# ANIMAL TESTING REVIEW PANEL

## REPORT FOR 2012

## INTRODUCTION

Shell seeks to implement the 3Rs philosophy of animal testing (replace, reduce, refine) wherever possible while meeting legal obligations and striving to protect human life and the environment. Any Shell-owned or -operated company must follow Shell's animal testing standards when any laboratory-based toxicology experiments are conducted on animals, even in those countries that have less stringent requirements.

Each year, an external Animal Testing Review Panel critically examines and comments on the implementation of Shell's animal testing requirements. The panel works with Shell to ensure best practice in laboratories and discusses Shell's external engagement to support the development and application of the 3Rs. The membership and terms of reference for the panel are provided at the end of this report.

This document details Shell's use of vertebrate animals in 2011 to assess the safety characteristics and environmental impact of Shell products and manufacturing processes. The document also reports on Shell's activities and external engagement related to animal testing in 2011. A new version of this report has been issued, as an error was noted whereby animal use numbers were incorrectly assigned between Shell, and Shell Joint Ventures.

## WHAT SHELL REPORTS

In line with industry practices, Shell reports on animal testing activities of Shell-owned and Shell-operated companies. Testing programmes that are supervised by industry consortia in which Shell participates are reported separately. Shell reports all experimental animal use on a 100%-basis (i.e., each animal is counted as Shell's even if the testing programme is undertaken by multiple companies). Testing data are collected from internal sources and from reports provided by external testing laboratories.

## SHELL'S USE OF ANIMALS

Animal use to assess the safety characteristics and environmental impact of Shell's products, manufacturing processes from 2007 to 2011 is reported in Table 1. On the whole, mandatory testing of fish to meet regulatory requirements constituted 93% of all animal use by Shell-owned and Shell-operated companies. Fewer rodents were used in 2011 compared to 2010 because industry consortia pursued less testing.

### TABLE 1: NUMBER OF LABORATORY ANIMALS USED IN YEARS 2007-2011

| Tests commissioned by | Type of animal used | Number of animals used | | | | |
|---|---|---|---|---|---|---|
| | | 2007 | 2008 | 2009 | 2010 | 2011 |
| Shell | Rodents | 420 | 592 | 64 | 2501 | 2497 |
| Shell | Rabbits | 9 | 6 | 21 | 9 | 6 |
| Shell | Fish | 50,052 | 54,986 | 43,093 | 38,524 | 33,753 |

| Tests commissioned by | Type of animal used | Number of animals used | | | | |
|---|---|---|---|---|---|---|
| | | 2007 | 2008 | 2009 | 2010 | 2011 |
| Shell | Birds | 0 | 0 | 0 | 0 | 90 |
| Industry consortia | Rodents | 3,151 | 2,009 | 3,194 | 4,411 | 748 |
| Industry consortia | Rabbits | 0 | 7 | 0 | 9 | 0 |
| Industry consortia | Fish | 0 | 0 | 0 | 271 | 0 |
| JVs | Rodents | 325 | 0 | 0 | 0 | 0 |
| JVs | Rabbits | 6 | 0 | 0 | 0 | 0 |
| JVs | Fish | 1,420 | 1,280 | 7,388 | 4,190 | 11,763 |
| **Total** | | **55,383** | **58,880** | **53,760** | **49,915** | **48,857** |

**Notes: Industry Consortia** are groups of companies (including Shell) that co-operate, usually within the framework of an industry trade association, to share available data and the costs of testing programmes on particular chemicals or groups of chemicals. **Joint ventures (JVs)** include companies where Shell is the operator and companies under Shell control.

The use in 2011 of rodent species and birds is detailed in Table 2. Regulatory test method guidelines that are used to assess the potential health effects of industrial chemicals typically require the use of rats, mice, rabbits or guinea pigs. The main use of rats was to conduct a two-generation reproductive toxicity study required by an Asian country. Mice were used to assess the modes by which certain substances exert toxic effects. Rabbits were used to assess skin and eye irritation end-points to meet regulatory requirements in those countries where alternative tests are not yet accepted. No guinea pigs were used. Regulatory requirements were imposed on Shell by an Asian country to test a substance on birds. Shell's arguments that the tests were unnecessary were not accepted by the regulatory authority.

Shell used 3,341 mammals and birds to assess product safety. Through application of the 3Rs, Shell avoided the use of approximately 180 mammals and 100 birds, primarily by lowering the number of animals in preliminary studies to determine the appropriate doses for chronic toxicity testing studies, by sharing groups of control animals and by applying read-across techniques.

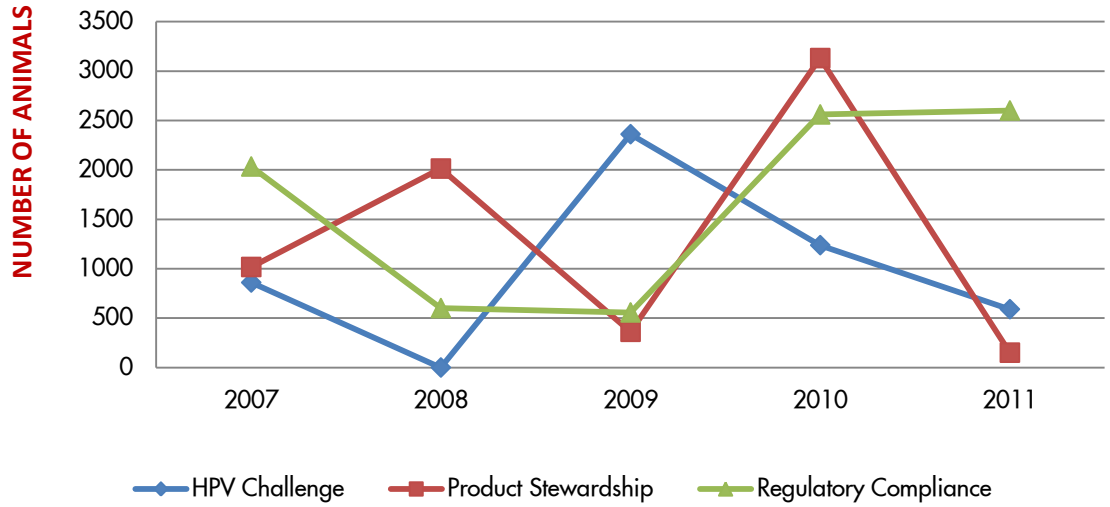
## TABLE 2: VERTEBRATE SPECIES OTHER THAN FISH USED IN 2011

| Species | Numbers |
|---|---|
| Rats | 3,095 |
| Mice | 150 |
| Guinea pigs | 0 |
| Rabbits | 6 |
| Birds | 90 |
| **Total** | **3,341** |

The number of vertebrate species (other than fish) and the purpose for which they were used is illustrated in Figure 1. In general, Shell expects that animal use is likely to increase in the near-term to meet requirements related to the European Union's REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) regulation. The industry's voluntary testing on high-

volume materials for the US Environmental Protection Agency's (EPA) High Production Volume (HPV) Challenge programme is largely complete.

FIGURE 1: NUMBER & PURPOSE OF TESTING IN NON-FISH SPECIES




**Notes:** The US EPA HPV Challenge programme is a voluntary initiative by the industry to provide a standard data set, mainly based on tests using animals, for substances produced in excess of one million pounds per annum (see www.epa.gov/HPV). **Product Stewardship:** Data is required to understand the health and environmental hazards of a product and are not collected for regulatory purposes. **Regulatory Compliance:** Testing required by law.

The use of fish from 2007-2011 is summarised in Table 3. Regulatory requirements in North America were the main driver for this. Shell's operational footprint expanded in regions where mandatory effluent testing on fish was required. Shell also had to conduct increased testing at certain locations to demonstrate compliance with effluent discharge permits after incidents of non-compliance.

TABLE 3: USE OF FISH, 2007-2011

| Purpose of test | 2007 | 2008 | 2009 | 2010 | 2011 |
|---|---|---|---|---|---|
| HPV Challenge | 0 | 0 | 0 | 72 | 0 |
| Product Stewardship | 0 | 160 | 0 | 0 | 17 |
| Regulatory Compliance | 51,472 | 56,106 | 50,481 | 42,913 | 45,499 |
| **Total** | **51,472** | **56,266** | **50,481** | **42,985** | **45,516** |

**Notes:** In addition to product safety testing, some countries (particularly US and Canada) require the use of fish to assess the toxicity of discharges to water and certain waste streams. Operating permits for industrial sites, such as oil refineries, chemical plants, supply and distribution terminals and retail sites require that the toxicity of effluent waters is tested on a range of aquatic organisms, including fish. Table 3 also includes fish used in response to US regulatory requirements to estimate environmental hazards during site clean-up operations.

**The panel agreed that Shell's uses of animals were clearly identified and was pleased with Shell's ongoing commitment to transparently report this information. The panel noted that the main challenge for Shell is to work with regulatory authorities to make scientifically-defensible reductions in animal use, especially fish, while protecting health and the environment.**

## REDUCTION, REPLACEMENT AND REFINEMENT OF FISH TESTING

Shell apprised the panel on two recent research projects to reduce the use of fish. An industry trade association in Canada in which Shell participates worked with a local university to assess the use of fish cell lines to support reclamation planning for oil sands process waters. This work was completed in 2010. The trade association is considering whether to support additional work.

A second R&D project was initiated in 2011 to assess the use of fish-embryos (zebra fish and fathead minnow) as an alternative for chronic aquatic toxicity tests. Fathead minnow frequently are specified as the test species in US National Pollutant Discharge Elimination System permits. The study participants include US EPA, the International Life Sciences Institute - Health and Environmental Sciences Institute (ILSI-HESI), Shell and three other companies. Preliminary results were presented at the 8th World Congress on Alternatives to Animal Testing.

**The panel was pleased with the progress and supportive of Shell's efforts to reduce fish use.**

## ADOPTING THE USE OF ALTERNATIVES IN SCREENING-LEVEL ASSESSMENTS OF PETROLEUM PRODUCTS

The panel discussed Shell's efforts to develop a toolbox of alternative assays to fill key gaps in understanding the safety characteristics of petroleum products. In 2011, Shell examined selected alternative assays and *in silico* models for skin and eye irritation and skin sensitisation to evaluate whether they are applicable to Shell substances. Shell also tested a method to facilitate ecotoxicity analysis of poorly soluble chemicals. Additional work to establish the reliability and predictability of these approaches will be conducted in 2012.

**The panel felt that Shell's efforts to evaluate the applicability of certain alternative assays, analysis methods and *in silico* models was a positive development and provided some guidance on prioritising Shell's efforts to develop its alternative testing toolbox.**

## IMPACT OF REACH ON SHELL'S ANIMAL USE

The first REACH registration deadline for high-hazard and high-volume substances was December 1, 2010. In 2011, the EU Chemicals Agency (ECHA) in several instances challenged the use of categories, read-across methods and the use of computer models to estimate toxicity. Shell and its consortium partners had used these methods to propose waivers for most animal testing in submitted REACH dossiers. Shell and its industry partners continue to engage with ECHA to address any concerns with REACH dossiers.

The most common data gaps identified in Shell's registration dossiers were for reprotoxicity testing, which historically has not been required by regulatory authorities. Current REACH guidelines indicate that a two-generation reproductive toxicity test, OECD 416, meets REACH information guidelines. This test requires the use of approximately 2,400 animals. The EU Commission has not yet determined whether the extended one-generation reproductive toxicity study (EOGRTS), OECD test guideline 443, will meet REACH information requirements. Although EOGRTS is not a direct

replacement for the two-generation study, the EOGRTS guideline can be applied to design tests that use fewer animals.

Shell remains committed to the goals of REACH in terms of demonstrating the safety of chemicals and reducing the use of animals in testing. The second REACH registration deadline is mid-2013. Shell will register substances that are manufactured or imported into the EU in amounts greater than 100 tonnes per year. Shell will continue to advocate for the application of EOGRTS and is working with industry partners to minimise any required REACH testing where scientifically justified.

**The panel encouraged Shell to work with its industry partners to pursue tiered testing strategies, to re-open discussions with ECHA as appropriate when lower tier testing delivers negative results and to use good science to advance the use of alternative test methods in the REACH context. The panel was disappointed that ECHA does not appear to be embracing the necessary change in mindset to reduce animal use and encourage *in vitro* and other alternative approaches.**

## GOVERNANCE AND CONTROL OF ANIMAL TESTING ACTIVITIES

Animal testing is governed by Shell's HSSE risk control framework, which specifies clear requirements for Shell-owned and –operated companies to apply the 3Rs to product safety evaluations. The panel discussed a recent application of the Shell Animal Testing requirements that stopped a proposed research project because Shell determined that it contravened Shell's requirements. The panel felt that Shell sent a good, strong message on its commitments to avoid unnecessary animal testing.

**The panel was very encouraged that Shell's animal testing standard is applied globally because it helps to avoid potential relocation of animal testing from countries that have strong animal welfare controls to countries where requirements are less stringent.**

## SHELL'S EXTERNAL ENGAGEMENT

Shell is active in a number of groups with the long-term aim of developing humane and alternative means to evaluating the health and environmental effects of oil and chemical products. Shell's current external engagement includes:

- Membership on the Advisory Board of CAAT (Johns Hopkins Centre for Alternatives to Animal Testing), providing oversight and direction to the research programmes that CAAT sponsors;
- Participation in CEFIC's (EU Chemical Industry Council's) Long-Range Research Initiative (LRI), which coordinates industry efforts in support of the 3Rs;
- Engagement with a joint European Commission-Industry initiative, the European Partnership on Alternatives to Animals (EPAA) through CEFIC;

- Participation in the Regulatory Steering Group and a separate task force that is focusing on alternatives to fish testing at the UK National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs);
- Membership in ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals), which supports task forces and convenes workshops to advance the science necessary to replace animal testing;
- Participation in an ILSI-HESI project and task force on animal alternative needs in environmental risk assessment; and
- Participation by Shell scientists in forums and conferences on animal testing in Europe and North America.

**The panel felt that Shell's external engagement was appropriate in scope given the importance of the animal testing issue.**

## CONCLUSION

The panel has:

- Critically reviewed Shell's use of animals;
- Commented on Shell's application of the 3Rs;
- Discussed the implications of REACH and the new EU animal welfare directive on Shell's use of animals; and
- Challenged Shell to further pursue alternatives for fish testing and the application of tiered testing strategies that maximise use of 3Rs approaches.

## ABOUT THE ANIMAL TESTING REVIEW PANEL

Energy and chemical companies face an increasing dilemma in responding to potentially conflicting societal demands to demonstrate the safety of their products, while at the same time reducing the use of animals in testing. The Animal Testing Review Panel was established in 2001 to provide credible, independent scrutiny of Shell's activities in this area.

## PANEL MODUS OPERANDI AND TERMS OF REFERENCE

Individual panel members are invited to serve for a period of three years, with the possibility of being invited to serve for a second period of three years. The panel recommends candidates who could be invited by Shell to join the panel, either as replacements for current members when their terms are completed, or to supplement the current panel membership.

The panel meets twice a year with key Shell personnel. It does not verify the accuracy of the data in the report. In addition to comments on Shell's reporting, the panel offers observations on the company's performance with respect to animal testing. In recognition of their time and expertise,

panel members are offered an honorarium; travel and accommodation expenses are also reimbursed.

## PANEL MEMBERSHIP 2012

**Kees van Leeuwen (Principal Scientist, KWR Watercycle Research Institute), Panel Chair**
Kees van Leeuwen is currently a principal scientist at KWR Watercycle Research Institute and is involved in issues related to risk assessment of chemicals, emerging compounds in the urban water cycle and sustainability of the urban water cycle. He was previously Principal Scientist at TNO (The Netherlands Organisation for Applied Research), Director of the Institute for Health and Consumer Protection in the European Commission and Professor in Toxicology at the University of Utrecht. He has written numerous scientific articles and edited two editions of a book on risk assessment of chemicals. He has a special interest in intelligent testing strategies.

**Grahame Bulfield (Senior Honorary Professorial Fellow and Emeritus Professor of Genetics, The University of Edinburgh)**
Grahame Bulfield spent the first 24 years of his career as a research geneticist. He was Chief Executive of the Roslin Institute from 1988-2002 where he transformed Roslin from being a traditional farm-animal research institute to one leading the application of modern biotechnology to animals. In 2002, he was appointed Vice-Principal of The University of Edinburgh and Head of the College of Science and Engineering. Since his retirement in 2008, he has been a Non-Executive Director and a Consultant in the life sciences sector. He has advised the UK government on animal testing and welfare issues.

**Charles Gentry (Independent Consultant on Laboratory Animal Science)**
Charles Gentry is a Company Director with international expertise in Laboratory Animal Science and specialist interest in compliance with UK and EU legislation and implementation of good practice. He is a former Director and Certificate Holder under the A(SP)A 1986 at the University of Cambridge. Charles is Chairman of the Certificate holders Forum UK, a member of the Fondazione Guido Bernadini Scientific Committee and Chairman of Lantra Advisory Group on Laboratory Animal Science.

**Alan Goldberg (Professor of Toxicology and Chairman of the Board, Center for Alternatives to Animal Testing, John Hopkins University)**
Alan Goldberg is a toxicologist focusing on in-vitro toxicology and the use of in-vitro data in risk assessment. As the Chairman of the Board for the Center for Alternatives to Animal Testing (CAAT), he is deeply committed to the 3Rs of alternatives (humane science). He was a commissioner and recently completed a study for the Pew Charitable Trust on the impact of Industrial Farm Animal Production on public health, the environment, animal welfare, and social justice. He has served on governmental and non-governmental boards dealing with laboratory animals.