

Putting animal welfare principles and 3Rs into action



European Pharmaceutical Industry
2011 Report



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European Federation of Pharmaceutical Industries and Associations



Putting animal welfare principles and 3Rs into action

European Pharmaceutical Industry 2011 Report

The research-based pharmaceutical member companies of EFPIA are constantly looking for solutions to meet the unmet medical needs of millions of patients who suffer from a wide range of diseases. These include chronic diseases such as cancer and diabetes, disorders of the central nervous system (dementia, parkinson’s and schizophrenia), as well as rare diseases, infectious diseases (HIV and hepatitis) and diseases affecting people primarily in developing countries. As an industry, we continue to improve the quality of life for both people and animals by developing new products and services for the diagnosis and treatment of diseases. Medical breakthroughs that benefit millions of patients would not be possible without animal testing.

Pharmaceutical innovation has and will always require a great deal of research and development – If we could not study animals, we would not get the crucial insights of the fundamental processes both in healthy and in sick organisms that prove medicines are reliable and effective. When a new concept has been confirmed in the lab, it is in the interests of the safety of the patients who receive the new treatment for the first time that the medicines have undergone the appropriate safety tests, some of which may involve animals. Without animal research, we would put these patients at high risk. Before the first human receives a new treatment, we need animals as a bridge to determine its basic safety for patients. Without this, no medicines and treatments, from which society and patients benefit from today, would exist. Although pharmaceutical companies cannot avoid the use of laboratory animals to

prove that medicines work, we must ensure we meet high standards of animal welfare. To put animal welfare principles into action, we only use animals where no alternative exists, use the minimum numbers to achieve the scientific objective and ensure that the animals suffer the minimum pain and distress (3Rs). This report explains how we are putting these 3Rs and animal welfare principles into action.

The 2011 European Pharmaceutical Industry Report shows how we not only comply with the letter of the law, but how our approach is to go **beyond compliance**, and how we are **leading by example**. It is also important that we are open to scrutiny and dialogue about this issue, hence our commitment to **open communication**. This report is part of fulfilling that commitment.





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Science is incremental. Breakthroughs often look from afar like giant leaps but they are in fact just the latest in a series of small steps. The same goes for the people whose work on the brains of songbirds gave us much of our current understanding of the pre-frontal cortex – an area associated with personality and behaviour but also with addiction and psychological disorders. All of that basic science involving the use of animals, conducted 30 years ago, was the first step on the long road that gave us medicines for people with schizophrenia and depression.

Richard Bergström

Director General of the European Federation of Pharmaceutical Industries and Associations (EFPIA)



EFPIA companies who are members of the standing Research and Animal Welfare working group have compiled and produced this report. The EFPIA working group on Research and Animal Welfare was established to allow on-going exchange of information and good practice within the pharmaceutical industry. It works to reconcile research needs with animal welfare imperatives, and promotes development and uptake of 3R approaches in research and testing both within the pharmaceutical industry and beyond.

Companies:

- | | |
|----------------------|---------------------|
| Abbott | Merck Serono |
| Astellas | Merck Sharp & Dohme |
| AstraZeneca | Novartis |
| Bayer HealthCare | Novo Nordisk |
| Boehringer Ingelheim | Orion Pharma |
| Eisai | Pfizer |
| Eli Lilly | Roche |
| GlaxoSmithKline | Sanofi |
| Ipsen | Servier |
| Janssen | UCB |

Associations:

- Verband Forschender Arzneimittelhersteller (VfA) (Germany)
- Associazione delle imprese del farmaco (Farmindustria) (Italy)
- Vereniging Innovatieve Geneesmiddelen Nederland (Nefarma) (Netherlands)
- Interpharma (Switzerland)
- The Association of the British Pharmaceutical Industry (ABPI) (United Kingdom)

Beyond Compliance

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Beyond Compliance



- * **How do we ensure that animal welfare standards and practices are put into action throughout the sector both in our industry and among the laboratory and research community more broadly?**

The European pharmaceutical industry's animal welfare standards and practices often go beyond those required by regulators. In addition to carrying out their own review of internal animal welfare standards and practice controls, companies also carry out regular monitoring and systematic audits of external partners. (P.6) [READ MORE...](#)

- * **How do we make sure that global regulations reflect 3Rs strategies?**

We continuously contribute to reviews of European and international regulatory requirements to make sure we implement the most up to date 3R strategies across the industry. (P.8) [READ MORE...](#)

- * **What internal and external industry initiatives facilitate the implementation of training programmes on animal welfare and care?**

The European pharmaceutical industry runs education and training programmes and courses on animal welfare and care for its employees. In addition, companies develop educational tools in partnership with the research community to help spread knowledge and good practices both in the pharmaceutical industry and amongst the wider scientific community. (P.9) [READ MORE...](#)

Leading by Example

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- * **How do we share and encourage good practices based on 3R principles across the pharmaceutical industry?**

The European pharmaceutical industry collaborates within and cross sectors to identify opportunities to implement the 3Rs (i.e. to systematically and verifiably Replace, Reduce and Refine) and increase the welfare of animals used for scientific purposes. (P.12) [READ MORE...](#)

- * **How do we stimulate putting into practice global animal welfare standards?**

The European pharmaceutical industry supports international research projects and development of standards and policies, as well as their application in companies' research sites worldwide. (P.14) [READ MORE...](#)

- * **What is being done to rapidly implement and enforce across Europe the revised European Directive 2010/63/EU on the protection of animals used for scientific purposes?**

The European pharmaceutical industry supports and stimulates rapid implementation and enforcement of the revised Directive 2010/63 within the EU and contributes to expert discussions on implementing measures at EU level. (P.16) [READ MORE...](#)

- * **Are companies independently assessed on how animal welfare standards are applied?**

European pharmaceutical companies are independently assessed and they work to improve existing external and independent assessments of internal animal welfare standards and facilities on a European and global level. (P.17) [READ MORE...](#)

Open Communications

Dialogue

Reporting

Committing to Open Communication

- * **How do we contribute to an open and constructive dialogue on animal welfare?**

The pharmaceutical industry understands the sensitivities around the issue of animal research. For this reason, we actively seek to engage in dialogue. We contribute to a continuous, open and constructive dialogue on animal research and welfare, with the public, legislators, policy makers, and interested parties. (P.18) [READ MORE...](#)

- * **How is industry communicating the progress made with animal welfare activities, specifically the 3Rs?**

European Pharmaceutical companies report progress made on a regular basis and the amount and quality of information in the public domain is increasing. Companies produce annual corporate social responsibility reports which detail the progress made year on year, as well as dedicated websites, blogs and brochures. (P.20) [READ MORE...](#)





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Question: How do we ensure that animal welfare standards and practices are put into action throughout the sector both in our industry and among the laboratory and research community more broadly?

The European pharmaceutical industry's animal welfare standards and practices often go beyond those required by regulators. In addition to carrying out their own review of internal animal welfare standards and practice controls, companies also carry out regular monitoring and systematic audits of external partners.



Checking standards of animal welfare with company audits and certifications

– Use of animals in laboratories comes with stringent guidelines for animal welfare. In Europe, the guidelines are among the most stringent in the world and laboratories are subject to mandatory legal inspections. Wherever we operate in the world, European pharmaceutical companies monitor compliance with defined quality standards of housing, care and handling of animals. Veterinary inspections, internal and external audits as well as company

ethical committees and certifications all contribute to the industry checking its standards. We do this not only to fulfill legal requirements, but also to go beyond them, and actively increase animal welfare standards. In many companies, internal procedures enable staff to raise concerns related to animal welfare. Research-based pharmaceutical companies and the contract research organisations the industry works with, voluntarily seek certification by external auditors from either national authorities, or certification bodies such as the

Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

Ethical considerations under constant scrutiny

– Animal welfare goes far beyond mere compliance with legislation. It involves finding the right answers to difficult ethical considerations, weighing up how we go about discovering new medicines and vaccines, and using animals to test whether they will be effective and safe for patients. Today, all the pharmaceutical company research facilities,



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wherever they operate, have an ethics committee on animal welfare, or use external ethical committees. These committees scrutinize the proposed research process to ensure that animal welfare standards and the 3R principles have been effectively applied to the research plan. Throughout 2011, company ethical committees have been providing guidance and support on ethical issues raised by employees or external persons, such as animal welfare experts, NGO representatives, lawyers or lay persons. Companies review and update their training programmes to ensure consistency of ethical standards across all sites worldwide. Ethical committee oversight and training makes

certain we live up to our ethical responsibility, and ethics remain a top priority.

Constantly raising the bar on animal welfare standards – As progress in science is constantly evolving, we regularly review existing agreements and contracts with external partners, such as medical labs or contract research organisations, to incorporate specific requirements to ensure animal welfare standards are put into practice. In 2011, many of our member companies reviewed and recommended animal welfare provisions in their contractual agreements. Furthermore, formal auditing processes are in place for contractors and animal

breeders, which focus on internal and contract animal research activities, and collaborations with academia and industry. Controls for animal welfare compliance of external partners are continuously being improved. Methods for doing this include sharing external ethical protocols within ethical committees, and introducing animal welfare compliance standards into our external agreements.

Animal welfare standards beyond European pharmaceutical companies – Each company currently has their own checklist of requirements, which standardise assessment criteria and determine whether external partners comply with the relevant animal welfare regulations. In 2011, a number of pharmaceutical companies went even further by developing global audit checklists to evaluate contractors and animal vendors across all their international operations. Steps are currently being taken to agree a common checklist for auditing that could be used by all European pharmaceutical companies to review the work of all contractors and contract research organisations. This aims to raise the bar even higher on standards for animal welfare.

One way of ensuring that animal welfare principles are being employed consistently is to review the topics being examined by the local ethical review committees across all of

a company's animal research and testing sites. A member company that did this in 2011, confirmed a high level of consistency between the topics that local committees look at during their review process. It also recognised the need for supplementary principles to help local ethical review groups apply the company policies consistently. Principles were produced to clarify expectations for the composition of ethical review panels; use of trained and competent personnel; and ways in which pain and distress of the animals in their care could be evaluated and alleviated.





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Question: How do we make sure that global regulations reflect 3Rs strategies?

We continuously contribute to reviews of European and international regulatory requirements to make sure we implement the most up to date 3R strategies across the industry.



Supporting review of regulations and international guidelines – Our industry is global and so we conduct our research worldwide; therefore solutions such as replacing, reducing, and refining animal studies need to be applicable and implemented worldwide. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) brings together the regulatory authorities and pharmaceutical industry of Europe, Japan and the USA as well as members of the scientific community to deliberate on the scientific and technical aspects of drug registration. By providing data and expertise, the European pharmaceutical industry participated in a significant effort to review ICH guidelines on safety, immunotoxicity and evaluation of anti-cancer products. This process resulted in waiving or rationalising and optimising certain tests, with the potential to reduce by up to 50%, the numbers of the animals required for toxicity testing. For a medium sized company, per year, up to 2000

animals (mostly mice and rats) need to be used for such testing. A potential halving of the numbers is therefore an important step in reducing the number of animals needed for toxicity testing. The 2011 revision of the ICH guidelines has led to a significant reduction in animal use without compromising safety and effectiveness, and has led to a number of other important decisions:

- * Separate acute toxicity studies were eliminated,
- * Some studies, like reproductive toxicity were postponed to a later stage of the development process, which means that less compounds are ultimately tested,
- * Abuse liability can be assessed using rodents rather than non-human primates,
- * Certain tests will be combined, and more data derived from one study.

Contributing to change across sectors – EFPIA has actively engaged in discussions on streamlining the application of regulatory requirements, including the 3R strategies. Through a cross-sector European Partnership for Alternative Approaches to Animal Testing (EPAA), the European pharmaceutical industry was able to share its experience and learnings from its review

of acute toxicity. The information sharing was conducted under the auspices of the UK National Centre for 3Rs (NC3Rs), and led to the waiver of acute toxicity tests in the pharmaceutical industry, with the objective to replicate this approach in other industry sectors. The cross-sector application of the waiver of acute toxicity tests is an important step in improving animal welfare, wherever possible. Other EPAA projects that European pharmaceutical companies have supported include:

- * Looking into the potential of using stem-cells to replace single organ animal testing,
- * Enhancing Integrated Testing Strategies, which involve mathematics and computer models to carry out cell-based tests, with the potential to reduce the number of animals needed for tests.

Finally in 2011, a number of companies participated in a cross-sector review conducted by the European Centre for the Validation of Alternative Methods (ECVAM) to test methods used in reproductive toxicity testing. The results of this review are expected in 2012, and it is hoped that the combined data will clearly demonstrate that fewer animals than previously had been thought, are necessary for these tests.



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Question: What internal and external industry initiatives facilitate the implementation of training programmes on animal welfare and care?

The European pharmaceutical industry runs education and training programmes and courses on animal welfare and care for its employees. In addition, we develop educational tools in partnership with the research community to help spread knowledge and good practices both in the pharmaceutical industry and amongst the wider scientific community.



Sharing best practices – We use alternative methods wherever we can, and our improved research methods, and best practices are widely shared through presentations at conferences and scientific publications. Sharing data can demonstrate that alternative methods either reduce or are far less distressing for animals. At the 8th World Congress on Alternatives in the Life Sciences in 2011, companies demonstrated their innovative 3R methods to other researchers, NGOs and academia, and updated regulators on

these new alternative methods. Another example of sharing best practices is the educational seminar held to update the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) on the use of Dried Blood Spot (DBS) technology. This educational seminar was able to demonstrate that it would be safe to use only a minuscule drop of blood from mice or rats for drug tests.



European Federation of Pharmaceutical Industries and Associations



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Education and Training – During 2011, each pharmaceutical company member of EFPIA conducted internal training programs related to the use of animals in research and 3R principles. They also supported participation in education and training programmes sponsored by organisations like the Federation of Laboratory Animal Science Associations (FELASA). This is in line with the European Directive on the protection of animals used for scientific purposes, which came into force in September 2010, and requires Member States to set minimum requirements for education and training. In addition to training to ensure all pharmaceutical company employees in Europe who deal with animals comply with legal requirements, exchanges of trainee researchers also took place in a few companies. Dedicated training on 3Rs is carried out for researchers, scientists, lab assistants, carers and others

directly in contact with animals. Building on our industry’s training experience, we have worked together with regulators to contribute to a trilingual e-learning tool on animal experiments, which was launched in 2011, and is now being promoted as a teaching aid. As well as training our staff, we ran lectures for various courses organized in major universities around the EU. For example, the SafeSciMet program, part of the Innovative Medicines Initiative (IMI), included courses for using telemetry. Telemetry devices have major benefits for reducing numbers of animals used in research. Much like a pacemaker that is fitted to a patient suffering from a heart condition, once the small device is fitted to the animal under anaesthesia, researchers can permanently monitor its blood pressure and other vital signs remotely, without handling the animal further. The more researchers learn about the advantages of

telemetry, and are trained to use it, the more animal welfare standards for animals used for cardiovascular studies will improve. For example, using a telemetric data transmission over a three year period, we can reduce the number of dogs used in pharmacological tests to detect cardiovascular symptoms from 65 to 10.

Similarly, education and training for in vitro toxicology methods should lead to reducing the number of animals used in toxicology research. As part of the Federation of Laboratory Animal Science Associations (FELASA) accreditation, our leading researchers have delivered lectures throughout 2011 to laboratory animal scientists and researchers on topics such as surgical procedures, administration and blood sampling procedures, handling as well as anaesthesia and euthanasia.





Leading by Example

Question: How do we share and encourage good practices based on 3R principles across the pharmaceutical industry?

The European pharmaceutical industry collaborates within and cross sectors to identify opportunities to implement the 3Rs (i.e. to systematically and verifiably Replace, Reduce and Refine) and increase the welfare of animals used for scientific purposes.

IMI projects aim at providing innovative solutions to finding new medicines, that also replace, reduce, refine use of animals used for scientific purposes –

EFPIA is one of the founding members of the Innovative Medicines Initiatives (IMI), Europe's largest public-private partnership that tackles scientific bottlenecks in medicines R&D. While the focus of IMI projects is finding breakthrough medicines, they also strive to reduce animal numbers, and develop more precise and refined animal models to test human diseases. One area of 3R focus is to apply *in silico* and *in vitro* methods thereby avoiding animal testing completely. The eTox IMI project has shown that it may no longer be necessary to carry out toxicity testing for clinical research. This project

has developed computer based prediction models of *in vivo* toxicity, using toxicity data provided by pharmaceutical companies, removing the need for certain animal tests.

eTox and other IMI projects will reduce the need to use animals for testing the safe doses before human clinical trials are conducted:

* **MARCAR:** A five-year project, which aims to establish for the first time, proof of the concept that early biomarkers can reliably and robustly predict later cancer development. One of the main drivers behind finding early biomarkers for risk assessment, is the potential to reduce animal use in drug and chemical risk assessment.



* **MIP DILI:** The aim of the project is to develop new tests that will help researchers detect potential liver toxicity problems much earlier in the development of a medicine. This will reduce the numbers of animals needed for testing in the later stages of drug development, and save many patients from the trauma of liver failure.

* **NewMeds project:** This project is one of the largest ever research academic-industry collaboration projects to find new treatment pathways for schizophrenia and depression. Central to discovering these new treatments, is developing and recommending animal research models, that are not only quicker and more efficient, but reduce the use of animals.

Joining forces with others – Together with the European Commission and other industry sectors, including the chemical, animal health and cosmetics industry, EFPIA is one of the founding members of the European Platform for Alternatives Approaches to Animal Testing (EPAA). A number of EFPIA companies are also direct members of this public-private partnership. In 2011, the European Commission and participants from academia, NGOs, and pharmaceutical companies, collaborated on EPAA projects. A true breakthrough was achieved with the Acute Toxicity project, when EPAA was able to provide evidence to regulators that only one testing route was necessary to show the toxicity of a substance, and not two as was formerly compulsory. EPAA also worked

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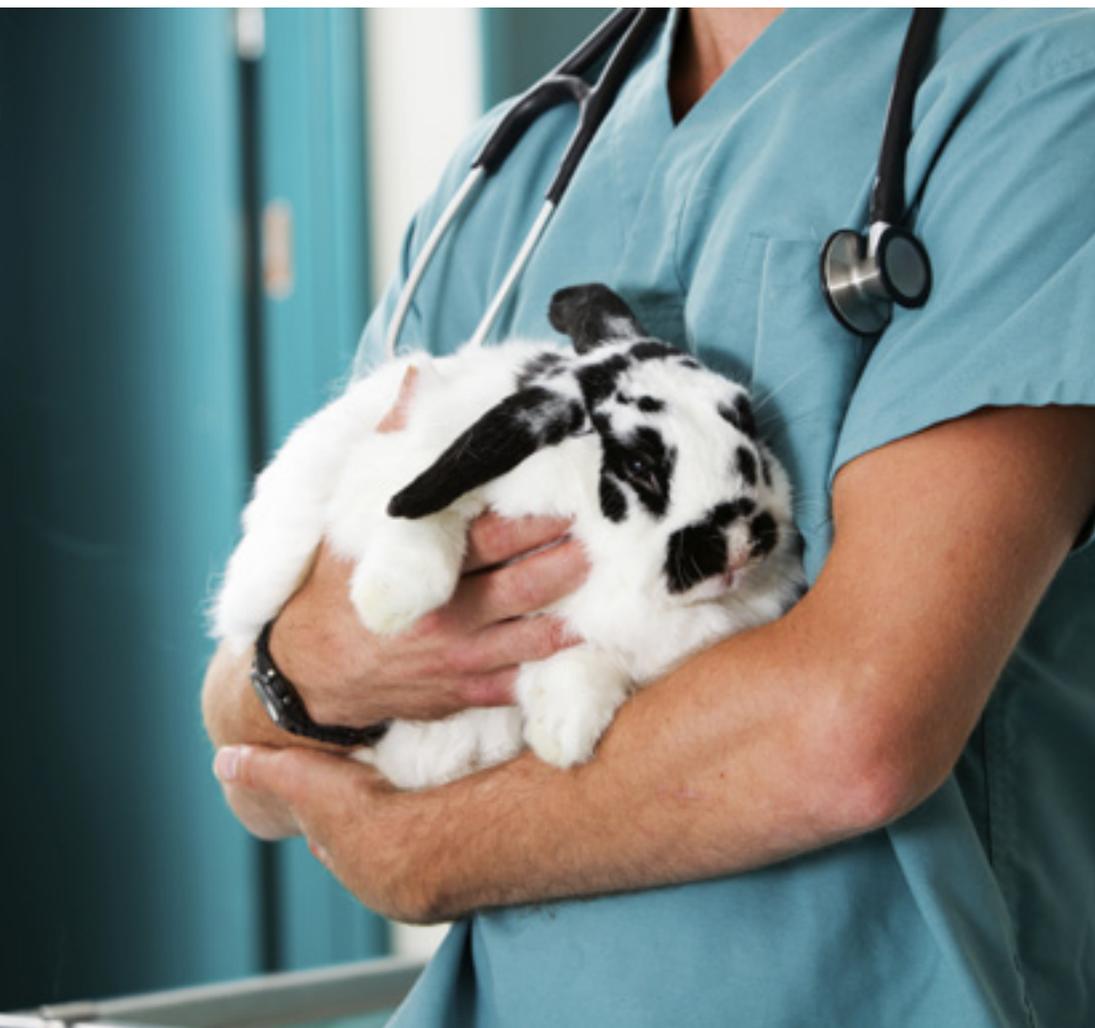
Leading by Example

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Leading by Example



on Integrated Testing Strategies (ITS) making the case to provide more data than current existing methods, with an agreement that “industry, academia and regulators need to educate each other, and ITS is among the most efficient solutions to address 3Rs”. (P.6) [READ MORE...](#)

Funding to develop better 3Rs – In 2011, the European pharmaceutical industry has continued to support science-based organizations which work to improve the development and implementation of 3Rs in medicines discovery. This support has been either financial or in kind, with the active contribution of experts, data or other resources. Funding has been provided for the Swiss 3Rs Foundation, the UK National Centre for 3Rs (NC3Rs) and the Federation of European Laboratory Animal Science Associations (FELASA). The funding for FELASA has been instrumental in defining and implementing education and training guidance, which sets standards, used in academic and industry laboratories across Europe. European pharmaceutical industry support has made possible:

* **3Rs prize:** The National Centre for the Replacement, Reduction and Refinement of Animals in Research (NC3Rs) awards an annual prize for an original contribution to scientific and technological advances in the 3Rs in medical, biological or veterinary

sciences published within the last three years. This is sponsored by industry.

- * **NC3Rs** leads a programme of work to identify and develop opportunities to minimise animal use in the pharmaceutical industry. Working closely with international scientists and regulators from Europe, the USA and Japan, the NC3Rs programme supports workshops where ideas and data sharing, as well as changes in approach in diverse areas of research and development are tackled, relating to a number of issues, such as:
 - Acute toxicity,
 - Regulatory toxicology of new chemical entities,
 - Research and development of monoclonal antibodies,
 - Prediction of human pharmacokinetics,
 - Abuse potential.
- * **The 3R Foundation** is a cooperative institution set up more than 20 years ago collaboratively by the pharmaceutical industry, NGOs, and the Swiss government. The aim of the 3R Foundation is to promote alternative research methods to animal experimentation, through grants for research projects, as well as to implement and promote the 3R principles. The organisation supports, first and foremost,



Leading by Example



projects aimed at developing new methods, or refining accepted methods (validation), which offer improvements vis-à-vis standard animal experimentation, in line with the 3R principles (Replace, Reduce and Refine).

Reward and recognition for 3R breakthroughs – Many EFPIA member companies incentivize development and promotion of alternative research approaches to the use of animals in research through

internal award schemes recognizing employees who have made outstanding advances in implementing the 3Rs. The German Verband Forschender Arzneimittelhersteller (VfA) is just one of the industry’s national associations that has successfully partnered with the chemical industry and the German Agriculture Ministry, to set up a Foundation for the Promotion of Alternative and Complementary Methods to Reduce Animal Testing (Stiftung Ersatzmethoden Tierversuche – SET). In 2011,

a company award was given to the scientists who brought a new monoclonal antibody medicine to clinical trials, on the basis of *in vitro* data and information from extensive testing, involving genetically altered mice. This avoided the use of non-human primates. The thoroughness of their work satisfied the regulatory authorities in the USA, Canada and EU that the medicines were safe for human use. Another important project was recognized in 2011, with a safety assessment team being given an award for using an external telemetry (radio-transmitter) method to assess the effects of potential new medicines on electrocardiogram (ECG – a study of heart function) in dogs. The new method reduces the adverse effects caused to the dogs, enhances the value of the scientific data obtained, and helps to avoid the use of around 120 dogs annually in this company.

Collaborating to help better measure 3R progress – Evaluating progress in 3Rs is difficult. There is limited information available in the public domain against which to measure progress. The statistics on animal procedures on living animals cannot be used as benchmark because the numbers of animals reported in annual statistics is influenced by a range of scientific and strategic factors independent of 3Rs. In 2011, EFPIA working group on Research

and Animal Welfare developed the first ever series of metrics (Key Performance Indicators - KPIs) to help assess the impact and investments in 3Rs on animals. This was presented at the 8th World Congress on Alternatives. The working group agreed a common set of priority KPIs to provide evidence of the investments in and benefits of 3R implementation, such as:

- * Examples in the reduction of severity,
- * Evidence of senior executive ownership of 3R,
- * Existence of internal 3R structures,
- * Number, subject and impact of internal 3R awards,
- * Involvement in external 3R initiatives.

This list reflects the importance of using a set of quantitative and qualitative KPIs in assessing the impact of, and communicating about 3R efforts.



Leading by Example

Question: How do we stimulate putting into practice global animal welfare standards?

The European pharmaceutical industry supports international research projects and development of standards and policies.



Dedication to the highest standards of laboratory animal care in research, testing and education – Applying high standards of animal care to research activities means that we ensure improvements in animal welfare standards are not only being put into practice, but are also having a real and tangible impact. The Bennett J. Cohen Award is the highest international honour awarded by the ICLAS (International Council for Laboratory Animal Science). It is awarded in recognition of promoting and advancing the principles of replacement, reduction, and refinement, and in the use of laboratory animals in research, teaching and testing. In 2011, this award was granted to Anne Dominique Degrijsse from the EFPIA Research and Animal Welfare group, thus recognising a European for her contribution to improving animal welfare standards. Internal award schemes go beyond reward

and recognition, by ensuring our companies consistently strive to implement the highest animal welfare standards, and that their efforts are shared to inform others about new methods of implementing the 3Rs.

Going beyond what is required – Finding new methods of carrying out scientific research is the backbone of the internationally recognised principles: the 3Rs. Thus, we go beyond what is prescribed to reduce the number of animals used in research. To protect the unborn child, new medicines need to be studied to make sure they would not damage the embryo, if used by a pregnant woman. Current international guidelines require studies on pregnant animals, but some of our companies are employing an *in-vitro* embryonic stem-cell test. This can reduce the number of tests performed on pregnant animals, by helping exclude compounds that are not suited for further development, and thus avoiding unnecessary testing.

Facilitating dialogue – Discussing how global animal welfare standards can be put into practice with other key stakeholders and interested parties, is essential to harmonising the implementation of these rules. EFPIA is represented on the Assessment and Accreditation of Laboratory Animal Care International (AAALAC) Board of Trustees, alongside other stakeholders and interested

parties, including medical researchers, veterinarians and representatives from ethical committees. The Board of Trustees facilitates dialogue about the need for harmonization of animal welfare standards according to the European standards between these groups to enhance the quality of research, teaching, and testing by promoting humane, responsible animal care and use.

Supporting international standards and international research – Putting international animal welfare standards into practice means not only adhering to the *status quo*, but also supporting research that will help form international standards in the future. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is unique in bringing together the regulatory authorities and pharmaceutical industry of Europe, Japan and the USA to discuss scientific and technical aspects of drug registration. Since its inception in 1990, ICH has evolved, through its ICH Global Cooperation Group, to respond to the increasingly global nature of drug development, so that the benefits of international harmonisation for better global health can be realised worldwide. Application of 3Rs is an integral part of the regular revision of existing technical and scientific guidelines that are aligned globally. The ICH process is essential to ensure global up take of alternatives.



Leading by Example



The downside is that the processes to ensure worldwide regulatory acceptance can take a long time. The industry supports this review process, and provides necessary information and data, which enhance acceptance of novel approaches and tools.

Coalitions deliver results – Pharmaceutical companies are also actively supporting various European and international research consortia providing data, expertise and know-how. The International Transgenic Mouse Model Consortia involves programmes from the USA, Canada and Europe coming together to either add or alter the DNA of a mouse, and to study the function or pathology involved with that particular gene. Such activities have the potential to greatly reduce animal use in future model generation and analysis. In Europe, pharmaceutical companies are also involved in the DETECTIVE project, which is part of an integrated research strategy towards the replacement of animal testing set up by the European Commission, and supported by Cosmetics Europe – The Personal Care Association. Within this collaborative project, 15 scientific and commercial partners are addressing the development of biomarkers of long-term toxicity in human target cells. In 2011, one company shared its non-invasive diagnostics technology for use in the project. Much collaboration is also taking place as part of the Innovative Medicines Initiative (IMI) partnership. The main goal of IMI is to optimise research tools. However, collaboration in areas related to animal testing, will result in the replacement, reduction or refinement of certain animal studies.

Internal Ethics Committees – All companies have ethics committees on animal welfare or use external ethics committees' advice. In many cases, these committees develop global guidance and recommendations and oversee the animal research practices using the same set of standards, and coordinating global prospective 3R strategies. In many companies, the review of non-human primates' studies is centralized to adopt a common 3R approach. Biostatisticians are often included in ethics committees and a retrospective evaluation of performed protocols, ensures that there is no further need for animal testing as the records of previous tests can be used instead.





European Federation of Pharmaceutical Industries and Associations



Leading by Example

Question: What is being done to rapidly implement and enforce across Europe the revised European Directive 2010/63/EC on the protection of animals used for scientific purposes?

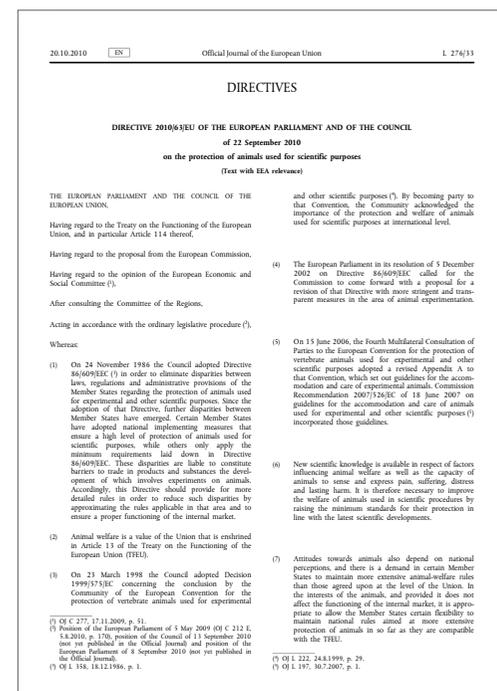
2011 has shown that we can support and are already stimulating the rapid implementation and enforcement of the revised Directive 2010/63/EC within the EU.

Contributing to the debate – EFPIA members are playing a leading role in guiding the implementation of the EU Directive on the protection of animals used for scientific purposes at an EU level, and also within Member States. We do this by contributing to responses to national consultations, participating in Expert Working Groups with the European Commission (e.g. statistical reporting) and being active members of Scientific Coalitions, such as the UK Bioscience Coalition. EFPIA is also part of a wider scientific community coalition, which provides input into EU level discussions on implementing guidance required by Directive 2010/63/EC (statistical reporting, genotyping, education and training). In 2011, this “transposition coalition” put forward important questions about the interpretation of the Directive to the European Commission, such as the interpretation of what



is a project or a procedure, and how delegation of powers from central to local level would work in practice. These questions also meant that pharmaceutical companies sought advice on how to achieve the best harmonization of transposition into national legislation in a way that balances research needs and welfare considerations. EFPIA also organizes webinars for the constituent members of the coalition, and participated in various laboratory animal science events to promote the Directive and explain its new provisions. In 2010 and 2011, EFPIA presented the new directive requirements at Eurotox, Charles River Associates short courses and national laboratory animal science events (including in some Central and Eastern European (CEE) countries).

In 2011, EFPIA also produced a position paper about how EU policy could better support the implementation of the Directive through training, communication, dissemination, sharing good practice and removing red tape, which does not translate into animal welfare benefits. Furthermore, EFPIA also made reference to how funding for upgrading public research animal houses, and specific budget lines in EU funding would also deliver direct and tangible outcomes. This is in addition to highlighting how the use of public-private partnerships could be considered to find additional financial and

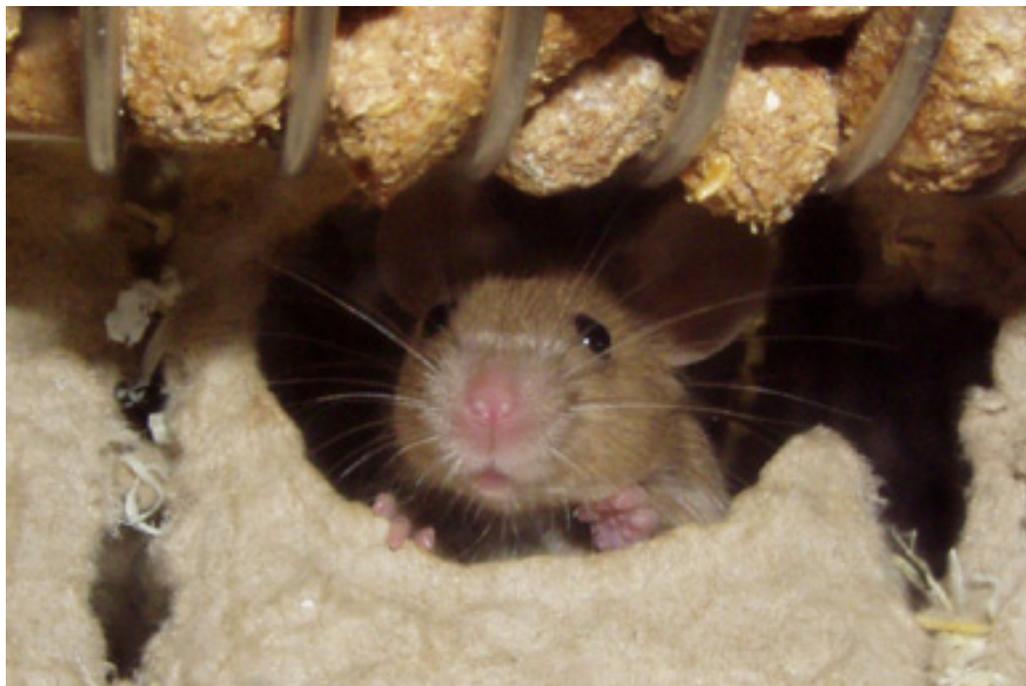




Leading by Example

Question: Are we independently assessed on how our animal welfare standards are applied?

We are independently assessed and we encourage improving existing external and independent assessments of internal animal welfare standards and facilities on a European and global level.



Certification – Almost 90% of our pharmaceutical companies’ facilities are subject to national and international certification, which goes beyond legal requirements, and is largely voluntary. Such certification is sought from external auditors, national authorities or the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). These certificates reflect our wish to maintain the highest standards in the treatment of animals used in research, teaching and testing across the industry. The objective is to reach 100% coverage.

Exchanging best practices for auditing – Several pharmaceutical companies have set up joint working groups on auditing to exchange best practice and join forces in external auditing efforts. Companies involved in Innovative Medicines Initiatives (IMI) projects have members on the ethical advisory groups, which review the animal care and use programs of the institutes performing *in vivo* studies.

Independent regulatory oversight – In Europe, regulatory bodies visit our facilities regularly and many of these visits are unannounced. In addition, veterinary inspections, internal and external auditing as well as national and company ethical

committees and certifications, all contribute to the industry checking its standards, not only to fulfil its legal requirements, but also to go beyond them, and actively improve animal welfare standards. Internal and external ethical committees serve as review boards that independently evaluate and approve our internal scientific protocols, before animal testing can even begin. Throughout 2011, company ethical committees have been active in providing guidance and support on how our animal welfare standards are applied. Furthermore, the committees ensure that people using, working and caring for the animals, are appropriately qualified. These committees include not only employees, but also external persons, such as animal welfare experts, NGO representatives, lawyers and laypersons.



Commitment to Open Communication

Question: How do we contribute to an open and constructive dialogue on animal welfare?

The pharmaceutical industry understands the sensitivities around the issue of animal research. For this reason, we actively seek to engage in dialogue. We contribute to a continuous, open and constructive dialogue on animal research and welfare, with the public, legislators, policy makers, and interested parties.



Collaborative projects at EU level – Working in partnership with other interested parties facilitates constructive discussion as to how animal welfare standards can be improved. EFPIA collaborates with five EU research organisations to facilitate the transposition of Directive 2010/63/EC on the protection of animals used in research. The constituent organisations of this coalition represent laboratory animal science experts (FELASA), academia and charities (European Science Foundation), veterinarians (ECLAM and ESLAV) and breeders (FELABA). The collaborative effort

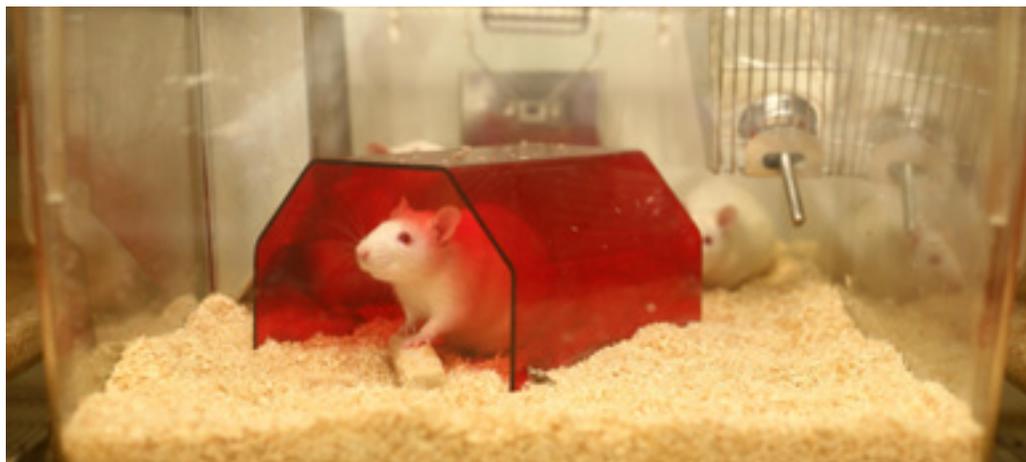
ensures that the legislation is implemented in day-to-day business in a way that balances biomedical research and animal welfare, and facilitates input in expert and legislative discussions. Our continuous participation in the European Partnership for Alternative Approaches to Animal Testing (EPAA) projects enables us to pool our knowledge, research and resources within a more general context. This helps in accelerating the development, validation and acceptance of alternative approaches for regulatory use.

Sharing best practice at national level too – We also go beyond the confines of the European institutions and share best practice, which promotes the use of the 3R methods worldwide. EFPIA members appreciate the importance of being involved in national and international dialogue, as this is where the implementation and benefits to animal welfare are really felt. EFPIA members are represented in national ethical committees, which are independent committees seeking multi-stakeholder engagement on issues concerning animal welfare, and gathering views from

a range of stakeholders and interested parties, including industry, NGOs and researchers. All of these activities seek to ensure regular exchanges on information relating to animals, aimed at increasing their welfare. Further dialogue and collaborative projects are in the pipeline with animal protection groups at national and European level.



Commitment to Open Communications

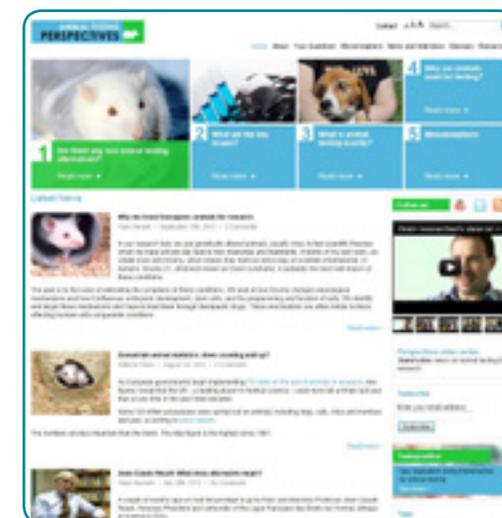


Show and tell – Showcasing our activities on animal welfare invites critical analysis from the general public, legislators, policy makers, and interested parties. We open the doors to our companies so that we can engage in such critical debates because they help us to understand better the many points of view involved when addressing animal welfare standards. During the revision of the EU Directive 2010/63/EC on the protection of animals used for scientific purposes, various companies invited representatives of the EU institutions and key stakeholders to visit animal facilities. In 2011, many of our sites opened their doors to students, investment

groups and politicians. Our scientists and animal technologists have been to schools to talk with pupils about the role of animals in pharmaceutical research. Since we understand that there are legitimate concerns, both ethical and scientific, with regards to the use of animals in research, our speakers listen carefully to objections and discuss opposing points of view.

Online presence – Ensuring our information is accessible to everyone is a prerequisite for informed dialogue. That is why our member companies ensure a strong online presence. This goes beyond information, and allows interested parties to engage actively in the debate on animal welfare. EFPIA hosts the website – [Animal Research For Life](#) - which openly explains what research on animals is, and for which purposes it is used. The website helps to inform the European public debate on animal welfare, by providing the legal background and key data. Throughout 2011, communication tools such as posters and publications about animal research

have been made available to members online, so that they can go out and engage in constructive dialogue with others. EFPIA members also use interactive tools. In 2010 EFPIA members launched a blog – [Animal Testing Perspectives](#). Throughout 2011, we have answered questions, and received comments on testing, and research on animals. In its first year, the Animal Testing Perspectives site has demonstrated that it is effective in engaging in an open, honest and balanced debate, and has contributed to helping stakeholders and the general public understand better the various views on the use of animals in scientific and medical research.





Commitment to Open Communications

Question: How is industry communicating the progress made with animal welfare activities, specifically the 3Rs?

European Pharmaceutical companies report progress made on a regular basis and the amount and quality of information in the public domain is increasing. Companies produce annual corporate social responsibility reports which detail the progress made, as well as dedicated websites, blogs and brochures.



Corporate Social Responsibility (CSR) Reports – The European pharmaceutical industry’s CSR reports for 2011 detail the progress made year on year. In 2011, as in other years, pharmaceutical companies ensure they monitor and comply with the spirit of the law and ethical standards in a number of key areas, including animal welfare. The 2011 batch of CSR reports will include the numbers of animals used, and provide indications on the species used as well as the type of research conducted. Building on this, we also assess the 3Rs and welfare methodologies that have been developed and applied. Putting pen to paper on an annual basis, and sharing this information externally, ensures that we are effectively communicating about our implementation and progress in the implementation of the 3Rs, and other animal welfare activities.

Sharing data – Actively contributing to the available scientific data on animal research is contributing to reducing the number of animals used in certain studies. In 2011, the European pharmaceutical industry has played a significant role in further developments made by third parties, who have been able to apply the data provided for their advanced research. Informing third parties of changes to current practices is also an important contribution. Such data sharing has led to a reduction in the numbers of non-human primates (NHPs) used in research. The industry has shared data to identify stages of the development process, offering opportunities for the reduction in use of NHPs. This information has been used to develop practical guidance and make recommendations to design studies using fewer animals. In addition, pharmaceutical companies provided data on general toxicology and information on a study design to support a project run by the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) and Laboratory Animal Science Association (LASA). The data gathered demonstrated variations in the number of animals used in toxicity and carcinogenicity studies. This variation in use made it possible to make recommendations so that small changes to current practice could further reduce the number of animals used in studying the adverse effects of chemicals in the future. Furthermore, the findings

of internal research dealing with developments made in the 3Rs, as well as collaborative projects, are published in a number of scientific peer reviewed publications, such as Laboratory Animals, Nature, Regulatory Toxicology and Pharmacology.

Showcasing our achievements – Presenting the European pharmaceutical industry’s achievements encourages more progress to be made by the entire scientific community. It also ensures that the community is aware of the good practices being applied. Throughout 2011, European pharmaceutical companies have presented their 3Rs and welfare achievements in scientific congresses and workshops where the information can reach a large number of professionals working in the field of biomedical research and animal studies. This includes national laboratory animal science organizations, such as Laboratory Animal Science Association (LASA, UK) or BCLAS (Belgian Council for Laboratory Animal Science) and European organizations, such as Federation of Laboratory Animal Science Associations (FELASA), CAAT-Europe, or national platforms for 3Rs, such as, UK National Centre for 3Rs (NC3Rs), Ecopa or Francopa and those European platforms for toxicology, such as Eurotox.

Beyond Compliance

Practices

Regulation

Training

Leading by Example

Sharing

Implementing

Enforcing

Assessing

Open Communications

Dialogue

Reporting

Useful links

Accreditation of Laboratory Animal Care International (AAALAC) - www.aaalac.org

Alternatives Approaches to Animal Testing (EPAA) - www.epaa.eu.com

European Centre for the Validation of Alternative Methods (ECVAM) – www.ecvam.jrc.it

Federation of Laboratory Animal Science Associations (FELASA) - www.felasa.eu

Innovative Medicines Initiative (IMI)- www.imi.europa.eu

Institute for Laboratory Animal Research (ILAR)- www.dels.nas.edu/ilar

Laboratory Animal Science Association (LASA) - www.lasa.co.uk

National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) - www.nc3rs.org.uk

3R Foundation - www.forschung3r.ch

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Photos have been sourced from a number of sources, including EFPIA and Understanding Animal Research. EFPIA would like to thank the members of the EFPIA working group on Research and Animal Welfare for the valuable contributions to this report.

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