INTRODUCTION

Shell seeks to implement the 3Rs philosophy of animal testing (replace, reduce, refine) wherever possible while meeting legal obligations and protecting human life and the environment. The Shell Standard on Animal Testing establishes requirements that any Shell-owned or -operated Company must follow when any laboratory-based toxicology experiments are conducted on animals.

Each year, an expert Panel reviews and comments on Shell’s implementation of the Standard on Animal Testing. The Panel works with Shell to ensure best practice in laboratories and discusses Shell’s external engagement to support the development and applications of the 3Rs. The membership and Terms of Reference of the Panel are provided at the end of this report.

This document details Shell’s use of animals in 2010 to assess the safety characteristics and environmental impact of Shell products and manufacturing processes. Shell’s activities and external engagement related to animal testing in 2010 also are reported. An annual report is published at http://www.shell.com/animaltesting.

WHAT SHELL REPORTS

In line with standard industry practices, Shell reports on activities of its companies, joint ventures under Shell control, and joint venture (JV) and associated companies not under Shell’s control but where Shell is the operator. Testing programs that are supervised by industry consortia in which Shell participates are reported separately. All animal testing is reported on a 100% basis (ie, each animal is counted as Shell’s use even if the testing programme was undertaken by an industry consortium). 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 and other operations in 2010 is reported in Table 1. Mandatory testing of fish to meet regulatory requirements constituted 86% of all animal use by Shell and its JVs.

TABLE 1: NUMBER OF LABORATORY ANIMALS USED IN YEARS 2006-2010

<table>
<thead>
<tr>
<th>Tests commissioned by</th>
<th>Animals used</th>
<th>Numbers of animals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2006</td>
</tr>
<tr>
<td>Shell Rodents</td>
<td>67</td>
<td>420</td>
</tr>
<tr>
<td>Shell Rabbits</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Shell Fish</td>
<td>23486</td>
<td>50052</td>
</tr>
<tr>
<td>Industry consortia Rodents</td>
<td>1796</td>
<td>3151</td>
</tr>
<tr>
<td>Industry consortia Rabbits</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
The use of mammalian species in 2010 is detailed in Table 2. Shell’s use of rodents increased in 2010 due to legal requirements for market entry in Asia. The regulatory authority required Shell to conduct two, two-generation reproductive toxicity studies (OECD 416) using rats. One of these studies was completed in 2010. Additional safety testing specifically for the Asia region is expected in 2011.

**TABLE 2: MAMMALIAN SPECIES USED IN 2010**

<table>
<thead>
<tr>
<th>Species</th>
<th>Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rats</td>
<td>5059</td>
</tr>
<tr>
<td>Mice</td>
<td>1781</td>
</tr>
<tr>
<td>Guinea Pigs</td>
<td>72</td>
</tr>
<tr>
<td>Rabbits</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>6930</td>
</tr>
</tbody>
</table>

Rabbits were used to assess eye and skin irritation. For eye irritation, negative results from the alternative in vitro tests were confirmed in rabbits to satisfy global safety regulations. Skin irritation tests were conducted on rabbits before the OECD issued its test guideline on in vitro alternative methods. Mice were used to assess skin sensitization and to comply with safety regulations in non-OECD countries.

Shell used 6930 mammals to assess product safety. Through application of the 3Rs, Shell avoided the use of approximately 870 mammals.

The purpose of the testing in mammalian species is illustrated in Figure 1. The figure shows the numbers of animals used in tests commissioned by Shell, by industry consortia, and by Shell-operated joint ventures. In addition to increased use of mammals to meet regulatory requirements, the number of mammals used for product stewardship purposes increased in 2010. These tests were pursued largely by US industry consortia in which Shell participates to research questions that may impact upon future regulation. Shell expects that animal use is likely to increase over time to meet increasing regulatory requirements, especially in the EU and North America.
The use of fish from 2006-2010 is summarised in Table 3. Regulatory requirements in North America were the main driver of the use of fish. The reduction in fish use compared to 2009 is mainly due to changes in operating permit requirements. Based on previous performance, some Shell sites were allowed to either decrease testing frequency or reduce the number of required analyses. Changes in permit requirements can have a material impact on fish use: a change in requirements implemented at one Canadian location resulted in 1000 fish saved.

### TABLE 3: USE OF FISH, 2006-2010

<table>
<thead>
<tr>
<th>Purpose of test</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV Challenge</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>72</td>
</tr>
<tr>
<td>Product Stewardship</td>
<td>57</td>
<td>0</td>
<td>160</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Regulatory Compliance</td>
<td>26629</td>
<td>51472</td>
<td>56106</td>
<td>50481</td>
<td>42913</td>
</tr>
<tr>
<td>Total number of fish</td>
<td>26686</td>
<td>51472</td>
<td>56266</td>
<td>50481</td>
<td>42985</td>
</tr>
</tbody>
</table>

Notes: Effluent and site waste biomonitoring - in some countries (particularly US and Canada), operating permits for certain 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.
REDUCTION, REPLACEMENT AND REFINEMENT OF FISH TESTING

Shell is consolidating its testing programmes on fewer, high quality facilities to enable more efficient use of fish. Shell expects that, if current trends continue, gains made in terms of more efficient use of animals most likely will be exceeded by increasing regulatory requirements to conduct testing. Shell continues to engage with the relevant regulatory authorities to address these issues.

The Panel encouraged Shell to broaden its efforts to develop alternative approaches to fish testing (see Shell’s 2009 report on animal testing). Already, Shell uses fish-embryo testing to fill gaps where legally allowed and scientifically valid. Shell also is working within industry and with other partners to advance the science that underpins the acceptance of alternative approaches. In 2010, Shell completed its participation in a multi-year UK DEFRA Link programme to develop new models for predicting fish toxicity. Shell also continued to support the assessment of fish cell-lines as an alternative to in vivo testing via the EU chemical manufacturers association’s (CEFIC) Long-range Research Initiative (LRI). The project’s work products currently are being disseminated. Shell started work with the US Environmental Protection Agency and other industry partners to explore the application of alternatives to fish testing in effluent monitoring programmes.

IMPACT OF REACH ON SHELL’S ANIMAL USE

The European Union’s REACH (Registration Evaluation, Authorisation and restriction of Chemicals) law required all companies that manufacture or import chemical substances in amounts greater than 1000 tonnes per year to perform chemical safety assessments and register their products with the EU Chemicals Agency (ECHA) by December 2010. Shell worked largely through industry consortia to achieve the registration deadline. The extensive use of read-across, trend analysis, data sharing, toxicity-prediction models and exposure-based waiving allowed Shell and its consortium partners to propose waivers for most animal testing in submitted REACH dossiers. The largest data gaps identified in Shell’s registration dossiers are for reprotoxicity testing, which historically has not been required by regulatory authorities. ECHA will review all animal testing proposals received with the 2010 registration dossiers by 2012. The Competent Authorities of the EU Member States are beginning to evaluate substances dossiers. ECHA and the Competent Authorities may challenge testing proposals and arguments made by industry to waive testing requirements. Addressing these challenges will be part of a learning process for all stakeholders to improve confidence in the use of non-animal methods to assess product safety.
The Panel noted that Shell’s approach to REACH has contributed to reducing uncertainty about health and environmental effects for whole classes of chemicals. The Panel was pleased to see that Shell’s application of 3Rs principles has delivered promising results so far in terms of animal use avoided.

GOVERNANCE AND CONTROL OF ANIMAL TESTING ACTIVITIES

Shell has had an animal testing standard since 2001. In 2009, these requirements were incorporated into Shell’s Health, Safety, Security and Environment (HSSE) Risk Control Framework. All Shell-owned and –operated companies must comply with these requirements. In 2010, Shell added requirements within this management system to ensure that each Shell business must report animal testing. The inclusion of this requirement is an additional control to provide assurance that Shell collects data from all relevant testing programmes. A gap assessment was completed by each Shell business against the Control Framework requirements. No material gaps in performance were identified with respect to animal testing.

Shell’s internal guidance for subject matter experts on animal testing was updated to conform to the HSSE Control Framework requirements and to take into account the new EU directive on animal welfare.

The Panel reviews each version of Shell’s internal guidance on animal testing. The Panel noted that the most recent draft is a considerable improvement in terms of clarity of responsibility and accountability for testing programmes.

SHELL’S EXTERNAL ENGAGEMENT

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

- Membership in 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 Long-Range Research Initiative (LRI), which coordinates industry efforts in support of the 3Rs (Replacement, Refinement and Reduction). Shell led efforts to organise a 2010 CEFIC LRI workshop and publication on comparative testing for the identification of skin-sensitizing potentials of nonionic sugar lipid surfactants;
- 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 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 of ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals), which supports taskforces and convenes workshops on issues related to new toxicology to
advance the science necessary to replace animal testing;

- Participation in an ILSI-HESI project 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 supported Shell’s external engagement strategy, which the Panel considered well targeted and proportionate to Shell’s overall use of animals.**

**CONCLUSION**

The Panel has:

- Critically reviewed Shell’s use of animals;
- Discussed Shell’s efforts to reduce fish use;
- Reviewed implications of the EU chemicals testing law, REACH; and
- Reviewed Shell’s internal processes to control animal testing risks.

**The Panel is satisfied with Shell’s overall performance and has identified areas where further improvement in application of the 3Rs may be realised, especially to reduce fish use.**

**ABOUT THE 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. Regulatory drivers are likely to result in an increasing requirement for the use of animals in testing in the next few years. Against a background of increased external debate, Shell reviewed its established laboratory animal testing policy and practices during 2001. Shell concluded there was a need to formalise its practices on animal testing, to put in place a more structured and demonstrable management process, and more effectively to communicate the Shell position both internally and externally. The Review Panel was established to provide externally credible, independent scrutiny of Shell’s activities in this area.

**MODUS OPERANDI AND TERMS OF REFERENCE OF THE PANEL**

Individual Panel members are invited to serve on the Panel 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 term is completed, or to supplement the current Panel membership.
The Panel meets twice per year with key Shell personnel. The Panel does not verify the accuracy of the data underlying 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 receive an honorarium. The Panel also is reimbursed for the expense of travel and accommodation.

**PANEL MEMBERSHIP 2011**

University of Newcastle Professor Paul Flecknell concluded his service on the Shell Panel in 2010. The Panel was joined by Charles Gentry in January 2011.

**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 an international expertise in Laboratory Animal Science and a 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.