

# Guaranteeing ethics in research/

Scientific research has paved the way for major advances and today researchers are able to work directly with living organisms, in particular human beings. Although national and international ethics regulations exist, they are not all harmonized. In order for the Group's research to be carried out properly across all Group sites worldwide, it seems essential to take a stance regarding the main topics in bioethics.

## 01. The challenges of bioethics

### STEM CELLS

<b>Definition</b>	Stem cells are involved in the processes of tissue regeneration and homeostasis (cell equilibrium). These processes are triggered in the event of surgery, injury and disease. Stem cells also represent major potential for research because they have not only the ability to renew themselves, but also to differentiate into several types of cells.
<b>Why it's important</b>	The use of stem cells in research gives rise to many questions primarily for three reasons: the embryonic origin of certain cells, the use of such cells for reproductive purposes, and the question of patenting living organisms.
<b>How sanofi-aventis is affected</b>	As one of the global leaders in pharmaceutical research, sanofi-aventis wants to explore the opportunities provided by the therapeutic applications of stem cells. The Group uses these research tools to develop new treatments based on chemical or biotherapeutic compounds.
<b>Current regulations/trends</b>	Europe: <ul style="list-style-type: none"> <li>• European Directive 2004/23/EC;</li> <li>• in most European countries, a legal framework is currently being developed.</li> </ul> United States: <ul style="list-style-type: none"> <li>• the situation is judged on a case-by-case basis from one state to another.</li> </ul>
<b>Group policy or position</b>	The use of stem cells (human and mouse) within the Group is limited to non-human embryonic stem cells.

### BIOPIRACY

<b>Definition</b>	The term biopiracy describes the process by which natural resources identified through bioprospecting of biogenetic resources (or knowledge and traditional practices) are patented. The result is to make them subject to intellectual property rights that limit their use.
<b>Why it's important</b>	Biopiracy poses an ethical problem because most of the time it occurs to the detriment of developing countries, without respecting the sovereignty of States.
<b>How sanofi-aventis is affected</b>	Natural products currently play an important role in the discovery and process of developing new medicines. Over the past twenty years, nearly half of the new chemical entities produced worldwide originated from compounds found in nature.
<b>Current regulations/trends</b>	<ul style="list-style-type: none"> <li>• The Convention on Biological Diversity (CBD).</li> <li>• The Rio de Janeiro convention (1992).</li> </ul>
<b>Group policy or position</b>	The Group's position is to discover and develop, on a case-by-case basis, in common with the original source(s), certain natural resources with potential therapeutic properties so that the benefit will be shared fairly by all stakeholders, in full compliance with the CBD.

### USE OF LABORATORY ANIMALS IN R&D

<b>Definition</b>	In addition to widely used experimental <i>in vitro</i> studies, the purpose of using laboratory animals is to collect as much information as possible about the therapeutic or toxic effects of a new drug.
<b>Why it's important</b>	This topic gives rise to two major issues: <ul style="list-style-type: none"> <li>• the animal's sensitivity leads one to question the experiment's legitimacy;</li> <li>• the animal's status compared to humans. Do people have the right to conduct experiments on living animals?</li> </ul>
<b>How sanofi-aventis is affected</b>	It is necessary to use laboratory animals for the research and development of new products, and they are mandatory before beginning clinical trials in humans. In addition to R&D toxicology studies, sanofi pasteur uses animals to ensure the efficacy and quality of its vaccines before they are brought to market, in compliance with specific regulations pertaining to vaccines.
<b>Current regulations/trends</b>	<ul style="list-style-type: none"> <li>• European Directive 1986/609/CEE.</li> <li>• European Convention ETS/123.</li> <li>• Animal Welfare Act (USA, 1996)</li> <li>• ILAR Guide, NRC, 1996</li> </ul>
<b>Group policy or position</b>	Beyond strict compliance with the various regulations in effect and the 3R's principle, the Group's proactive approach is illustrated by the creation of the "sanofi-aventis charter on the humane care and use of laboratory animals" and by the fact that it obtains accreditation for its programs on the care and use of laboratory animals.

### GENETICALLY MODIFIED ORGANISMS

<b>Definition</b>	GMOs, or genetically modified organisms, are those that have been modified in order to improve specific characteristics (such as a plant's resistance insecticide) or to produce a particular compound (such as the production of food aromas).
<b>Why it's important</b>	The traceability and confinement of these organisms and their products are the main issues in connection with GMOs.
<b>How sanofi-aventis is affected</b>	Sanofi-aventis uses GMOs for research purposes in order to better understand diseases, but also to develop treatments with fewer side effects. A number of treatments on the market today, such as insulin or certain cancer therapies, are produced thanks to GMOs.
<b>Current regulations/trends</b>	Regulations vary widely according to the country.
<b>Group policy or position</b>	In line with regulatory requirements, the use of GMOs takes place in confined laboratories. Their elimination is also regulated and respected by sanofi-aventis. In 1993, the Group established "TRIBIO", a committee of experts devoted to the prevention of biological risk. This committee conducts site audits on a regular basis.

**CLINICAL TRIALS**

<b>Definition</b>	A clinical trial is a research study in human volunteers carried out to answer specific health questions. It may test a drug, a medical device or surgery. Clinical trials are necessary to identify those patients who will best be able to benefit from therapeutic innovations, depending upon their disease or condition. They also make it possible to determine what adverse events may occur, as well as the drug's dosage and conditions of use.
<b>Why it's important</b>	Patients are vulnerable in view of their disease or risk factors. Whether a trial focuses on products designed to cure or treat a disease or condition, or preventive products that act on risk factors and make it possible to prevent or delay the occurrence of disease, the trial must protect the safety of participating patients and ensure their free consent is based on clear, complete information.
<b>How sanofi-aventis is affected</b>	Before new treatments can be offered to patients, it is crucial to ensure that they are effective and safe. This is why clinical trials are a mandatory part of the marketing approval process, both for the registration of new drugs and for the introduction of new indications for products already on the market.
<b>Current regulations/trends</b>	Stringent national and international regulations include: <ul style="list-style-type: none"> <li>• European Directive 2001/20/EC;</li> <li>• CFR 21 regulations issued by the FDA;</li> <li>• regulations issued by the Japanese Ministry of Health, Labor and Welfare;</li> <li>• directives of the International Conference on Harmonization (ICH), specifically Good Clinical Practice (GCP).</li> </ul>
<b>Group policy or position</b>	Sanofi-aventis supports efforts to improve clinical trial transparency so that patients and/or healthy volunteers will be better informed about the trials in which they participate and that their rights are guaranteed. It publishes information about its own clinical trials via specialized Internet sites. Regardless of the country where the Group carries out clinical trials, it ensures compliance with ethical standards for the protection of those enrolled in the trials.

**HUMAN BIOSPECIMENS AND PROTECTION OF PERSONAL DATA**

<b>Definition</b>	Human biospecimens include in particular: organs, tissues, cells, bio-fluids (blood, serum, urine, etc.), ribonucleic acid (RNA), and genomic deoxyribonucleic acid (DNA).
<b>Why it's important</b>	Genetic material makes it possible to identify a person and may give access to a great deal of information about the donor. As a result, it is important to protect these informations.
<b>How sanofi-aventis is affected</b>	Within the framework of its research activity, sanofi-aventis makes use of human biospecimens to further develop its scientific knowledge.
<b>Current regulations/trends</b>	<ul style="list-style-type: none"> <li>• Article 21CFR Part 11 (FDA) concerning the protection of personal genetic data.</li> <li>• French Data Protection Act (CNIL).</li> </ul> Moreover, for work conducted in France on genetic data involving "the examination of genetic characteristics," a request must be made for explicit, written and informed personal consent.
<b>Group policy or position</b>	Sanofi-aventis has defined the "General principles on the ethical use of human biospecimens". In addition, the two applications enabling the examination of genetic databases comply with the French Data Protection Act concerning the protection of personal data (CNIL) and Article 21CFR Part 11 (FDA) concerning the protection of personal genetic data.

**GENE THERAPY**

<b>Definition</b>	Gene therapy consists of introducing genetic material into certain cells of the body as a means to fight disease.
<b>Why it's important</b>	This technique gives rise to three major questions: <ul style="list-style-type: none"> <li>• when a viral vector is used, is there a risk of spreading this virus among the population;</li> <li>• is there a risk of transmission to future generations;</li> <li>• how long will a gene introduced into the body be expressed, and in particular, its replication in the cells.</li> </ul>
<b>How sanofi-aventis is affected</b>	Sanofi-aventis has an innovative gene therapy approach (NV1FGF), currently in phase III clinical trials, for the treatment of critical limb ischemia.
<b>Current regulations/trends</b>	<ul style="list-style-type: none"> <li>• In Europe, there are several directives concerning how gene therapy clinical trials are to be conducted: Directive 2001/83/EC, Directive 2001/20/EC.</li> <li>• In the United States, each State determines its own legislation.</li> </ul> The United States and all European countries have banned germ-line gene therapy research and any modification of human nature.
<b>Group policy or position</b>	Currently, NV1FGF is the only gene therapy approach being pursued by sanofi-aventis. Moreover, no virus vector is used; DNA is injected directly into the affected tissues.

**HUMAN CLONING**

<b>Definition</b>	Human cloning consists of reproducing a genetically identical being.
<b>Why it's important</b>	Human reproductive cloning raises a considerable number of ethical, philosophical and religious questions.
<b>Current regulations/trends</b>	According to a report published in 2004 by UNESCO: <ul style="list-style-type: none"> <li>• 46 countries have passed legislation banning human reproductive cloning;</li> <li>• 3 countries have placed a temporary moratorium on human reproductive cloning, for a limited period of time.</li> </ul>
<b>Group policy or position</b>	Sanofi-aventis does not conduct human cloning research.

**NANOTECHNOLOGY**

<b>Definition</b>	Nanotechnology refers to the techniques and manufacturing processes that make it possible to create particles on the nanometric or molecular scale.
<b>Why it's important</b>	Due to their small size, nanoparticles raise the issue of how to control and monitor their effects on health and the environment.
<b>How sanofi-aventis is affected</b>	By producing compounds of the same size as most biological molecules and structures, nanotechnology paves the way for a number of medical applications, both therapeutic and diagnostic.
<b>Current regulations/trends</b>	Currently there are no specific regulations, although expert committees meet in the United States and Europe.
<b>Group policy or position</b>	Discovery research at sanofi-aventis evaluates the use of: <ul style="list-style-type: none"> <li>• nanocrystals (Quantum dots) as imaging tools;</li> <li>• "squalene nanoparticles" to study their active compounds' mechanisms of action (chemical entity, gene or protein).</li> </ul> The Group has entered into university collaborations concerning nanoparticle formulations, and a collaboration with Elan.