to the benefits of the tax treaty if you are:

- The beneficial owner of ordinary shares or ADSs (and of the dividends paid with respect to such ordinary shares or ADSs);
- A "US person" (i.e., an individual resident of the US, a US corporation, or a partnership, estate or trust to the extent your income is subject to taxation in the US as the income of a resident, in your hands or in the hands of your partners or beneficiaries);
- Not resident in the Netherlands for Dutch tax purposes; and
- Not subject to an anti-treaty shopping rule.

You generally will not be eligible for the benefits of the tax treaty, and therefore will not be an eligible US holder, if you hold ordinary shares or ADSs in connection with the conduct of business through a permanent establishment, or the performance of

services through a fixed base in the Netherlands, or you are not resident in the US for US tax purposes.

If a partnership (or other entity treated as a partnership for US tax purposes) holds ordinary shares or ADSs, the tax treatment of a partner generally will depend upon the status of the partner and the activities of the partnership. If you are a partner in a partnership (or other entity treated as a partnership for US tax purposes) that holds ordinary shares or ADSs, you should consult your own tax advisor regarding the specific tax consequences of owning and disposing of ordinary shares or ADSs.

Based on our audited financial statements and relevant market data, we believe that we were not treated as a 'passive foreign investment company' or 'PFIC' for US federal income tax purposes with respect to the year 2008. In addition, based on our current expectations regarding the value and nature of our assets, the sources and nature of our income, and relevant market data, we do not anticipate becoming a PFIC in the year 2009 or thereafter. We believe, however, that we were or may have been a PFIC for US federal income tax purposes with respect to the years before 2005. See 'Passive Foreign Investment Company Rules,' below. *US holders that held our ordinary shares or ADSs at any time before 2005 should consult their own tax advisors regarding the possible application of the PFIC rules to their ordinary shares or ADSs.*

For US federal income tax purposes beneficial owners of ADSs will be treated as the owners of the underlying ordinary shares represented by those ADSs.

Taxation of dividends

The gross amount of distributions paid by us (including amounts withheld in respect of Dutch withholding tax) generally will be subject to US federal income taxation as foreign source ordinary dividend income to the extent paid or deemed paid out of our current or accumulated earnings and profits (as determined under US federal income tax principles), and will not be eligible for the dividends received deduction allowed to corporations. Distributions in excess of current and accumulated earnings and profits will be treated as a non-taxable return of capital to the extent of your basis in our ordinary shares or ADSs and thereafter as capital gain. However, we do not maintain calculations of earnings and profits and you should therefore assume that any distribution we make with respect to our ordinary shares and ADSs will constitute ordinary dividend income.

Subject to certain exceptions for positions that are hedged or held for less than 60 days, an individual US holder generally will be subject to US taxation at a maximum rate of 15% in respect of dividends received before January 1, 2011, unless we were in the year prior to the year in which the dividend was paid, and are, in the year in which the dividend is paid, a PFIC. As described above, we believe that we were not a PFIC for US tax purposes with respect to the year 2008, and also do not anticipate becoming a PFIC with respect to the year 2009.

Dividends paid in Euro will be included in income in a US dollar amount calculated by reference to the exchange rate in effect on the date of receipt by you (or by the depositary in the case of ADSs). If such dividends are converted into US dollar on the date of receipt, you generally should not be required to recognize foreign currency gain or loss in respect of the dividend income. If you receive a refund of Dutch withholding tax under the tax treaty between the Netherlands and the US, you may be required to recognize foreign currency gain or loss to the extent the amount of the tax treaty refund (in dollars) received by you differs from the US dollar equivalent of the refund amount on the date the dividends were received.

You may claim the benefit of the reduced withholding rate of 15% that is available under the tax treaty between the Netherlands and the US by submitting a duly completed Form IB 92 (USA) (available at **www.belastingdienst.nl**) that has been certified by a financial institution (typically the entity that holds the ordinary shares or ADSs as custodian for the holder). If we receive the required documentation prior to the relevant dividend payment date, we may apply the reduced withholding rate at source. If you fail to satisfy these requirements prior to the payment of a dividend, you may claim a refund of the excess of the amount withheld over the tax treaty rate by filing Form IB 92 (USA) together with a supplemental statement with the Dutch tax authorities. Pension funds and tax-exempt organizations qualifying for a complete exemption from tax are not entitled to claim tax treaty benefits at source, and instead must file claims for refund by filing Form IB 95 (USA) (also available at **www.belastingdienst.nl**).

Subject to applicable limitations and to the special considerations discussed below, Dutch withholding tax at the 15% tax treaty rate will be treated as a foreign income tax that is eligible for credit against your US federal income tax liability or, at your election, may be deducted in computing taxable income. Foreign tax credits will not be allowed for withholding taxes imposed in respect of certain short-term or hedged positions and may not be allowed in respect of arrangements in which your expected economic profit, after non-US taxes, is insubstantial. You should consult your own advisers concerning the implications of these rules in light of your particular circumstances.

Taxation of capital gains

Subject to the discussion below under 'Passive Foreign Investment Company Rules', gain or loss realized by you on the sale or other disposition of ordinary shares or ADSs will be capital gain or loss in an amount equal to the difference between your basis in the ordinary shares or ADSs and the dollar-value of the amount realized on the disposition. (If the amount realized is denominated in a foreign currency, such amount shall be determined at the spot rate on the date of disposition, or, at the spot rate on the settlement date if the shares or ADSs are traded on an established securities market and you are a cash basis eligible US holder or an accrual basis eligible US holder that so elects). The gain or loss will be long-term gain or loss if the ordinary shares or ADSs were held for more than one year. Long-term capital gain recognized by an individual US holder before January 1, 2011 generally is subject to taxation at a maximum rate of 15%.

Passive foreign investment company rules

Unfavourable US tax rules (the 'PFIC rules') apply to companies that are considered passive foreign investment companies ('PFICs'). We will be classified as a PFIC in a particular taxable year if either (a) 75% or more of our gross income is treated as passive income for purposes of the PFIC rules; or (b) the average percentage of the value of our assets that produce or are held for the production of passive income is at least 50%.

As explained above, we believe that we were not a PFIC for US tax purposes with respect to the year 2008, and also do not anticipate becoming a PFIC with respect to the year 2009 and thereafter. We believe, however, that we were or may have been a PFIC for US federal income tax purposes with respect to the years before 2005.

If we were a PFIC in the past, US holders that held our ordinary shares or ADSs at any time during the years when we were a PFIC and did not make certain US tax elections (a "mark-to-market election" or a "QEF election") will be subject to adverse tax treatment. For instance, such holders will be subject to a special tax at ordinary income tax rates on certain dividends that we pay and on gains realized on the sale of ordinary shares or ADSs ('excess distributions') in all subsequent years, even though we ceased to qualify as a PFIC. The amount of this tax will be increased by an interest charge to compensate for tax deferral, calculated as if the excess distributions had been earned ratably over the period the US holder held its ordinary shares or ADSs. It may be possible, in certain circumstances, for a holder to avoid the application of the PFIC rules by making a "deemed sale" election for its taxable year that includes the last day of our last taxable year during which we qualified as a PFIC. *The PFIC rules are extremely complex, and you should consult your own tax advisers regarding the possible application of the PFIC rules to your ordinary shares or ADSs and the desirability and availability of a "deemed sale election."*

US backup withholding tax and information reporting

Payments in respect of the ordinary shares or ADSs that are made in the US or by a US-related financial intermediary will be subject to information reporting and may be subject to backup withholding unless you: (a) are a corporation or other exempt recipient; or (b) provide an IRS Form W-9 or an acceptable substitute form, certifying your taxpayer identification number and that no loss of exemption from backup withholding has occurred.

If you are not a US citizen or a 'US person' (as defined in the introduction to this discussion), you generally are not subject to these rules, but may be required to provide certification of non-US status in order to establish that you are exempt.

Documents on display

We are subject to the informational requirements of the Securities Exchange Act of 1934, as amended, and in accordance therewith file information with the US Securities and Exchange Commission ('SEC').

You may read and copy this information at the following location:

Public Reference Room
100 F Street, N.E.
Washington, D.C. 20549
USA

Please call the SEC at 1 800 SEC 0330 for further information on the public reference room. Copies of these materials can also be obtained by mail at prescribed rates from the Public Reference Section of the Securities and Exchange Commission, 100 F Street, N.E., Washington, D.C. 20549. Our ADSs are quoted on the NASDAQ National Market, and consequently, the periodic reports and other information filed by us with the Commission can be inspected at the offices of the NASDAQ National Market, 1735 K Street, N.W., Washington, D.C. 20006. The primary market for our ordinary shares is NYSE Euronext Amsterdam. We make our filings with the SEC by electronic means. Any filings we make electronically are available to the public over the internet at the Commission's website at www.sec.gov and at our website at www.crucell.com.

Exchange Controls
There are currently no Dutch laws, decrees or regulations that restrict the export or import of capital, including, but not limited to, foreign exchange controls, or that affect the remittance of dividends or other payments to non-Dutch residents or to US holders of our securities except as otherwise set forth in 'Taxation' in this section.

Significant changes

Other than as disclosed in this Annual Report, no significant change has occurred since December 31, 2008, the date of our most recent audited financial statements.

Limitation of liability and indemnification matters
Pursuant to Dutch law, each member of our Supervisory and Management Boards is responsible to us for the proper performance of his or her assigned duties. They are also responsible for taking measures to prevent the consequences of any improper performance of duties by another member of our Supervisory Board or our Management Board. Our articles of association provide that our Management Board members and our Supervisory Board members are discharged from liability for their actions as board members if our General Meeting of Shareholders adopts a resolution to that effect. This discharge extends only to actions or omissions disclosed in or apparent from the adopted annual accounts or otherwise communicated to our General Meeting of Shareholders.

This discharge of liability may be limited by mandatory provisions of Dutch law, such as in the case of bankruptcy. Under Dutch law, our Supervisory Board members and members of our Management Board generally cannot be held personally liable for decisions made exercising their reasonable business judgment.

Our articles of association provide that we shall generally indemnify any person who is or was a member of our Supervisory Board or our Management Board or one of our employees, officers or agents, and who suffers any loss as a result of any action in connection with their service to us, provided they acted in good faith in carrying out their duties.

This indemnification generally will not be available if the person seeking indemnification acted with gross negligence or wilful misconduct in the performance of their duties to us. A court in which an action is brought may, however, determine that indemnification is appropriate nonetheless.

Appendix Overview Licensees and Partners

As of year-end 2008, the Group had the following licensees and partners:

Vaccines

Partner/licensee	Starting date	Technology	Disease target	Development stage
Aeras Global TB Vaccine Foundation	Mar. 2004	PER.C6 and AdVac	Tuberculosis	Phase 2
Bestewil Holding B.V.	Jan. 2006	Co-micelles	Influenza	Pre-clinical
Harvard School of Medicine	Dec. 2003	AdVac + Ad5HVR48	HIV	Pre-clinical
International AIDS Vaccine Initiative (IAVI)	Sep. 2004	AdVac	HIV	Phase 1
Kimron Veterinary Institute	Jul. 2003	PER.C6	West Nile virus – Veterinary vaccine (avian)	Marketed in Israel
Merck & Co., Inc.	Sep. 2007	PER.C6 and AdVac	2 Infectious disease areas	Pre-clinical
National Institutes of Health (NIH)	Mar. 2002	PER.C6 and AdVac	Ebola, lassa and Marburg	Phase 1
National Institutes of Health (NIH)	Mar. 2004	PER.C6 and AdVac	Malaria	Phase 1
Novartis Vaccines and Diagnostics	Dec. 2004	PER.C6	Alphavirus vectors	Pre-clinical
Okairos Srl.	Oct. 2005	PER.C6	Hepatitis C	Pre-clinical
Sanofi pasteur	Dec. 2003	PER.C6	Influenza	Phase 2
Tibotec Pharmaceuticals Ltd.	Nov. 2005	PER.C6	Undisclosed vaccine	Pre-clinical
Transgene SA	Dec. 2007	PER.C6	Undisclosed vaccine	Pre-clinical
Vaxin, Inc.	Sep. 2004	PER.C6	Alzheimers disease and veterinary	Pre-clinical

Proteins

Partner/licensee	Starting date	Technology	Disease target	Development stage
Abraxis Bioscience, LLC.	Oct. 2008	PER.C6	Protein production	Pre-clinical
Affitech AS	Nov.2008	PER.C6	Undisclosed Antibodies	Pre-clinical
Arana Therapeutics, Ltd.	Oct. 2008	PER.C6	Portfolio antibodies	Pre-clinical
Bioceros B.V.	May 2008	STAR	Portfolio antibodies	Pre-clinical
Biotecnol SA	Jan. 2007	PER.C6	Portfolio antibodies	Pre-clinical
Cangene Corp.	Oct. 2008	PER.C6	Undisclosed Antibodies	Pre-clinical
Celltrion, Inc.	Apr. 2008	STAR	Portfolio antibodies	Pre-clinical
Centocor, Inc.	Dec.2008	STAR	Monoclonal antibodies	Pre-clinical
CSL Ltd.	Dec. 2008	PER.C6	Undisclosed protein	Pre-clinical
Daiichi Sankyo Co., Ltd.	Nov. 2007	PER.C6	Portfolio antibodies	Pre-clinical
Ferring International Center SA	May 2005	PER.C6	Women's healthcare	Pre-clinical
Ferring International Center SA	Dec. 2005	PER.C6	Women's healthcare	Pre-clinical
Gedeon Richter PLC	Nov.2008	PER.C6	Undisclosed biopharmaceutical	Pre-clinical
GlaxoSmithKline Biologicals SA	Dec. 2008	PER.C6	Recombinant protein	Pre-clinical
Invitrogen Corp.	Sep. 2007	STAR	Monoclonal antibodies	Pre-clinical
IQ Corporation B.V.	Oct. 2005	PER.C6	Anti-anthrax antibody	Pre-clinical
LFB Biotechnologies	Jul. 2007	PER.C6	Undisclosed antibodies	Pre-clinical
JSC Masterclone	Jul 2007	PER.C6	Undisclosed antibodies	Pre-clinical
Medarex, Inc.	Dec. 2007	PER.C6	Portfolio antibodies	Pre-clinical
Medarex, Inc.	Mar. 2008	STAR	Monoclonal antibodies	Pre-clinical
MedImmune	Oct. 2007	PER.C6 and MAbstract	Anti-bacterial antibodies	Pre-clinical
Merus B.V.	Jun. 2004	PER.C6	Portfolio oligoclonics	Pre-clinical
Micromet AG	Nov. 2004	PER.C6	Portfolio antibodies	Pre-clinical
MorphoSys AG	Mar. 2008	PER.C6	Oncology	Pre-clinical
MorphoSys AG	Aug. 2006	PER.C6	Inflammatory diseases	Phase 1
MorphoSys AG	Aug. 2004	PER.C6	Portfolio antibodies	Pre-clinical
Novartis Vaccines and Diagnostics	Jun. 2004	PER.C6	Portfolio antibodies	Pre-clinical
Patrys PTY Ltd.	Feb. 2007	PER.C6	Portfolio antibodies	Pre-clinical

ProFibrix B.V.	Dec. 2007	STAR	Portfolio antibodies	Pre-clinical
ProFibrix B.V.	Dec. 2008	PER.C6	Recombinant fibrinogen	Pre-clinical
ProFibrix B.V.	Dec. 2008	PER.C6	Recombinant thrombin	Pre-clinical
PR&D Biotech SA (Recepta Biopharma SA)	Nov. 2007	PER.C6	Portfolio antibodies	Pre-clinical
Synthon B.V.	Nov. 2008	PER.C6	Biosimilar protein	Pre-clinical
Taiwanese Development Center for Biotechnology	Mar. 2007	PER.C6	Undisclosed proteins	Pre-clinical
Talecris Biotherapeutics Inc.	Dec. 2008	PER.C6	Undisclosed proteins	Pre-clinical
Talecris Biotherapeutics Inc.	Sep. 2008	PER.C6	Undisclosed protein	Pre-clinical
Toyobo Gene Analysis Co. Ltd.	Apr. 2008	STAR	Portfolio antibodies	Pre-clinical
UCB Celltech	Sep. 2006	STAR	Portfolio antibodies	Pre-clinical
UMN Pharma Inc.	Mar. 2006	PER.C6	Undisclosed protein	Pre-clinical

Gene therapy

Partner/licensee	Starting date	Technology	Disease target	Development stage
Ark Therapeutics Ltd.	Jan. 2006	PER.C6	Portfolio	Phase 3
Elm Biotech Pty Ltd.	Dec. 2008	PER.C6	Adenovirus-vectored product	Pre-clinical
TAPImmune Inc.	Aug. 2003	PER.C6	Portfolio	Pre-clinical
Merck & Co., Inc.	Nov. 1998	PER.C6	Portfolio	Pre-clinical
NeoTropix, Inc.	Mar. 2004	PER.C6	Oncology	Pre-clinical
Transgene SA	Apr. 2001	PER.C6	Portfolio	Phase 2
Vascular Biogenics Ltd.	Mar. 2005	PER.C6	Portfolio	Pre-clinical

Alliances with contract managers for production

Partner/licensee	Starting date	Technology	Area
Biochrom AG	Nov. 2008	PERMEXIS	Medium Development
Cambrex	Aug. 2004	PER.C6	Medium development
DSM Biologics	Dec. 2002	PER.C6	Therapeutic proteins (including antibodies)
Hyclone, Inc.	Dec. 2003	PER.C6	Medium development
Invitrogen Corp.	Jun. 2003	PER.C6	Medium development
JRH Biosciences Inc.	May 2004	PER.C6	Medium development Recombinant vaccines
Lonza	Nov.2008	PERMEXIS	Medium Development
Molecular Medicine BioServices, Inc.	Dec. 2001	PER.C6	Recombinant vaccines & gene therapy products (US)
Sigma-Aldrich Corp.	Dec. 2003	PER.C6	Medium development

Functional Genomics

Partner/licensee	Starting date	Technology	Area
Galapagos Genomics N.V.	Jun. 1999	PER.C6	Genomics

Cross-reference to Form 20-F

Part I

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Exhibits

Exhibit Number	Description
1.1	Deed of Incorporation of the Company (incorporated by reference as Exhibit 3.1 to Crucell N.V.'s amended Registration Statement on Form F-1/A, as filed with the Securities and Exchange Commission on October 24, 2000)
1.2	Amended articles of association (incorporated by reference as Exhibit 1.2 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 13, 2007)
4.1	Summary and Lease Agreement dated November 18, 1998, between IntroGene B.V. and Amboz B.V. (incorporated by reference as Exhibit 4.1 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 28, 2001)
4.2	Summary and Lease Agreement dated November 27, 1997, between IntroGene B.V. and CAM Implants B.V. (incorporated by reference as Exhibit 4.2 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 28, 2001)
4.3	Lease Agreement dated July 1, 2002 between Crucell Holland B.V. and Oppenheim Property Services B.V. (English translation) (incorporated by reference as Exhibit 4.3 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on April 18, 2003)
4.4	Collaboration Agreement dated December 18, 2002 by and between Crucell N.V. and Crucell Holland B.V., and DSM Biologics Holding, Inc., DSM Biologics Company, Inc., and DSM Biologics Company, B.V. (English translation) (incorporated by reference as Exhibit 4.4 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on April 18, 2003)†
4.5	Employment Contract dated June 30, 2006 between Crucell Holland B.V. and R.H.P. Brus (incorporated by reference as Exhibit 4.5 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 13, 2007)
4.6	Employment Contract dated June 30, 2006 between Crucell Holland B.V. and Prof. Dr. J. Goudsmit (incorporated by reference as Exhibit 4.6 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 13, 2007)
4.7	Employment Contract dated June 30, 2006 between Crucell Holland B.V. and L. Kruimer (incorporated by reference as Exhibit 4.7 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 13, 2007)
4.8	Collaboration and License Agreement dated December 31, 2003 by and between Crucell Holland B.V. and Aventis Pasteur S.A. (now sanofi pasteur) (incorporated by reference as Exhibit 4.6 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on February 27, 2004)†
4.9	Transaction Agreement dated December 1, 2005 by and between Crucell N.V. and Berna Biotech AG (incorporated by reference as Exhibit 4.9 to Crucell N.V.'s amended annual report on Form 20-F/A, as filed with the Securities and Exchange Commission on June 30, 2006)
4.10	Supply Agreement dated November 12, 2001 and the Letter of Amendment to the same Agreement, dated June 18, 2004 between CSL Limited and Berna Biotech Limited (incorporated by reference as Exhibit 4.10 to Crucell N.V.'s amended annual report on Form 20-F/A, as filed with the Securities and Exchange Commission on December 7, 2007)*

4.11	Collaboration Agreement dated April 30, 2001 between Chiron Behring GmbH & Co. and Rhein Biotech N.V. and Green Cross Vaccine Corporation (incorporated by reference as Exhibit 4.11 to Crucell N.V.'s amended annual report on Form 20-F/A, as filed with the Securities and Exchange Commission on December 7, 2007)*
4.12	Employment contract dated September 1, 2007 between Crucell N.V. and C. De Jong
8.1	List of subsidiaries of Crucell N.V.
12.1	Certification of CEO pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
12.2	Certification of CFO pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
13.1	Certification of CEO and CFO pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
99.1	Crucell Code of Conduct

Confidential treatment has been granted with respect to portions of the exhibit indicated by a dagger (†). The omitted portions have been filed separately with the Securities and Exchange Commission.

* Confidential treatment requested as to certain portions, which portions have been filed separately with the Securities and Exchange Commission by Crucell N.V.

General information

Supervisory Board

J.P. Oosterveld (Chairman)
A. Hoevenaars
S. Davis
S.P. Lance
P.M. Satow
C.E. Wilhelmsson

Management Board

R.H.P. Brus (President and Chief Executive Officer)
L. Kruimer (Chief Financial Officer)
C. De Jong (Chief Operating Officer)
J. Goudsmit (Chief Scientific Officer)

Registered Office
Archimedesweg 4-6
PO Box 2048
2301 CA Leiden
The Netherlands

Financial Calendar 2009

Publication first quarter results 2009	May 6, 2009
Annual General Meeting of Shareholders	June 5, 2009
Publication second quarter results 2009	August 11, 2009
Publication third quarter results 2009	November 3, 2009
Publication annual results 2009	February 9, 2010