News
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****Alternatives to Draize test proposed to predict eye safety of products

DALLAS -- Saying the words "Draize test" to an animal rights activist is like sounding a call to battle. So most researchers just don't say the words. But now a group of responsible scientists suggests that alternative testing probably can and should be developed, and they hope that everyone will listen.

The Draize test, in which substances being tested are dropped into the eyes of animals, is required by several U.S. regulatory agencies to determine whether proposed products will damage or irritate the eye. A product must be tested before it can be put on the market. The test evokes emotional controversy because it is performed on rabbits and may cause pain and/or blindness.

Dr. James P. McCulley, chairman of the Department of Ophthalmology at The University of Texas Southwestern Medical Center at Dallas, is one of the authors of A Critical Evaluation of Alternatives to Acute Ocular Irritation Testing. He will present information on the subject during the annual meeting of the American Academy of Ophthalmology held in Dallas Nov. 8-12.

McCulley's co-authors are Drs. John M. Frazier and Alan M. Goldberg of the Johns Hopkins Center for Alternatives to Animal Testing, Baltimore; Dr. Shayne C. Gad of G.D. Searle & Company, Skokie, Ill.; and Dr. Dale R. Meyer, UT Southwestern Medical Center at Dallas.

McCulley and his colleagues believe that alternative in vitro tests can be developed, using cell cultures rather than live animals, that will be just as valid as the Draize test for preliminary screening. They also suggest that some testing is needless and can be eliminated. Still, the assurance that products will not harm the consumer if used properly is the priority.

Eye irritation testing became a requirement by the Food and Drug Administration 40 years ago after the marketing of an untested eyelash dye (Lash Lure) caused blindness in some consumers and one fatality. The FDA called for testing, and FDA administrator Draize suggested a grading system that linked his name to eye irritation tests.

Today eye irritation testing is required for four classes of products: pharmaceutical, cosmetic and toiletries, consumer products and industrial chemicals.

For the pharmaceutical industry, testing is performed when a material is intended to be put in the eye either as medication or as a means of lubrication. For these purposes, the test must be both sensitive and accurate.

Cosmetics and toiletries are frequently used in the area of the eye and may come in contact with it unintentionally. In this case, the tests need to be sensitive. On the other hand, they might be less sensitive in the case of toiletries like deodorants or depilatories for which eye contact is unlikely and moderate irritation might be acceptable.

Consumer products not intended for personal care, such as detergents or drain cleaners, are tested so that they can be labeled to provide information about potential danger and treatment in case of accidental exposure to the eye. Agricultural chemicals also fall into this category.

Finally, users of industrial chemicals, a much smaller population than general consumers, usually take active precautions to guard themselves against contact. However, these chemicals are tested to provide information in case of accidental exposure.

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Although requirements for testing in each category differ to some extent, a common test consists of placing either .1 milliliter of a liquid or .1 gram of a powder or other solid onto one eye of each of six rabbits. The material is not washed out, and both eyes of each animal are graded according to the Draize scale at 24, 48 and 72 hours. (The untreated eye acts as a control.) The test is considered 85 percent predictive of reactions in humans. The Federal Hazardous Substance Act of 1964 and the Consumer Product Safety Commission guidelines of 1976 have helped to establish the methods.

"There is good reason to have some kind of toxicity testing," said McCulley. "However, I think we can eliminate some of the testing in animals if the regulatory agencies would allow it.

"What I envision for the future is a battery of tests that will predict whether the substance is going to be toxic or not, whether it will kill or damage cells. If we know it is toxic in vitro, there is no point in putting it in a rabbit to see the toxic effects."

A pharmaceutical product for use in the eye would be dropped as soon as toxicity was shown. In the cosmetic industry, cutoff points would be developed for acceptable and unacceptable toxicity, and a product that exceeded the level would also be dropped before further testing. In either case, a product either non-toxic or within an acceptable range would then be tested in an animal to be certain that the in vitro test was accurate.

"No alternative test would be 100 percent accurate, just as the animal tests are not 100 percent. With some things they will be accurate; acids and alkalis will always kill cells. It's better to be as certain as possible to prevent human blindness," said McCulley.

He anticipates two batteries of in vitro tests: one to predict whether the product is cytotoxic, capable of killing cells or preventing their multiplication, and one to measure irritation not related to cell death. "I would hope there would eventually be four tests -- two in each category -- but that's a personal opinion.

McCulley says that the search for alternatives to Draize testing is just in its infancy. The first step will be to develop multiple tests and select from them a battery of tests that will prove workable in the hands of a number of people. Then the tests must be validated as predicting the same reaction in animals and in man. "I think we will have a fairly good battery of tests that is acceptably predictive within five years. But then it will probably take several years to get the regulatory agencies to accept the tests."

Meanwhile, there are several ways that some Draize testing can be eliminated before alternatives are developed. Tiered testing would eliminate products that were obviously toxic, those with pH factors less than 2 or above 12. After that, skin tests to determine irritancy could screen out the need for some tests. Only products that appeared mildly irritant or non-irritant need to go to Draize testing.

"I also hope that some mechanism for publishing test results can be made available," said McCulley. There is needless duplication of tests because there is no way to determine which substances have already undergone testing. "These tests are usually done for private companies and are not the sort of thing that gets published in scientific journals."

The authors of A Critical Evaluation of Alternatives to Acute Ocular Irritation Testing conducted a survey that determined 190 laboratories in the United States conduct some Draize testing. These include contract research companies and laboratories in pharmaceutical and chemical companies. More that 24,600 tests are conducted annually involving over 122,700 animals, according to a sampling.

"I have a dual goal in seeking alternatives," said McCulley. "One is to develop alternatives for their own sake, and one is to be responsive to what I think is a reasonable, but unfortunately often overstated, public concern. Scientists must be responsible so that necessary use of animals in research will be protected."

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Note: The University of Texas Southwestern Medical Center at Dallas was formerly The University of Texas Health Science Center at Dallas. The name was changed on Oct. 9.