



THE WAY FORWARD

STRATEGY FOR A FUTURE CHEMICALS POLICY

A NON-ANIMAL ALTERNATIVES POSITION PAPER



The British Union for the
Abolition of Vivisection



European Coalition to
End Animal Experiments

Foreword

INTRODUCING THE EUROPEAN COALITION AND THE BUAV

The European Coalition to End Animal Experiments, (hereafter 'the European Coalition'), is Europe's leading alliance of animal protection organisations who have come together to campaign for effective and long-lasting change for laboratory animals. Formed in 1990 by animal groups across Europe, the Coalition now represents members across member states of the European Union plus a range of international observer groups drawing together organisations with a range of legislative, scientific and political expertise. Its membership base is currently expanding to include those member groups in EU accession countries. Current Observer/Member groups of the European Coalition are as follows:

Members: ADDA (Spain); Animal Rights Sweden; Animalia (Finland); BUAV (UK); BTVVG (Germany); Danish Society for the Protection of Laboratory Animals; Deutscher Tierschutzbund (Germany); GAIA (Belgium); LAV (Italy); One Voice (France); SSPA (Switzerland) and Vier Pfoten (Austria). The Chair group of the European Coalition is the British Union for the Abolition of Vivisection (UK).

Observers: Animal Alliance of Canada; Doris Day Animal League (US); Dierenbescherming (Holland); Dr Hadwen Trust for Humane Research (UK); EFAP (Greece); IAVS (Ireland); International Fund for Animal Welfare EU; JAVA (Japan) and Eurogroup for Animal Welfare.

Established in 1898, the British Union for the Abolition of Vivisection (BUAV) is Europe's leading single-issue organisation campaigning to end animal experiments. The BUAV has an established record stretching over 100 years; we combine legal and scientific expertise, research skills, media liaison, public campaigning, undercover investigations and political lobbying in order to work effectively for an end to animal experiments and their replacement with modern and humane alternatives. The BUAV chairs the European Coalition to End Animal Experiments.

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The European Commission's proposals for a future Chemicals Policy envisage the testing of thousands of 'existing chemicals' (those in use before 1981) and will influence how new chemicals are tested and regulated in the future. The Strategy relies heavily on toxicity tests on laboratory animals. Not only are these tests cruel, but their scientific validity is in doubt. Their use is based on established practice rather than proven reliability or predictive value; in fact most have never been validated to modern standards¹. Furthermore, the commitment of time, personnel and resources needed to test chemicals using standard animal methods would delay results by decades, if not centuries.

The replacement of animal tests with a modern, non-animal alternative testing strategy would lead to a number of improvements. It would tell us more about the toxic properties of chemicals, be cheaper to perform and therefore more cost-effective to run, and produce results more quickly than traditional animal methods. This would both encourage innovation and benefit all stakeholders concerned with human safety, environmental protection, animal welfare and consumer confidence.

The European Commission, Council, and many Members of the European Parliament have made it clear that the EU Chemicals Policy should avoid animal testing wherever possible. Animal tests *can* be avoided, and be eliminated completely provided there is enough political will to create the necessary changes.

Data from *in vitro* tests could permit the hazard identification of existing chemicals and their prioritisation for control. Testing should begin by initially screening substances using existing validated and approved *in vitro* methods² as part of a carefully designed stepwise programme³. At the same time, whilst that screening is taking place, a targeted Europe-wide effort should be undertaken to perfect the non-animal methods that are close to validation. In this way animal tests can be avoided entirely, and the EU will lead the world in development of a scientifically rigorous and humane strategy for toxicity testing.

Human health,
environmental
and wildlife
protection

There is undoubtedly a need to identify and regulate substances that may pose a threat to the environment, or hazards to human and wildlife health.

Rather than being a solution, the present system of outdated animal-based test methods is actually part of the problem. Because results obtained from animal tests can vary between species (and even between laboratories), the call for further testing can be used to delay regulation of dangerous substances. A full programme of non-animal tests will stop species variability in results being used to prevent classification and regulation.

1. For each substance, up to twelve test areas are investigated, as required by legislation. In the majority of cases, the animal tests are accepted for use but not validated to modern standards; they have not undergone the validation process that is required for new non-animal tests.
2. Such as mutagenicity, skin corrosion, skin penetration and photo-irritation tests *in vitro*, all of which are already validated and authorised by the EU.
3. For an explanation of the use of stepwise screening processes, and non animal tests, see 'Action to End Animal Toxicity Testing', BUAV 2001.

THE BUAV AND THE EUROPEAN COALITION SUPPORT THE FOLLOWING PRINCIPLES:

- **The 'right to know'** what chemicals are present in products, and what the potential risks are of these chemicals⁴.
- **The "precautionary principle"**, action to reduce exposure without waiting for 'absolute proof' of harm. The European Coalition therefore supports a **phase-out of persistent, bio-accumulative or hazardous chemicals**⁴ in order to reduce or eliminate exposures to such chemicals. Many chemicals could be phased out immediately, based on data available today demonstrating a strong likelihood to bio-accumulate, persist in the environment, or be carcinogenic or mutagenic.
- **The principle of substitution**⁴ (whereby industry is compelled always to use the safest substance where alternatives to dangerous substances exist) applied without further animal testing.
- **A commitment to stop all releases to the environment of hazardous substances by 2020**⁴.

Closing the
'knowledge gap'

The European Commission has made the assumption that there is a lack of basic toxicity data for existing chemicals, but this perceived 'knowledge gap' for existing chemicals does not mean that data does not exist *at all*. A significant amount of data, both animal and human, already exists for many of these chemicals in publicly accessible databases, from epidemiological studies, forensic institutes, hospital and workplace records and poisons information centres, and in the privately held databases of individual chemical companies.

Mandatory data sharing between companies and countries is needed, together with an obligatory 'amnesty period' for chemical companies to share previously withheld information on chemicals. (Such an 'amnesty' in the USA in 1999 produced over 10,000 data submissions that would have otherwise been assumed non-existent.)

Concern over property rights to data must not be allowed to cause increased or duplicate testing. Safety testing data can be made public in ways that do not compromise commercial confidentiality.

4. These principles are in accordance with the Copenhagen Chemicals Charter, October 2000, supported by the leading consumer and environmental NGOs.

Animal tests are cruel

The cost in animals' lives cannot and should not be ignored. Producing exact figures for numbers of animals likely to be used as part of an animal-based strategy for the EU would depend on a number of factors including the results of previous tests. There can be no doubt, however, that traditional animal-based methods for testing chemicals involve a massive amount of animal suffering. The following is an illustrative example of the estimated number of animals likely to be used to test a single High Production Volume (HPV) chemical for which no data currently exists.

Animal tests are impractical

The backlog of chemicals which the Commission suggests may need some additional testing is estimated at 30,000 to 100,000 substances. The Commission has set a timeframe for the testing of existing chemicals, envisaging that all the data gaps for these chemicals will be filled by the end of 2012 and that some chemicals will be fully tested by 2005 (including long-term rodent tests for carcinogenicity which take five years to complete).

This timetable is unrealistic if it depends on animal testing. A large programme of animal tests does not make scientific or economic sense, especially since some long-term methods are resource-intensive.

In contrast, non-animal tests are often faster than their animal test counterparts. For example, the animal test for carcinogenicity takes five years. The non-animal SHE test could be validated in two years, and takes a few days per chemical to conduct.

ANIMAL TESTING FOR CHEMICALS: AN IMPRACTICAL SOLUTION

- 1. A dedicated programme of chemical testing on animals, solely for long-term toxicity and carcinogenicity, conducted jointly by the US National Toxicology Program and the US National Cancer Institute, has taken 36 years to achieve results for only 500 chemicals⁵. At this rate (14 chemicals per year) an EU animal test programme for 30,000 existing chemicals would take 2,143 years to complete.**
- 2. The OECD⁶ has been overseeing a chemical testing programme called the Screening Information Data Set (SIDS) programme. Under this scheme, limited screening information includes acute and repeat dose tests, and reproductive and genetic toxicity tests, conducted mainly on animals. In the first ten years of international co-operation under the SIDS programme, only 60 chemicals have been evaluated⁷. At this rate (6 chemicals per year), an EU animal test programme for 30,000 existing chemicals would take 5,000 years to complete.**
- 3. Research toxicologists from the USA and the Netherlands have written: "At the present mode and rate of study of these chemicals, it is doubtful that our society will ever have a thorough toxicologic evaluation on the majority of chemicals that are now used or may be used in the future."⁸**

Animal tests are unreliable

There is already a considerable body of scientific evidence documenting the failure of animal-based toxicity studies to accurately predict human reactions to chemicals. Significant species differences in anatomy, physiology, biochemistry and metabolism make extrapolation of results from animal tests to humans, at best, highly questionable. (See the BUAV's booklet Action to End Animal Toxicity Testing.)

Extrapolating from one species to another, or from one strain to another of the same animal, is fraught with so many problems that one is drawn to the conclusion of Dr Erik Millstone who, reviewing the methods and practices of animal experimentation, concluded that *"the main conclusions to be drawn from this discussion [of a range of techniques to assess the predictability of animal experiments for the assessment of danger to humans of various chemicals] are that the use of animals in toxicological studies does not provide a reliable basis for extrapolation to human health."*⁹

In the same vein Dr Michael Festing of the MRC Toxicology Unit at the University of Leicester, in a review of safety testing of chemicals using a single outbred strain of genetically undefined, heterogeneous animals (in the main rats and mice) says that *"the poor quality of present experimental designs is leading to inaccuracies that make it extremely difficult to validate alternative in vitro and short-term tests."*¹⁰

Animal tests frequently fail to mimic the most common pattern of human exposure to chemicals ie. little and often, and multiple exposures. Animal tests address only one chemical at a time, and often involve injecting or force-feeding high doses in order to shorten test times and to achieve statistical significance. Even then, the animal data are limited by species extrapolation problems, requiring 'guestimated' uncertainty factors. *In vitro* tests, by focusing on toxic mechanisms in a sensitive, simple system, do not suffer from these problems and, moreover, enable chemical mixtures to be tested.

5. International Life Sciences Institute (1998). Assessing the toxicity of exposure to mixtures of disinfection by-products – research recommendation. ILSI: USA.
6. The OECD is the Organisation for Economic Co-operation and Development whose Test Guideline programme has formed the basis of EU test methods for many years.
7. Goldberg, A (2000). Developments in Animal & Veterinary Sciences 31B: 1639.
8. Yang, RSH et al (1998). Environmental Health Perspectives 106: 1385-1393.
9. E Millstone (1989) in: Animal experimentation: the consensus changes, G Langley (Ed.) Macmillan Ltd, London pages 72-87
10. M F W Festing (1997), Nature, 388, 321-322

ANIMALS USED PER HPV CHEMICAL

Eye irritancy:	3 rabbits minimum
Skin irritancy:	3 rabbits minimum
Skin corrosivity:	0 if <i>in vitro</i> test used
Skin allergy:	30 guinea pigs minimum or 20 mice minimum
Acute oral toxicity:	15 – 25 rats or
Acute skin or inhalation toxicity:	30 rodents
Acute toxicity and prolonged toxicity (14 days)	80 fish
Repeat dose toxicity:	40 rats (28 day), and/or 80 rats and/or 32 dogs (90 day)
Mutagenicity:	40 rodents minimum
Carcinogenicity:	400 rats or mice minimum
Chronic toxicity:	160 rodents + 32 dogs
Teratogenicity:	80 rats + 48 non-rodents
Bioaccumulation	320 fish
Early life stage fish toxicity	420 fish
Fertility, reproductive/developmental toxicity and Level 2 peri- & postnatal reproduction toxicity:	240 rodents minimum
Toxicokinetics:	60 rats or mice minimum, and sometimes dogs
Estimated animals per chemical:	2123

In a report by the Institute for Environment and Health, for the UK's Department of the Environment, Transport and the Regions¹¹, calculations suggest that, as a minimum, 12.8 million animals (8.4 million mammals and 4.4 million fish) would be required to test 30,000 substances. This would rise to 50.2 million animals (45.8 million mammals and 4.4 million fish) if the offspring produced in reproductive studies and animals used in some higher tier tests are taken into account. In addition, inclusion of novel tests for mammalian neurotoxicity and endocrine disruption would further increase the number of animals used.

Each animal test causes pain and distress, often prolonged. Studies that condemn animals to years of slow poisoning, painful cancers, or repeated force-feeding with poisonous substances are outdated and inhumane. It is time to replace animal based toxicity tests.

11. IEH (2001) Testing Requirements for Proposals under the EC White Paper 'Strategy for a Future Chemicals Policy' (Web Report W6), Leicester, UK, Institute for Environment and Health (at <http://www.le.ac.uk/ieh/webpub.html> posted July 2001.

Alternative non-animal tests

The European Coalition welcomes the inclusion of animal welfare as one of the political objectives of the European Commission's proposed strategy for a future chemicals policy. However, there is a real danger that without a strictly enforced timetable relating to the introduction of alternative non-animal tests, the strategy would bring about vastly increased levels of animal testing and fail in its objective of encouraging the development of alternative tests.

There are already a number of validated non-animal methods that are in use and have replaced many animal tests. These include *in vitro* tests for skin corrosion, for light-sensitive skin irritation, for skin absorption and for mutagenicity.

There are also several non-animal tests that are already in use at member-state level or by industry. Many of these could be validated in 1 – 3 years time, allowing them to be ready in time for implementation of the Chemicals Strategy.

The tests awaiting validation include: an *in vitro* method to identify moderate eye irritants; a non-animal test for skin allergy; cell culture and target tissue tests for acute and repeat dose testing; the SHE cell transformation assay for carcinogenicity; computer simulation and *in vitro* studies for toxicokinetics; a test for reproductive toxicity; and *in vitro* endocrine disruptor tests.

The validation process – animal tests / non animal tests

Most of the animal tests still used today have never been scientifically validated to prove their accuracy, relevance and repeatability. By contrast, before acceptance, non-animal alternatives are subjected to extremely detailed validation studies which even then may lead to years of discussion by bodies such as the OECD before full implementation.

These barriers have resulted in continuing use of the flawed animal test regime, and the delay of new tests which are more useful in determining the toxic properties of substances.

The European Commission, together with ECVAM¹² and other alternatives experts, must carefully review the existing validation and acceptance process to improve techniques for considering non-animal alternatives, dramatically reduce the time taken to validate and accept tests and harmonise international validation and acceptance systems. The EU should not wait for the cumbersome decision-making process of the OECD before approving valid new methods. The European Council (7th June 2001) notes that 'the Community should play a more active role in the OECD, to encourage wider adoption of validated, alternative, non animal testing methods'. Animal test methods must be deleted from the OECD's Test Guidelines as soon as replacement non-animal alternatives are added.

12. European Centre for the Validation of Alternative Methods

THE 7 STEP ACTION PLAN FOR A NEW *IN VITRO* EU CHEMICALS STRATEGY

The European Coalition proposes a 7 step action plan which will ensure that animal tests are eliminated, and that non-animal methods are brought into use as soon as possible. It recommends swift action on transparency and mandatory data sharing as well as targeted and time-tabled prioritisation of the validation and implementation of alternative methodologies.

THE 7 STEP ACTION PLAN FOR A NEW *IN VITRO* EU CHEMICALS STRATEGY

ACTION 1. make public (for a significant period before testing starts) lists of all chemicals nominated for testing at each stage of the chemicals testing strategy. For example, they could be published on a website, in order to allow for public comment, as occurred in the US with the HPV Program.

ACTION 2. impose mandatory data-sharing between companies and countries of existing chemicals information and global coordination of chemical testing programmes to make use of existing chemicals data and avoid duplicate testing. As well as existing animal test data, sources of human data would include epidemiological studies and accidental human and environmental exposure data held by pathology and forensic institutes, poisons centres, institutes of occupational health etc. The European Chemicals Bureau, in its extended role, should co-ordinate the assessment and collection of existing data, and sharing of new data.

ACTION 3. target the progress of non-animal test methods and prioritise the validation of new tests. A targeted timetable for validation of non-animal tests should be written into the chemicals strategy and strictly enforced. To achieve this there must be a significant commitment to increase the funding available to both the development and validation of alternative methods, for example, through ECVAM.

ACTION 4. further harmonise the international validation and acceptance process to maximise the use of alternative methods and avoid repeat validation studies.

ACTION 5. evaluate all available data (related to Action 2.) of each chemical and immediately restrict, phase out or impose a moratorium on the production and use of those chemicals that are most hazardous.

ACTION 6. where testing is required, a battery of non-animal tests should be applied in a stepwise strategy and chemicals classified and controlled accordingly (see BUAV's booklet, 'Action to End Animal Toxicity Testing').

ACTION 7. where safety evaluation is not possible for certain chemicals after performing all available *in vitro* tests, suspect chemicals should be restricted on the precautionary principle. Any further testing should await the final validation of new alternative methods under the Commission's new, co-ordinated initiative (see Actions 3 and 4).