

# Humane Regulatory Testing: The United Kingdom Experience

**Jon D. Richmond**

*Animals (Scientific Procedures) Inspectorate, Home Office, P.O. Box 6779, Dundee DD1 9WN, UK*  
E-mail: [jon.richmond@homeoffice.gsi.gov.uk](mailto:jon.richmond@homeoffice.gsi.gov.uk)

**Summary** — Regulatory testing requirements are considered by some to be rigid and inflexible. In fact, there is often considerable discretion in the animal test requirements and the endpoints that can be applied. This paper reviews the steps taken by government departments, agencies and professional associations in the UK to ensure that the Three Rs are reflected when animal testing is undertaken to satisfy regulatory requirements. The Home Office and other relevant government departments and agencies have agreed upon and implemented concordats on animal welfare and data sharing, and a joint guidance on humane regulatory testing has been published with the assistance of appropriate professional bodies. This paper describes these initiatives and reviews their impact to date on policy and practice at home and abroad.

**Key words:** *animal testing, data sharing, regulation, regulatory testing.*

## Introduction

In Great Britain, the Home Office (HO) is the government department charged with regulating the use of animals for experimental and other scientific purposes (1).

It is one of the few government departments that neither funds nor commissions animal testing, does not determine test requirements, and does not require animal test data to discharge its statutory functions. Thus, conflicts of interest that would arise from a department regulating its own activities are avoided. However, there is a price to be paid for this.

Influence and control over policy and practice with respect to regulatory testing, and other aspects of the use of animals for experimental and other scientific purposes, are spread across several government departments with different departments leading for different classes of substances. This separation of responsibilities requires that care be taken to ensure that all relevant stakeholder views are heard and balanced as policy and practice evolve. The departments and agencies involved cannot operate as “free agents” — a coordinated approach is required to ensure that coherent, consistent and defensible policies and practices are devised and implemented. In short, there is a need for “joined-up government”.

## Joined-up Government

Good practice has always required that government departments and agencies take all relevant views into account when planning and implementing policy. At times, however, the interests, needs and activities of departments and agencies have been

identified on an *ad hoc* basis, rather than on a systematic basis, and sometimes commitments have been entered into by one department that unwittingly confound the best laid plans of others.

The HO is the department that “owns” government policy with respect to the regulation of the use of animals for experimental and other scientific purposes, and it operates the regulatory system. The HO has worked particularly closely with other government departments, agencies and other stakeholders over the last five years to raise awareness of the principles underlying the regulatory system relating to animal use for experimental and other scientific purposes, and to ensure that our priorities are properly reflected in the policies and practices of others.

Animal research is regulated by the *Animals (Scientific Procedures) Act 1986*. Not only must each proposal for animal use be subjected to a statutory cost–benefit assessment, but all animal use must be justified, and all reasonable and relevant replacement, reduction and refinement strategies must be taken into account. These principles must also be visible in the policies and practices of other government departments that impact on animal use.

To that end, formal networks have been established to ensure that all relevant UK government departments and agencies acknowledge that it is essential that the Three Rs are reflected in their policies and practices.

## A Partnership Approach

A partnership approach has proved to be the best means to carry this forward. The common goals and

objectives identified are often of such a nature that no single party can achieve success on its own. The partnership approach has allowed government departments to pool resources (including skills and knowledge, contacts and leverage over other stakeholders) and to share ownership of, and the benefits arising from, the outputs that are now being achieved.

### **In Addition to Dialogue . . .**

Establishing a constructive dialogue was the starting point: it takes time to establish confidence and trust and to identify and agree priorities. Early discussions quickly identified the benefits of sharing common values, objectives and goals. We identified some Three Rs-oriented approaches already adopted by some departments and agencies that could be adapted and incorporated into the practices of others. Equally important, we are now guaranteed the opportunity to play a formal part in future policy developments within other departments very early in the planning process.

In addition to working with various third parties to produce a number of technical guides, we have, as a group, produced and adopted two formal concordats on animal welfare and data sharing, and, with the relevant professional bodies, produced a joint guidance on humane regulatory testing (2).

### **Animal Welfare: Assessment of Safety**

As a partnership formed by government departments and agencies, our first formal venture was a formal concordat on animal welfare. Whilst acknowledging that some animal use continues to be necessary to protect human health and the

environment, it commits the signatories to ensure regulatory requirements are devised, reviewed, interpreted and implemented to minimise any necessary animal suffering, whilst making proper provision to protect human health and the environment. The five key obligations are reproduced in Table 1.

### **Actions and Outputs**

Our dialogue continues. Progress has been made against each of these headings both by sharing existing best practices and in developing new policies and practices. Government strategy and involvement in developing alternatives is now better focused. The Three Rs are central to the UK Government's involvement in both the International Conference on Harmonisation (ICH) and the emerging chemicals testing strategies.

Those supplying excessive or inappropriate animal test data to UK regulatory authorities are being formally warned that this is the case and are advised to behave more responsibly in the future.

The UK has tried to be at the forefront of accepting the most refined data required properly to assess acute oral toxicity in mammals and skin sensitisation potential. The Health and Safety Executive (HSE), for example, has recently informed stakeholders that the murine local lymph node assay is now the preferred method of establishing the skin sensitisation potential of chemicals.

### **Data Sharing Concordat**

Data sharing is seen as a significant means of minimising the use of animals. Responsible data shar-

**Table 1: Animal welfare concordat: obligations**

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Encourage the development of alternative methods through cooperation with, or participation in, national and international initiatives aimed at refining, reducing or replacing the use of animals

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Seek to influence intentional harmonisation initiatives to ensure that policies and practices take full account of the ethical duty to protect the welfare and minimise the numbers of animals used in safety assessments

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Alert applicants/clients to instances where data submitted in support of registration or safety evaluation are considered excessive in terms of animal suffering or numbers, or where internationally accepted alternatives replacing, reducing or refining animal use have not been employed

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Accept for assessment internationally recognised, non-animal alternative tests conducted to appropriate standards

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Not to require repetition of data produced by the applicant for other safety evaluation agencies where such data accord with internationally accepted guidelines and have been generated in compliance with appropriate standards

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ing not only brings animal welfare benefits, but it also sets the scene for more timely regulatory decisions.

An initial review of current data sharing requirements and practices was not encouraging. Although many European Directives contain “data sharing provisions”, data sharing at the European level is often only encouraged rather than required, and practices differ for different classes of material and from country to country.

The available information concerning current levels of data sharing (3) suggests that the most effective data sharing takes place under regimens that encourage, rather than require data sharing. Specifically, within the European Union (EU) between 1994 and 1996, the UK, where the relevant data sharing provisions operate on a voluntary basis, accounted for approximately one-third of all intents to notify new chemicals (323 of 974), over 80% of data sharing enquiries (336 of 382) and over 80% of known instances of data sharing (22 of 27).

In August 2000, a number of government departments and agencies (the HO; the Department of Health; the Department for Trade and Industry; the Department of the Environment, Food and Rural Affairs; the HSE; the Medical Devices Agency; the Pesticides Safety Directorate; the Veterinary Medicines Directorate; and the Food Standards Agency) agreed upon a formal concordat to further encourage data sharing.

The essential obligations of the concordat are reproduced in Table 2.

## Actions and Outputs

The actions taken by the parties to implement the data sharing concordat have recently been reviewed with a view to identifying and spreading best practices.

More information is now being provided on time-expired data protection. There is an increasing preparedness to accept public domain information. The responsible extrapolation of existing knowledge in lieu of additional testing is being encouraged. Increasing consideration is being given to accepting similar data generated for other purposes.

In addition, at the international level, the UK is advancing data sharing as a key part of ICH and as a practical means of minimising the use of animals for reproductive studies.

## Barriers to Data Sharing

The barriers and obstacles to data sharing have been enumerated in order that strategies to further encourage data sharing can be devised.

1. The various, and variable, data sharing requirements, between regions and with respect to different classes of materials, would benefit from harmonisation once best practice is defined.
2. The confusion about possible sources of animal test data needs to be clarified.

**Table 2: Essential obligations of the concordat**

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Minimise data requirements for animal tests as far as possible

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Review . . . relevant powers and procedures, and identify any procedural or legal barriers to data sharing, looking for opportunities to extend data sharing

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Encourage data sharing between clients whenever appropriate, but particularly at the intent to notify stage

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Accept adequately constructed animal test data generated under different assessment requirements or regimens (i.e. support mutual acceptance in the UK international settings)

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Press for agreement on behalf of the UK Government for the fullest provisions and procedures which enable data sharing when negotiating, updating or transposing relevant EU Directives and when taking part in other international harmonisation processes

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Discuss data sharing with relevant trade associations and other parties, in order to help resolve practical and legal obstacles and to set a climate of expectation that data sharing should take place, whilst recognising the need not to place unreasonable additional burdens upon business

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Actively encourage companies to search for relevant test data (directing potential notifiers to sources which reduce the chances of substances and products being tested under more than one national or international requirement), to collaborate over animal testing, and to place data in the public domain

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3. Communication between national competent authorities needs to be improved.
4. More effective and equitable means must be found to properly reward those who are prepared to share proprietary data.
5. Legitimate means must be found to overcome possible problems relating to third-party liability should problems arise due to the quality of information shared.

### Guidance on the Conduct of Regulatory Toxicology and Safety Evaluation Studies

A partnership approach has the advantage of bringing together groups with different responsibilities and expertise and ensuring "buy-in" to the resultant outputs.

In February 2001, the HO, the Department of Health, the British Toxicological Society and the British Society of Toxicological Pathologists, jointly produced *Guidance on the Conduct of Regulatory Toxicology and Safety Evaluation Studies* (2). It reinforces the UK Government's commitment, and that of the scientific community, to the highest scientific and animal welfare standards and the effective implementation of the Three Rs. It offers practical advice to ensure that the Three Rs are properly considered and implemented in regulatory safety testing without compromising scientific validity or the resulting risk assessment.

The Guidance is premised on four essential requirements.

1. There must be a reasoned, sustainable justification for the new test data. There must be no appropriate, validated replacement alternative test method. All relevant reduction and refinement measures must be identified and implemented. The protocols should be those most likely to produce the data required to meet the specified objective.
2. The Guidance reviews the competencies required to undertake regulatory testing involving animals. It explores the scope and limitations of available test methods and the nature of test requirements. It stresses the importance of early consultation with appropriate parties to clearly define what testing must be conducted, the value of appropriate pilot studies and a tiered and hierarchical approach to testing, and the benefits of undertaking studies to recognised quality assurance standards. Data sharing is encouraged.
3. It offers thematic advice on reviewing existing data, *in vitro* screening and a hierarchical approach to testing, selection of test methods/species/numbers, sampling methods and humane endpoints.
4. Work has recently begun on the second edition. This will take account of technical progress since the first edition was prepared, will broaden the range of stakeholders involved, and will hopefully be available in time to influence and shape animal testing when the proposed chemical testing strategies take effect.

### References

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