

# ISSUE

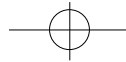
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## THE USE OF ANIMALS IN PRODUCT SAFETY TESTING

Scientists have significantly reduced the number of animals used in product safety testing in recent times. Because this reduction has been possible, animal rights activists would like the public to believe that the use of laboratory animals can be eliminated in this field altogether. It is often claimed that valid alternatives to the use of animal tests already exist to evaluate product safety. This is not true.

The FDA states, “many procedures intended to replace animal tests are still in various stages of development...While the best means may begin with valuable adjunct tests, ultimately testing must progress to a whole intact, living system — an animal.” Not using animal tests when necessary would subject humans and other animals to unreasonable risks.

- ▶ Manufacturers of food, drugs, household goods, cosmetic products, pesticides and other chemicals have both ethical and legal obligations to protect the safety of consumers.
- ▶ Federal statutes including the Food, Drug, and Cosmetic Act; Toxic Substances Control Act; Federal Insecticide, Fungicide, and Rodenticide Act; Clean Air and Water Acts and the Consumer Product Safety Act mandate that the federal government be involved in assuring product safety and in protecting public health.
- ▶ Federal agencies such as the Food and Drug Administration, the Environmental Protection Agency, the Consumer Product Safety Commission and the Occupational Safety and Health Administration play a significant role in monitoring product safety.
- ▶ Federal agencies and professional groups agree that alternative methods are not available at this time to completely replace the use of animals in product safety testing. Nevertheless, in a formalized interagency effort, the federal government is actively working to establish the validity of new nonanimal tests that may be accepted for regulatory purposes and further reduce animal use.
- ▶ The vast majority of test animals are rodents (primarily mice and rats).
- ▶ The “classic” LD-50 test has been replaced, in almost all cases, by modified tests that require fewer animals. However, there are still rare instances when statistically precise acute-dose toxicity data are needed.
- ▶ The Draize test, developed in 1944, has changed considerably over the years to reduce or eliminate any pain test animals may experi-



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ence. It is the FDA's position that "the Draize test is currently the most meaningful and reliable method for evaluating the hazard or safety of a substance introduced into or around the eyes."

- ▶ Companies that claim their products are not tested on animals — and, therefore, are "cruelty free" — mislead consumers since almost all products, or the chemical compounds that comprise them, were previously tested on animals. Such testing need not be repeated.

### What is product safety testing?

The purpose of safety testing is to ensure that a product is safe when used as directed and, perhaps more important, to provide scientific data for poison control centers and emergency room personnel should a product be misused. Toxicology is the study of the harmful effects of substances on living systems. Toxicologists test prescription drugs, over-the-counter drugs, food additives, household products, pesticides, chemicals and cosmetics which include items like shaving cream, sunscreen and shampoo. A substance's relative safety is judged according to its effects under various conditions, such as dose, route of administration, duration and frequency of exposure, as well as the actual chemical structure.

### Do we really need to use animals for testing?

Because scientists have drastically reduced the number of animals needed for product safety testing, animal rights activists have led the public to believe that the use of laboratory animals can be eliminated from this field altogether. This is not true.

According to Dr. James Mason, former Assistant Secretary for Health at the Depart-



ment of Health and Human Services, "Whole animals are essential in research and testing because they best reflect the dynamic interactions between the various cells, tissues and organs comprising the human body."<sup>1</sup>

The Food and Drug Administration (FDA) has stated that "many procedures intended to replace animal tests are still in various stages of development and that it would be unwise for us to urge manufacturers not to do any further testing....While the best means may begin with valuable adjunct tests, ultimately testing must progress to a whole intact, living system — an animal."<sup>2</sup>

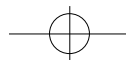
While scientific societies, such as the Society of Toxicology, have issued strong statements in support of the development of nonanimal methodologies, they also caution that "at present, tests in intact animals are the only means of assessing the potential hazard from (dermal and ocular) exposure other than direct testing in man."<sup>3</sup>

Not performing adequate testing violates both our moral and legal obligation and places people as well as animals at risk.

### Which federal agencies regulate product safety testing?

Federal laws require that the public be protected from hazardous commercial products, but specific animal tests are not statutorily mandated. Related federal regulations explicitly or implicitly call for animal testing. Four principal federal agencies have a significant role in animal testing for regulatory purposes. (See cover page.)

The FDA is responsible for administering statutes that regulate human and animal food and drugs, medical devices, biological products for human use, cosmetics, color addi-



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tives and radiological products. The FDA expressly requires that laboratory animal tests be conducted both for prescription drugs and over-the-counter drugs before these products can be tested further in humans. Antiperspirants and dandruff shampoos, for example, are considered to be over-the-counter drugs.

The Environmental Protection Agency (EPA) uses toxicity data derived from animal testing, as well as other data, to protect humans, animals and the environment from harmful effects of pesticides, industrial chemicals, air and water pollutants and hazardous wastes.

The Consumer Product Safety Commission (CPSC) relies on animal data in identifying and regulating risks to consumers of personal care and household products, while the Occupational Safety and Health Administration (OSHA) uses such data indirectly in requiring employers to maintain a safe workplace.

### Types of Toxicology Tests

The nature and extent of testing may vary from one type of product to another. The intended use of the product, the ways in which people are likely to be exposed to it, the specific properties of the product and the dictates of federal law are all factors in determining which tests are needed and the extent of the evaluation.

Some of the common types of toxicology tests are acute lethality and skin and eye irritancy (Draize) tests. There are also chronic and sub-chronic studies that examine the risks of extended exposure to new chemicals and drugs, such as long-term cancer treatment. Teratology and reproduction studies address the causes of birth defects, while mutagenicity studies assess a chemical's tendency to cause adverse changes in the genetic makeup of an organism.

### What is the LD-50?

The LD-50 test is a measure of acute lethality. An LD-50 rating is calculated for the dose at which one-half of the test animals can be expected to die from ingestion of the test substance.

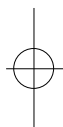
This "classic" LD-50 test, developed more than 50 years ago, has been discouraged by the EPA since 1984.<sup>4</sup> The FDA has no requirements for LD-50 test data obtained by using the classic, statistically precise test.<sup>5</sup> The CPSC also accepts estimated acute toxicity data.

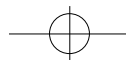
Federal agencies now suggest using a tiered testing approach rather than the "classic" LD-50 test. First, data already available from existing or structurally related chemicals are reviewed in order to make preliminary safety evaluations. One useful data source for this purpose is the 14-year-old, industry-funded Cosmetic Ingredient Review (CIR). It brings together all available published and unpublished data on the safety of cosmetic ingredients.

The second step is the "limit" test, which uses 10 to 20 animals, not 80 to 100 animals like the old LD-50. In this test, animals are given a single dose of a product according to their body weight. The vast majority of test animals are rodents (mice and rats). Although the results of the "limit" test may not be as precise, this form of testing is almost always sufficient in estimating the toxicity of the substance in question.

Lastly, if necessary, multiple endpoint testing is done. Dosed animals are observed for abnormal behavior and are carefully watched during recovery. They are also autopsied to evaluate internal evidence of toxicity to various organ systems.<sup>6</sup>

While the LD-50 usually can be replaced by other tests that utilize fewer animals, there





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are still rare instances when precise acute dose toxicity data are needed. For example, the “classic” LD-50 test may be necessary when examining the potency of highly toxic drugs, such as new cytotoxic cancer drugs. Also, when determining the effective strengths of certain pesticides, precise acute toxicity data may be desired.<sup>7</sup>

### Skin and Eye Irritancy Tests

Because many products are intended for topical use, or for use in and around the eyes, consideration for potential skin and eye irritancy is an important aspect of safety evaluation.

In some circumstances, it is not necessary to conduct any irritancy testing in animals. If, for example, initial chemical analysis shows that the product is a corrosive, the toxicologist assumes that the product will produce irritancy and that animal testing will yield no new information.

Similarly, testing for eye irritancy may not be needed if initial nonanimal or skin irritancy tests indicate that the product may injure eye tissue.

### What is the Draize test?

The Draize eye and skin irritancy tests are used to determine whether substances that may come into contact with the eye or skin will cause irritation or injury.

In the eye test, drops of the test substance are placed into one eye in each of as few as three test animals. Rabbits are commonly used because their eyes are at least as sensitive as the human eye. Affected eyes are observed at intervals, and results are scored based on the degree of various reactions — corneal clouding, percent of cornea involved, condition of iris, redness, etc. Scientists can also observe the

healing process after exposure to an irritant, since live animals, not test tubes, are used.

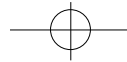
For the skin irritancy test, the fur of as few as three animals is clipped and the test substance is placed in contact with the skin. The site is covered for a day and then the patch is removed to evaluate any irritation for up to three more days.

While the basic Draize procedures are essentially the same as those used since the 1940s, modifications to reduce or eliminate any pain or distress in test animals are now employed. These modifications include using ophthalmic anesthetics whenever possible, using diluted solutions or lower doses of test substance and eliminating the use of stocks for restraint so animals can move freely and have continual access to food and water.<sup>8</sup>

### Is the Draize test really necessary?

As part of its overall effort to reduce or avoid unnecessary testing methods, the FDA has been carefully evaluating the use of the Draize test. It is the FDA's position that “the Draize eye irritancy test is currently the most meaningful and reliable method for evaluating the hazard or safety of a substance introduced into or around the eye.”<sup>9</sup>

While *in vitro* studies can be useful as screening tools to indicate the relative toxicity or safety of a substance, the FDA states that “the responses and results of alternatives alone cannot, at the present time, be the basis for determining the safety of a substance. It is more likely that these efforts will result in reduction or refinement as opposed to the replacement of the Draize eye irritation test.”<sup>10</sup>



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### What are the nonanimal alternatives for product safety testing?

As indicated previously, in recent years the scientific community has been successful in reducing the number of animals used in product safety tests as well as in refining test methods to reduce any pain or distress these animals may experience.

Mathematical models can be useful in helping to predict an organism's response to varying levels of exposure to a substance and in improving the design of scientific experiments.

Computer data banks allow for the reduction of test duplication. Computers also are useful in the initial evaluation of chemicals slated for further study. Unsuitable chemicals can be eliminated from consideration prior to starting any animal testing.

Cells, tissues and even whole organs obtained from animals and humans can be kept "alive" in the laboratory and used in preliminary screening of chemical compounds. However, testing on tissue culture will not reveal the effects of a substance on a complex living organism composed of many different physiological systems.

As important as nonanimal methods have proven to be, they have only limited utility and cannot totally replace the use of animals in safety testing at this time. Most researchers generally hold that nonanimal methods are adjuncts rather than alternatives to animals.<sup>11</sup>

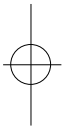
For economic and ethical reasons, industry is actively committed to the search for alternatives to animal testing. Internal and external efforts to develop and evaluate promising nonanimal procedures are receiving significant industry support.

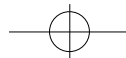
Government, academia, and industry support the "3 Rs" — reduction, refinement and replacement.

For its part, the federal government is actively working on the validation and future regulatory acceptance of new toxicological tests. These tests not only can improve risk assessment in order to better protect the public, but also continue to reduce animal use, refine procedures involving animals to make them less stressful, and replace animals where scientifically feasible and practical.<sup>12</sup> In 1998, a new skin irritation test was endorsed by the inter-agency committee dedicated to this purpose. The new test can reduce both the number of animals needed for study and the amount of discomfort these animals experience.

### What is the truth about so-called "cruelty-free" products?

The public may be confused by announcements that some companies do not test their products in laboratory animals, thus providing "cruelty-free" products. This notion can be misleading because most of these products or their ingredients have been tested previously in animals, or the safety of the products has been well-established based on a long history of human exposure to them; therefore, additional evaluation is not required. In some instances, animal testing may be conducted by raw material suppliers other than the manufacturer of the final product. If the safety of a consumer product





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has not been substantiated, federal agencies require a prominent declaration to that effect on the label.

The fact that a given product may not require additional animal tests does not mean that testing can be abandoned for all products. New chemicals, new uses of old chemicals and new mixtures of chemicals must be subjected to toxicity testing so that unsafe products will not be marketed inadvertently.

- <sup>1</sup> James O. Mason, M.D., Assistant Secretary for Health, U.S. Department of Health and Human Services, Statement before the U.S. Senate Committee on Commerce, Science and Transportation, Consumer Subcommittee, November 8, 1989.
- <sup>2</sup> U.S. Food and Drug Administration, Statement to the Maryland Governor's Task Force to Study Animal Testing, April 17, 1989.
- <sup>3</sup> Society of Toxicology, Comments on the LD-50 and Acute Eye and Skin Irritation Tests, July 24, 1989.
- <sup>4</sup> Environmental Protection Agency News, August 29, 1984.
- <sup>5</sup> Gerald B. Guest, D.V.M., Director, U.S. Food and

Drug Administration Center for Veterinary Medicine, Animal Testing — The Present, The Future, Food & Drug Law Institute, Sept. 7, 1989.

- <sup>6</sup> Environmental Protection Agency, Revised Policy for Acute Toxicology Testing, September 22, 1988.
- <sup>7</sup> Dr. David Rall, Director, National Institute of Environmental Health Sciences, National Institutes of Health, U.S. Department of Health and Human Services. Statement before the U.S. House of Representatives Energy and Commerce Committee, Subcommittee on Health and the Environment, May 16, 1988.
- <sup>8</sup> *Federal Register*, Vol. 49 No. 105. pp. 22523, May 30, 1984.
- <sup>9</sup> David A. Kessler, M.D., Commissioner, U.S. Food and Drug Administration. Letter to the Honorable Pete Wilson, Governor of California, September 3, 1991.
- <sup>10</sup> Mason, see 1.
- <sup>11</sup> Councils of the National Academy of Sciences and the Institute of Medicine, Committee on the Use of Animals in Research. *Science, Medicine and Animals*. National Academy Press, 1991.
- <sup>12</sup> *Validation and Regulatory Acceptance of Toxicological Test Methods: A Report of the ad hoc Interagency Coordinating Committee on the Validation of Alternative Methods*, NIH Publication 97-3981.

