

## 04. Use of laboratory animals

Animal research is a sensitive ethical issue demanding the utmost consideration and respect. Given the very nature of the pharmaceutical business, sanofi-aventis is obliged to conduct animal experiments for legal, scientific and ethical reasons. In addition to the widely used experimental *in vitro* models, *in vivo* studies aim to collect as much information as possible about the therapeutic or toxic effects of a new drug in a higher species before administration to man.

In addition to studies within the R&D framework, sanofi pasteur also carries out animal studies to assure the efficacy and quality of its vaccines in production before market release, in compliance with specific vaccine regulations.

### → STRICT REGULATIONS

Animal experiments are subject to strict regulations to which sanofi-aventis complies both nationally and internationally:

- country or region animal welfare laws (e.g., European Directive 1986/609/EC; Animal Welfare Act in the US; European Convention ETS/123);
- rules (standards) developed by:
  - Institute for Laboratory Animal Research (ILAR);
  - Universities Federation for Animal Welfare (UFAW);
  - FELASA (Federation of European Laboratory Animal Science Associations).

Sanofi-aventis continued its efforts to respect and protect laboratory animals by implementing "The sanofi-aventis charter on the humane care and use of laboratory animals," which are internal standards aimed to go beyond the regulations.

### → A TOTAL COMMITMENT TO THE 3R'S PRINCIPLE (REDUCTION, REPLACEMENT, AND REFINEMENT)

Sanofi-aventis believes in the need to adhere to the highest standards of animal care and is committed to the strict application of the 3R's principle:

- **reduction** consists of obtaining the same information while decreasing the number of animals used;
- **replacement** aims at using lower order species and alternative methods;
- **refinement** addresses animal welfare issues including minimizing pain.

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### SANOFI-AVENTIS COMMITMENTS TO THE 3R'S PRINCIPLE

#### REDUCTION

- Optimize research strategies in order to eliminate unnecessary experiments and ensure that approaches are scientifically sound.
- Obtain as much information as possible from each experiment.
- Animals are used only where there is the firm expectation that the results will contribute to protection and/or improvement of human health and safety.
- Choose appropriate animals: 95% of the animals used by the Group are rodents.
- Each protocol is reviewed by an internal Ethics Committee.
- Reduce where possible the use of non-human primates (for example, sanofi pasteur significantly reduced the use of primates over the past five years).
- As required by national laws, all animal use is recorded and reported to competent authorities. For each study or project, the number of animals is reviewed by Ethics Committees and the least number of animals is used to obtain the scientific or regulatory objective. Biostatisticians review all experimental protocols. These data are provided only to relevant national authorities.

#### REPLACEMENT

- Animals are only used when valid alternative methods do not exist. The justification of any animal use is reviewed by an internal Ethics Committee.
- Systematic use and the contribution to the development of *in vitro* systems: tissue cell cultures, high throughput screening (HTS), *in vitro* dosing.
- Replacement of higher evolutionary species with lower order species.

#### REFINEMENT

Each experimental protocol must be approved by an Ethics Committee that evaluates the scientific justification for the study, the appropriateness of the techniques employed and/or the animals used as well as taking into account the pain the animal may experience. Sanofi-aventis places particular attention on ensuring that pain is defined and monitored for each case.

The Ethics Committee is also in charge of defining and assessing the study's endpoint so that it is acceptable and as humane as possible. In addition, all animals are under the care of a veterinarian.

#### Other commitments to ensure the optimal well-being of animals include:

- utilization of non-invasive methods: in 2006, sanofi-aventis inaugurated a new building for animal imaging;
- personnel training: each employee working on animals has been trained in animal experimentation and receives periodic retraining. 30% of employees attended a retraining session in 2007, and another 30% will attend one in 2008;
- in-house workshop on the "Culture of Care" for sanofi-aventis R&D employees about the care and use of animals in research;
- ongoing surveillance to identify new techniques making it possible to improve the company's commitment to the 3R's.

#### Improving the animal's environment:

- cage adapted to each species, high quality litter is used;
- respect for the physiological and social needs of animals, with measures taken to enrich their environment. (e.g., providing opportunities for animals to socialize; physical exercise for dogs, etc.).

#### Transport:

- a great deal of attention is given to overseeing the conditions for animal transport between sites as well as between suppliers and sanofi-aventis, whether by road or air. We adhere to appropriate transport standards and ensure suppliers meet those standards as well. The supplier transport conditions were reviewed (or audited) and complied with international rules and national regulations in 2007;
- sanofi-aventis will continue to optimize the conditions for animal transportation between our research sites.

#### Employee empowerment:

- in order to continuously improve, sanofi-aventis encourages employees to express their concern for animals in experiments, enabling anonymous reporting.