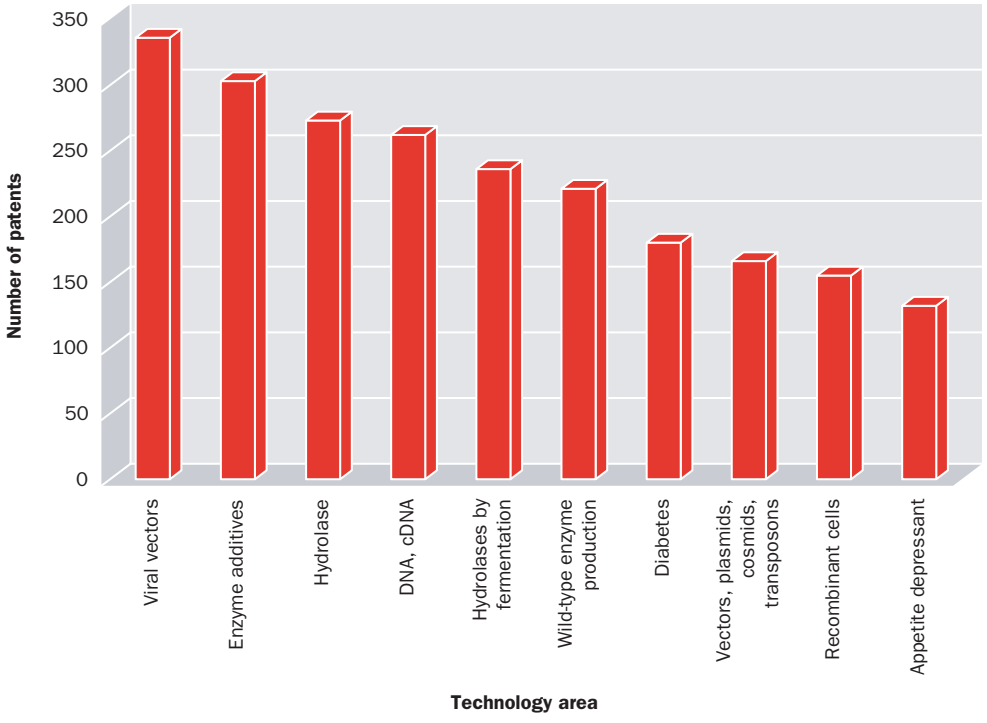
The Novo Nordisk strategy for patent success

With a coveted place at the top of the increasingly competitive anti-diabetes treatments market, Novo Nordisk is committed to the careful management of its intellectual property rights in order to maintain its position. Two key members of the company's IP team explain how they do it. By ***Joff Wild***

There are not many sectors in which a company with annual sales of over US$4 billion and a market capitalisation of more than US$15 billion could be described as mid-sized. But in the healthcare industry, where corporations such as GlaxoSmithKline and Amgen are valued in the hundreds of billions of dollars, that is exactly what Novo Nordisk is. Not that anyone working at the 18,000-employee Danish company seems to be that bothered.

Top 10 technology areas patented*



And why should they be? Sales have nearly doubled since 1999, the share price has increased by 40% in the last year and the long-term prospects for continued success look promising. The key to all of this is that instead of spreading its net wide in an attempt to find treatments for a number of diseases, Novo Nordisk has concentrated its expertise in one principal area so that today it is the world's leading provider of diabetes-related products. These include insulin analogues in state-of-the-art injection devices, a range of long- and short-acting insulin, and repaglinide - the first in a new group of oral drugs, the prandial glucose regulators.

And the demand for what the company produces continues to grow. There are 18.2 million people in the United States, or 6.3% of the population, that have diabetes. Whilst globally the total rises to 140 million, with predictions that the figure will increase to 300 million by 2025, including 22 million in the United States.

So, with the number of patients set to grow in such dramatic fashion over the coming years, and most especially in some of the world's most lucrative markets, it comes as no surprise to learn that Novo Nordisk is not alone in seeing the potential in providing anti-diabetic treatments. In fact, it is an area that becomes more crowded by the year, populated not just by almost every large research-based life sciences company in both the biotech and pharmaceutical spheres, but also by generic outfits, which are increasingly looking at the possibilities presented by what looks set to be a loosening of the controls on the production of generic biotechnology products in both the US and Europe.

Novo Nordisk patent strategy

Lessons learned in the 1990s

As in all areas of the life sciences therefore, the management of intellectual property rights – and most particularly patents – is of crucial importance. But this is especially so for a comparatively small company trying to maintain its pre-eminent position in such a lucrative niche. During the 1990s, Novo Nordisk learned to appreciate just how competitive the market was, and how patent portfolios can be used to block opponents, when it got into a long-running dispute with Genentech as a result of its attempts to enter the US growth hormone and insulin markets. Twice, in 1995 and 1996, Genentech won court orders – both subsequently overturned – restraining the sale of Novo Nordisk's branded growth hormone Norditropin, and also in 1996 Genentech claimed that five of its patents were infringed by Novo Nordisk's manufacture and marketing of recombinant human insulin Novolin in the US. The dispute was only settled in 1998 when the two companies agreed a global cross-licensing deal. Novo Nordisk was also granted a worldwide licence under Genentech patents relating to insulin with the American company receiving unspecified payments in return.

It was an eye-opening experience for the Danish company. So says Lars Kellberg who, as head of Novo Nordisk's Patent Department, has the overall responsibility for protecting the company's most important inventions. "We had legal opinions that we were not infringing and that some of the other side's patents were not actually valid. But this was not sufficient to guarantee market entry," he says. In the end, Kellberg explains, the case was settled because Novo Nordisk found it had intellectual property that caused Genentech some problems. "What worked was opening a claim against the other side. If the other party has low exposure you can only defend yourselves and their incentive to settle is low. But if you can expose the other side, then you have a much better chance of getting a settlement on your terms," he says.

From the mid-90s through to the early part of this decade, Novo Nordisk was involved in a number of high-profile cases on both sides of the Atlantic with companies such as Aventis, American Home Products and Eli Lily. "The disputes were disruptive to the company and expensive," says Kellberg. And the cost was not only financial. "Some scientists have to spend a long time on these things and they are not always treated very nicely by the other side. They have to be prepared to even have their credentials questioned. It is not a pleasant experience for them," Kellberg says.

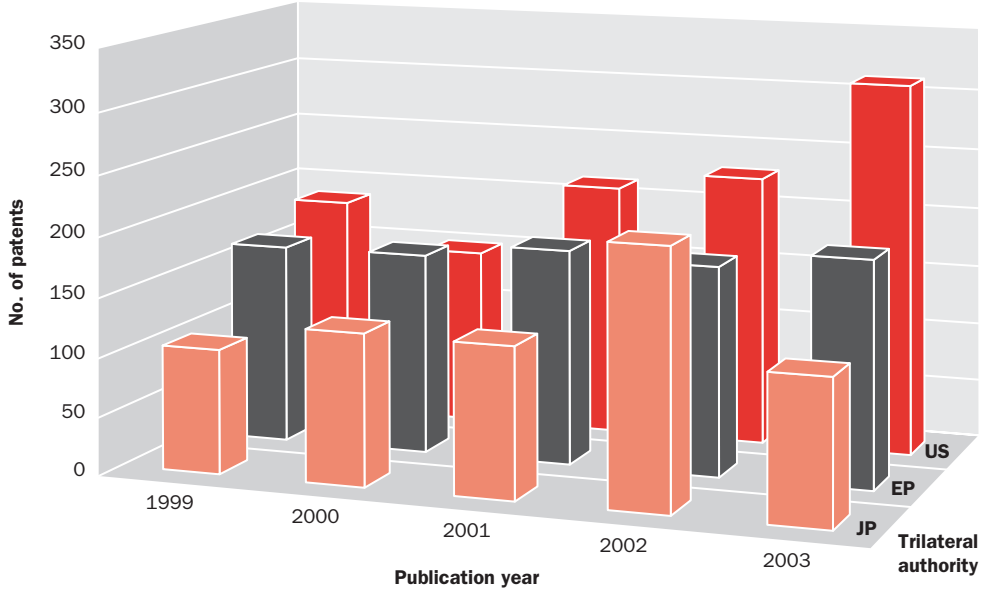
But although litigation may not be a pleasant experience, there are times when it cannot be ducked and Kellberg is clear that should such occasions arise the challenge will be met head-on. Indeed, the company has ongoing disputes in both the US and the UK at the moment. At the same time, however, where there is a chance that litigation can be avoided then Kellberg believes that such an option should be explored. "Previously the level of litigation we were involved in was like World War Three and the other parties felt the same way too," he says. In some cases, he explains, this has led to what he calls gentlemen's agreements designed to prevent the outbreak of World War Four. "Instead we have decided that should a dispute arise we will spend three months trying to resolve it amicably before initiating a lawsuit," he says. "While we will never rule out litigation, we feel there are times when it could be appropriate to use our resources in a more constructive manner. I think the tendency now would be to try to approach the other party before going to court," Kellberg adds.

The patenting process

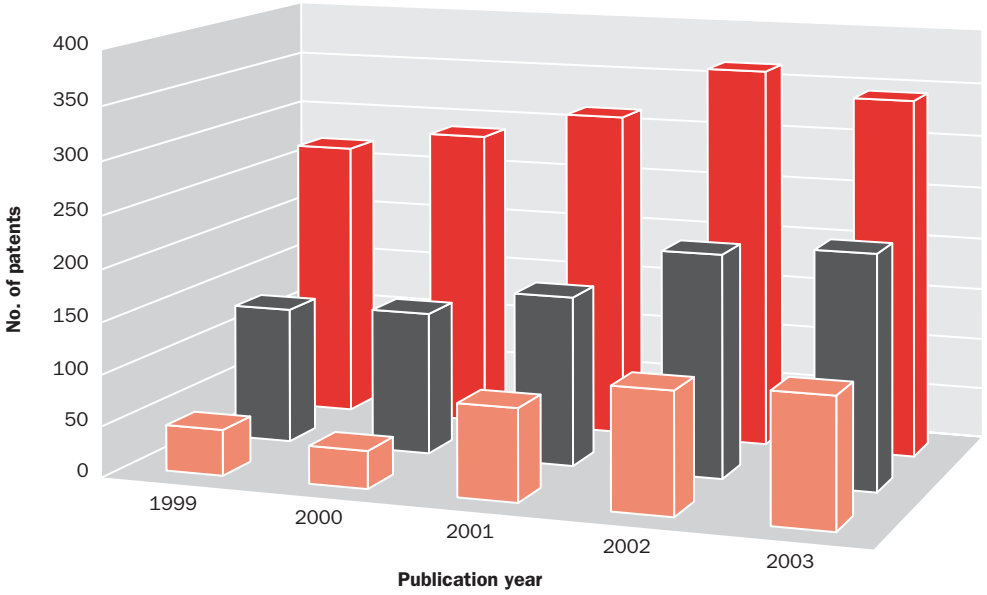
Of course, one way of staying out of court is to do everything possible to ensure that problems do not materialise in the first place. At Novo Nordisk this is done through an extensive series of patent-related checks and reports from the very birth of a research project.

Kellberg explains that one of his primary functions is to avoid freedom to operate issues. "When we launch a product we need to be independent of third-party patent rights or we have to have ensured that we have the

Novo Nordisk Trilateral Authority Patenting Activity* 1999-2003



Novo Nordisk Patenting Activity* 1999-2003
(Top 3 technology areas across JP, US and EP)



- Detergents - other than soap
- Natural products and polymers
- Fermentation industry

necessary licences," he says. To do this, the company begins at the very start of the R&D process. Once a potential line of research is mooted, but before a project begins, the Novo Nordisk market intelligence group will conduct a state-of-the-art analysis. "At this stage, we have no idea what any potential compound will look like; however, we do think it is important to define the patent landscape," Kellberg says. This means getting an idea of the level of competition in the area and seeing whether any parties have broad patents that may cause problems further down the line. "If the landscape does look crowded, we may decide not to go ahead. However, it could also indicate that this is a very attractive area," Kellberg explains. "At such an early stage, it would be unusual to turn down a project solely on the basis of intellectual property," he adds.

Once the green light is given for a project to proceed, a well-rehearsed series of procedures is ticked off. "It is mandatory for every project to have a patent attorney assigned to it. It is also compulsory to have a taskforce to deal with all patent-related issues coming out of the project," Kellberg says. The role of the taskforce, he continues, includes reviewing the invention-related disclosures generated by scientists and prioritising them. "This ensures that the right inventions get protection," he says. At the same time, the company conducts ongoing patent surveillance based on key words and competitors. "This information is assessed on a weekly basis so that we can keep track of what is happening. Then twice a year, an official report is produced as the project as a whole is reviewed," Kellberg explains.

Once the research has got to a point where it is time to select compounds for development, a thorough freedom to operate analysis is done. This is done not only by an internal team, but also by third parties from outside the company such as private practice patent attorneys, the search division in the Danish Patent Office and companies that specialise in freedom to operate issues. "It is important to have a new pair of eyes looking at things as they will see issues from a completely different perspective. We feel this is important because if we move into development and then discover we have a patent issue a few years down the line, we will already have spent millions of dollars," Kellberg explains. For the same reason, once the freedom to operate report has been prepared by the attorney shadowing the research project, this is subject to a challenge procedure. It involves putting together a group of senior managers and attorneys from the IP Group whose job is to scrutinise the report and ask the person who put it together to justify his or her findings. "We do this because there may be a tendency for someone who has been working closely with a project team to become biased and think, for example, that blocking patents may not be valid," Kellberg says. "We have learned to be cautious. You may think you have good arguments against the validity of a patent but that may translate into only a 50/50 chance of prevailing should a case go to trial," he adds.

When the challenge process is completed, the Patent Department makes a recommendation that is then sent to the senior executives, whose job is to decide whether the project should move forward into the development stage. "If there are critical issues we make sure that the relevant people are properly briefed before they sit down to make their decision," says Kellberg.

With the US having emerged as Novo Nordisk's primary market, the patent process is conducted in close consultation with the company's five attorneys based in Princeton, New Jersey. "An American perspective is crucial to us from the very start," says Kellberg. "Although we try to draft applications so that they fulfil requirements everywhere, the American market does pose unique problems in areas such as claim language and best mode requirements," he says. For this reason, the attorneys in Princeton handle all Novo Nordisk's US prosecution work. "We have best practice discussions with them on a constant basis and they are also integrated

into our organisation because a lot of the decisions we make will have a bearing on our US position," Kellberg adds.

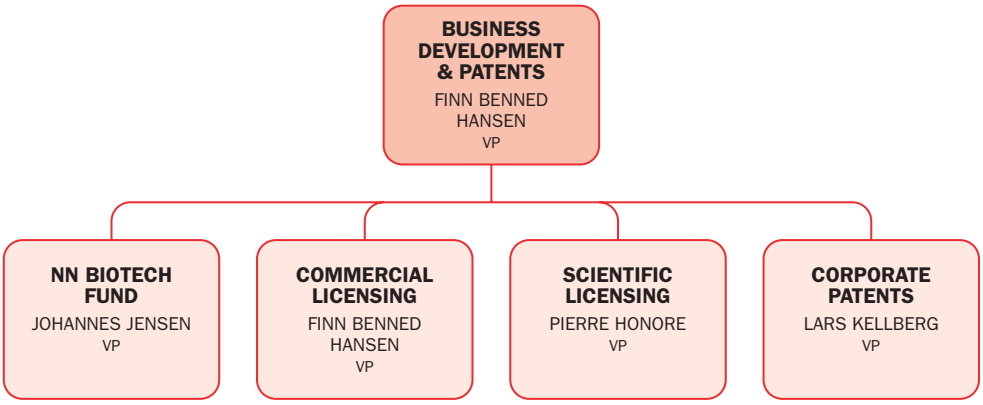
Always be prepared

Although it has not been common for Novo Nordisk over recent years, the threat of litigation will always hang over a company in the life sciences sector – especially if it is a market leader with a strong product pipeline. For that reason, the company has to remain very focused during the patenting process. "When a project moves into full-scale development, we have to interact with marketing and product management because as the process goes forwards there is always potential to capture new medical indications, unique selling points and so on," Kellberg says. Patenting the compound and also its differentiating aspects means not only that there is the potential to expand the life of the product, but also that Novo Nordisk gains competitive advantage over its rivals. "We are always competing and it is important to patent in such a way as to ensure freedom to operate. At a minimum it gives us some bargaining power should we get into a dispute," Kellberg explains. It is a philosophy the company has honed since its litigation experiences in the US during the 1990s. "You might have a very good case but if all you can do is defend yourself you do not have much flexibility or bargaining power," Kellberg says.

And should it come to litigation, despite attempts to settle a problem amicably, there is a set plan as to how to organise internally to maximise the chances of success. "Litigation is a cross-functional exercise. For example, someone with a licensing background will always be included in the decision-making process because we have to make a business case for going through the courts: they can help us understand the value of enforcing a patent as opposed to licensing it," Kellberg explains. For the same reason, he says, there will always be input from the marketing department. It is for this reason that each dispute will be assigned to a litigation team composed of representatives from many departments within the company, including the Legal Department, marketing, licensing and project management, in addition to members of the Patent Department. Then, if it comes to settling a case, a team of licensing experts will take over to negotiate the terms.

It is unusual, though, for a dispute to suddenly raise its head and catch Kellberg and his colleagues by surprise because, he explains, the Patent Department is almost always aware that there may be a problem well in advance. "Because we conduct so many regular freedom to operate analyses on our major competitors, and we report twice a year on what they are doing and evaluate the risks their activities pose, we know there is a good chance someone will infringe many years before they do," he says.

IP organisation at Novo Nordisk



Source: *Novo Nordisk*

Securing the right rights

Of course, the creation and protection of patents is only one part of the intellectual property equation at any life sciences company. And Novo Nordisk is no different. On top of the vital role played by Lars Kellberg and his colleagues in the Patent Department, there are three other major IP-related departments within the company to be factored in:

- The Novo Nordisk Biotech Fund – a business unit responsible for the company's venture activities which offers equity investments to companies in the biotechnology and medico technology sectors with a high level of relevance for the current and future business model of Novo Nordisk. The investment can be done as a stand-alone, but there are several examples where it has been done as part of an overall deal with a biotechnology company, in cases where Novo Nordisk is interested in establishing a collaboration on a defined project.
- The Commercial Licensing Group – this group works on worldwide and regional collaborative agreements relating to projects and products that have already been marketed or have passed the clinical proof of concept milestone.
- Scientific Licensing – this group deals with research collaborations and early development projects.

In charge of Scientific Licensing is Pierre Honoré. He divides his group's role into three major functions: first, to offer support to the

R&D organisation in the form of collaborative arrangements that will secure new project and product opportunities for Novo Nordisk's discovery and early development pipeline; second, to provide support to Novo Nordisk's in-house projects in relation to the testing of compounds in areas where Novo Nordisk does not have the in-house expertise or facilities to do the job on its own, or to get hold of technology and research that could be important to the work being done inside the company; and third, to commercialise Novo Nordisk technologies and patents that do not fit in with the company's strategic vision.

Of the three, probably the group's longest-standing jobs have been to secure agreements with outside organisations in relation to the R&D portfolio and project work being done inside Novo Nordisk. Honoré explains that the motives for doing this are various. "We have expertise in diabetes but even in this area there are times when we need access to targets or technologies we do not own," he says. On other occasions, it may not be technology that Novo Nordisk wants, but the specific expertise of individual scientists. In either case, the company's researchers are key in identifying what is necessary. "They come to us and say they want to make an agreement and then we go ahead and do it," says Honoré.

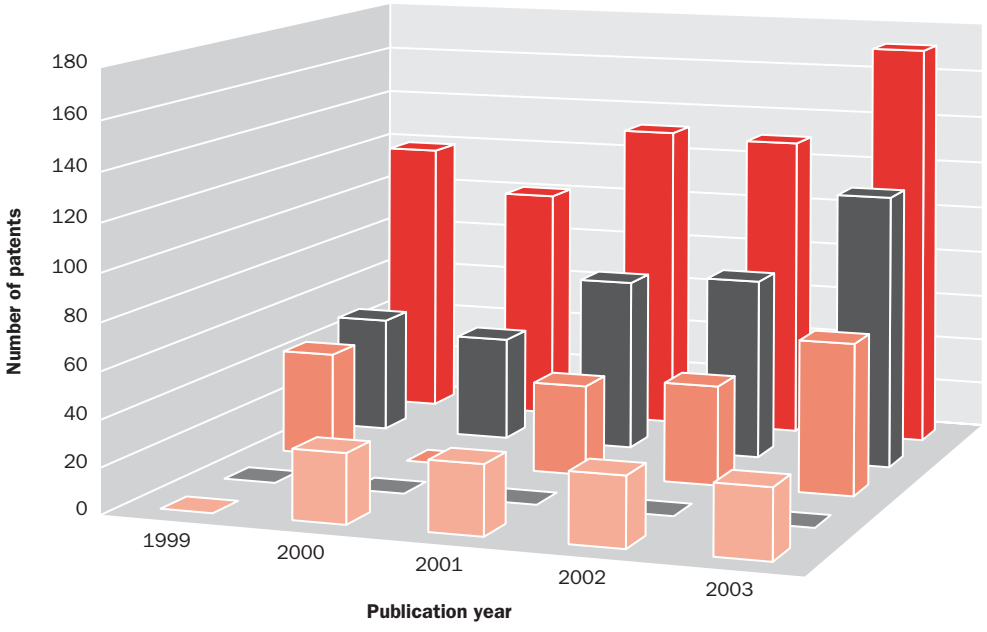
The type of deal negotiated will depend on a variety of factors but, in general, Novo Nordisk looks to retain all the intellectual property rights involved in this low-level type of collaboration. However, there are times when compromise is necessary, says Honoré. "If this is the case, we will tend to do a deal which allows us to keep the ownership of the rights relating to the compound itself, with the other party retaining the rights to, say, the test model," he explains. Sometimes, though, even that is not enough. "There are occasions when we have to agree that the other party keeps all the intellectual property rights and we get an exclusive licence to use them. It is a last resort because we find it important to control our IP position but sometimes you have no choice," he says. Then there is also the issue of publication – where the priorities of academics and businesses can be very different. It is another area where flexibility is key. "In our agreements we allow universities to publish their research independent of Novo Nordisk but we do have the right to preview the manuscript to see if it creates any IP problems. If it does we can delay publication for up to two months," says Honoré. "Ideally, we would keep the paper out of circulation for 12 months but you can't really do that these days," he adds.

One of the reasons for this is the competitiveness of the field in which it operates. A fact of life is that Novo Nordisk is not the only company looking for collaborations, so it has to act accordingly. "We have to make sure we are an attractive partner for research institutions and small companies because they are very important to our future plans," says Honoré. The ability to be flexible in deal-making is one important part of this, but so is the calibre of the company's research teams. "They are the people that are able to establish good links with fellow scientists and so they act as our ambassadors. If they have a strong relationship with a company or institution then it makes it much easier for us to come in and do our job. It is a matter of having the right scientists. They support the deal-making and are subsequently instrumental in making the collaboration a success," Honoré explains.

Expanding Novo Nordisk's core protein competences

Over recent years, the work of the Scientific Licensing group has increased as Novo Nordisk has made the strategic decision to see if some of its core protein technologies and competences can be applied in areas outside of diabetes. It is a move that makes sense given the fact that biopharmaceuticals of the type the company tends to produce are capable of multiple potential therapeutic applications – something that is greatly attractive at a time when Novo Nordisk's main markets are becoming increasingly crowded

Top three Technology Areas Patented* 1999-2003 - US Patents



Novo Nordisk patent strategy

and competitive. In particular, the company has seen potential for protein-based therapeutics in cancer treatments based on immunotherapy and autoimmune-related chronic inflammatory conditions.

Because these two areas lie outside the traditional Novo Nordisk disease biology expertise, the company does not have the means internally to identify and develop appropriate proteins. As a result, Honoré and his group have spent the last year trying to identify companies and universities around the world that can license them technologies that will help them do this. "Last year we put a big effort into screening biotech companies," Honoré says. He also estimates that there are about 200 technology transfer offices at universities that may be of interest and, during 2003, Novo Nordisk visited 20 of these in Europe. The company is now repeating the process in the US.

When it comes to negotiating deals, Honoré believes that Novo Nordisk offers good terms. "We like to secure worldwide rights and we are flexible about how we do this – it could be direct payments, loans or equity arrangements," he says. "It is very rare that we are not able to agree. It is all about ensuring a collaborative arrangement that is attractive to both parties, including who will control the IP in a project and how the rights to use are distributed. The US biotechs and universities tend to want to retain control over their rights and we are prepared to let them do this in a coordinated way with us," he adds.

Another recent move has been into out-licensing. Although the company has always been willing to give third parties access to its intellectual property under the right circumstances, it has not done so in a systematic way. But this is beginning to change. "We have realised that we are a specialist company and that some of what we produce could be useful in other areas. As a result, we have started to think about out-licensing compounds with patent coverage that we do not want to pursue on the basis that it is better to out-license than to kill projects," says Honoré. "Senior management sees this area as a potential income stream," he adds.

The company is still in the process of defining the issues surrounding out-licensing, such as timing and the allocation of resources, and as a result no deals have yet been finalised. "We have to work out how best to present the opportunities – we have to make them as attractive as possible and to allocate resources even after a deal is signed," Honoré says. But despite the lack of activity so far, his advice is to watch this space. "There are two projects that are a high priority where we are in talks, although we have not yet begun to look at precise terms," he says. What is clear is that it is now up to his group to be able to sell Novo Nordisk projects to potential licensees. "Our model is to identify opportunities in-house and then to take them to the earliest stage where they will be attractive to pharma companies," Honoré says. Novo Nordisk, he explains, might decide to retain a late-stage opt-in possibility if the opportunity can also be used in its core areas, but otherwise the company does not plan to be involved after the deal apart from the support needed in the first one or two years. In terms of letting third parties know about what is available, Honoré says that at the moment it is a matter of Novo Nordisk doing all the groundwork itself. "At this stage we are not interested in advertising what we have on websites or similar because we believe the likelihood of success will be greater by directly contacting companies that have the expertise and resources necessary to optimise the further development and marketing of a given opportunity," he explains. ■

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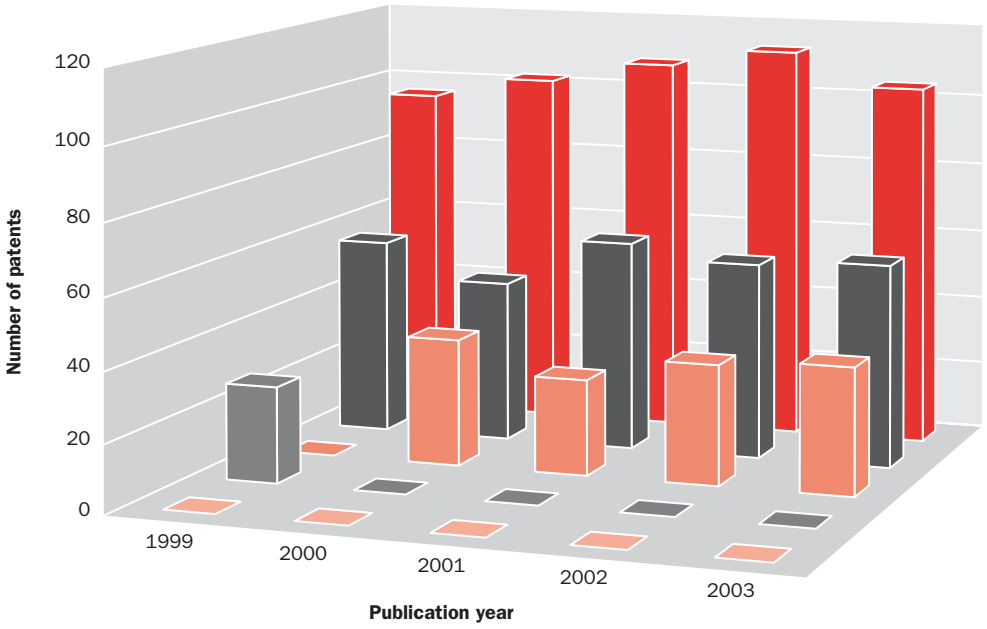
Top three Technology Areas Patented* 1999-2003 - EP Patents



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**Patent Applications (US patents were published for the first time in March 2001 - stats prior to this date show granted US patents).*