

three days – searching for better treatment

Bioethical challenges
within research and development
of new pharmaceuticals





About Novo Nordisk

Novo Nordisk is a healthcare company and the world leader in diabetes care. The company has the broadest diabetes product portfolio in the industry, including the most advanced products within the area of insulin delivery systems. In addition, Novo Nordisk has a leading position within areas such as haemostasis management, growth hormone therapy and hormone replacement therapy.

Novo Nordisk manufactures and markets pharmaceutical products and services that make a significant difference to patients, the medical profession and society. With headquarters in Denmark, Novo Nordisk has offices in 79 countries and markets its products in 179 countries. More than 23,600 people work at Novo Nordisk; around half of them are working with sales and marketing, production or research and development outside Denmark. More than 4,000 people are working with research and development.

Steering through a constantly shifting ethical landscape

The development of new pharmaceuticals is charged with exciting possibilities and daunting challenges, not least the fact that only one in 10 compounds tested in humans will ever become an approved pharmaceutical product. In the often decade-long journey of bringing a product to market, choices and decisions rest on individuals' and the company's ethics and values.

Novo Nordisk promotes awareness among all employees of bioethics and how decisions are founded on the company's bioethics policy and sets of guidelines. We also work closely with stakeholders and partners to improve and harmonise standards. The film, *Three days – searching for better treatment*, underlines that commitment.

Our approach to bioethics

At Novo Nordisk we strive to conduct our business in a financially, environmentally and socially responsible way. This is what we call the Triple Bottom Line business principle, which guides how we make decisions and how we operate.

This film illustrates how this principle applies to developing new pharmaceuticals. Bioethics is the expression used for all ethical issues related to the use of life science technologies for the discovery, development and production of pharmaceutical products. In essence it is about

how to make choices on what is the right thing to do to conduct clinical trials with respect for the individuals involved, to make responsible use of human material in research and development, to consider the welfare of experimental animals and to ensure safe use of gene technology in production.

The enclosed leaflet, *From idea to patient*, shows the exciting, but also long and difficult process of bringing pharmaceutical products to market, with no guarantees of success. Our goal is to develop products that meet critical health-care needs while balancing long-term business interests with those of our stakeholders and society.

The film invites you inside, offering a closer look into the search for better treatment.

Enjoy!

Mads Krogsgaard Thomsen

Executive vice president and
chief science officer



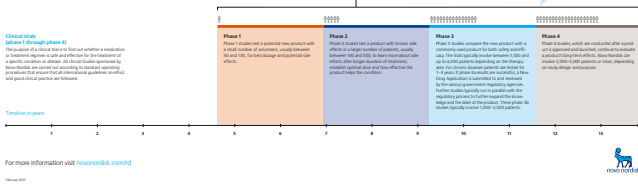
from idea to patient

In the pharmaceutical industry, the road from idea to patient for a new product is highly complex and time consuming. Industry estimates that out of 10,000 ideas that begin in the lab, just 10 will ever reach the stage where they are tested on people. Out of that, one may reach the market. The entire process requires some of the largest investments Novo Nordisk makes, both in terms of capital and manpower. The process typically takes 10 to 13 years from initial work in the lab

until a product is launched on the market. The further a product is advanced, the greater the loss if discontinued due to adverse events. This diagram illustrates the process. The number of people involved along the way depends on the stage of product and its priority, but generally, hundreds to thousands of Novo Nordisk employees have taken part in the development of the new product to succeed on pharmacy shelves.

The race for new solutions and patents within an environment of increasing demands from patients, government regulatory agencies and the medical profession, creates an intense pressure. Benchmarks show that Novo Nordisk performs at least in line with competitors in the process.

The chart illustrates a complex process. In most cases, the stages overlap and times vary depending on the product.



Dilemmas at work

In the film you will meet three scientists who are working on projects within three of Novo Nordisk's therapy areas – diabetes care, haemostasis management and cancer treatment – and the challenges and ethical dilemmas they face in their work.

What guide their choices are the company's values and ethical guidelines. We recognise that there are different and shifting perceptions of right and wrong to consider – and no easy answers. By confronting them openly and responsibly we seek to strike the right balance of business interests, the interests of society and those of affected stakeholders.

The challenge: Defeating diabetes

Novo Nordisk is a world leader in diabetes care. Diabetes is a disorder in the body's ability to produce and use insulin resulting in increased blood sugar levels. Some 245 million people have diabetes, and as many as two-thirds are insufficiently treated. Our vision is to defeat diabetes by providing improved diabetes prevention, detection and care. We focus on insulin therapy that helps people with diabetes to better control their blood sugar to avoid devastating long-term complications.

The project: Liraglutide

Liraglutide is a once-daily human analogue of the naturally occurring hormone Glucagon-Like Peptide-1 (GLP-1). The compound is being developed by Novo Nordisk for the treatment of type 2 diabetes, and is currently in phase 3 clinical development. Liraglutide works by stimulating the release of insulin only when glucose levels become too high, and the current data indicate that it will be a safe, convenient and effective way for people with type 2 diabetes to control their blood sugar. In contrast to most other antidiabetic treatments liraglutide also leads to weight loss instead of weight increase even when patients improve their metabolic control.

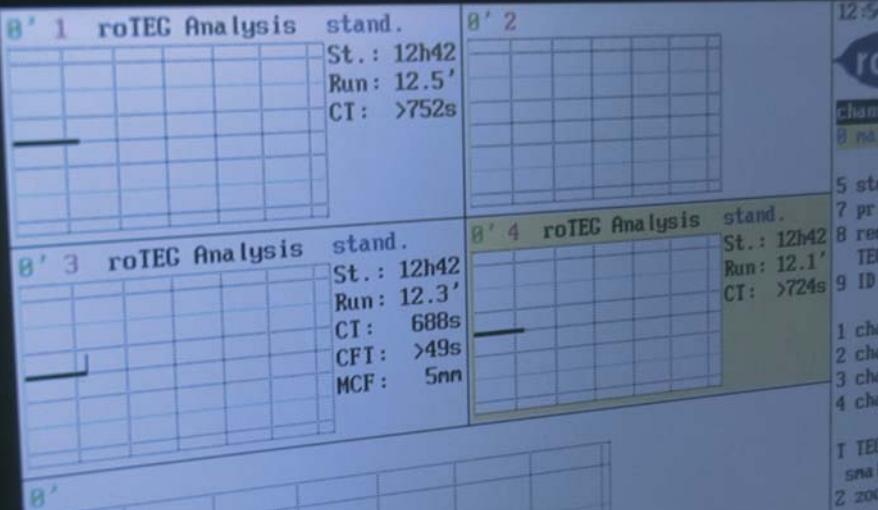
The ethical dilemmas: Clinical trials

It would not be possible to bring liraglutide – or any pharmaceutical product – to the market without doing clinical trials to document safety and efficacy before market authorisation is given. Doing clinical trials in developing countries can raise ethical dilemmas. Novo Nordisk has global standards for clinical trials to ensure the safety of participants and the same high ethical standards worldwide. We ensure that each person participating in a study fully understands the consequences, and we only initiate trials in countries that have ethical review boards.

Gene technology

Novo Nordisk uses gene technology and genetically modified organisms (GMOs) in biomedical research and the production of pharmaceuticals. The use of GMOs offers substantial benefits to the quality of products, the environment and opportunities to identify new treatment concepts for patients. It is expected that gene technology can help solve many health issues of today.

Yet we also recognise that gene technology causes some concerns. The GMOs used at Novo Nordisk in the production are handled under closed and contained conditions. We only use GMOs in the lowest risk category for production and the final products do not contain GMOs. We will use production strains without antibiotics resistance genes whenever technically possible and practically feasible.



The challenge: Living with haemophilia

Novo Nordisk is a leader within haemostasis management, expanding our project portfolio around the active ingredient in NovoSeven®, recombinant factor VIIa. NovoSeven® was initially developed for use in people with haemophilia with inhibitors. Haemophilia is an inherited disabling bleeding disorder that has tremendous medical, social, psychological and financial impact upon the person, his family and society. The most serious complication is the development of inhibitory antibodies to the coagulating factors used to stop bleeding episodes. When bleeds are not managed, there is a greater risk of injury and disabilities. Inhibitors occur in up to 30% of people with severe haemophilia A and 2–3% of those with severe haemophilia B. About 400,000 people have haemophilia – more than half of them are inadequately treated.

The project: Long-acting factor VIIa

The short duration of action of NovoSeven® has been considered a barrier to using this product prophylactically for long-term prevention of bleeding episodes. To develop a new factor VIIa product with a prolonged circulation time in the blood, it is necessary to test new drug compounds in blood from people with haemophilia. The film shows the challenges of this process. In June 2007 a phase 1 trial was initiated of long-acting factor VIIa, a long-acting version of NovoSeven®. The trial will assess the safety and pharmacokinetics of the new treatment concept.

The ethical dilemma: Use of human material

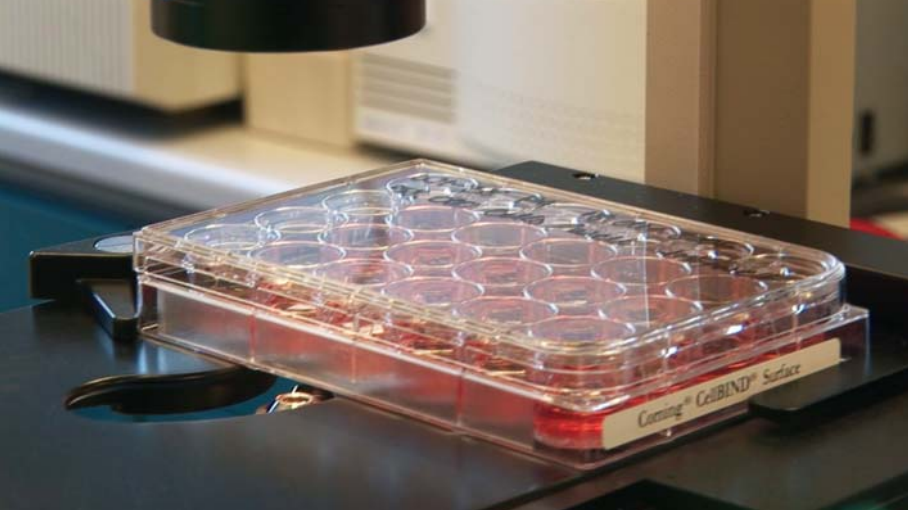
The use of human material such as blood is vital to the successful development of new pharmaceuticals. Human blood, human cells or tissue is used in the early stages of research. It is of key importance to be able to test drug compounds in human material at various stages of the development of new pharmaceuticals. This enables us to rapidly select viable compounds and to assess the safety, before tests are conducted on animals and people. The use of human material reduces the need for testing compounds in animals; still, ensuring responsible use of such material can present dilemmas that must be addressed with all the parties involved.

The challenge: Fighting cancer

In Novo Nordisk's second-largest business segment, biopharmaceuticals, we are expanding our portfolio within haemostasis management, growth deficiency and hormone replacement therapy, and building a presence in immunotherapies. Thirteen clinical development projects with biopharmaceutical products are underway. Among these are early projects within the areas of inflammation and oncology. With any individual having a 42% risk of developing cancer, and only a 50% chance of being cured, developing candidates for cancer therapies is one of our biggest challenges.

The project: Anti-KIR

Anti-KIR, a fully human monoclonal antibody, is a new treatment that may be able to cure cancer. It is a protein-based pharmaceutical that binds to Natural Killer (NK) cells, which are part of the immune system. These NK cells can kill diseased cells, such as cancer cells. Anti-KIR enhances the ability of NK cells to do that job. In 2006 Novo Nordisk obtained regulatory approval to initiate a phase 1 study to evaluate the safety of anti-KIR in patients with acute myeloid leukaemia. In January 2007 the first human dose was successfully administered. The film follows this process.



The ethical dilemma: Animal experimentation

Experiments on living animals are a necessary part of the discovery and development of new drugs. However, the use of experimental animals is a source of concern for Novo Nordisk as it is to many people. We cannot replace all animal experiments in the foreseeable future, but we continuously refine the care and use of animals and develop procedures that reduce and/or replace animal experiments. We act with due respect for the animals by establishing and ensuring high ethical and welfare standards, including an internal ethical review of all new types of experiments on animals. External partners, contract research organisations and suppliers are held to the same high standards and we monitor their performance. Experimental animals are housed according to their needs, with appropriate training and socialisation of the animals.



Dilemmas at work

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We welcome feedback and comments on the film and this brochure as part of our ongoing dialogue and engagement with stakeholders.

Send your comments to:

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For more information, visit: novonordisk.com/science/bioethics

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