Physicians Committee for Responsible Medicine

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Thank you for the opportunity to address the committee as it considers this important legislation.

It is well-known that the Draize test is cruel to animals. But what is not commonly appreciated is that the Draize test is not used as a safety test. If it were, then products that were Draize-tested and appeared to be unsafe would not be marketed. But the test is not used that way. Numerous products fail the test and are marketed anyway.

Take Clairol products, for example. In response to new federal guidelines, Clairol released information on the safety of its products to beauticians who use them regularly. Many are clearly eye irritants. Some can cause permanent eye damage.

Clairol's notice regarding its permanent (oxidation) hair colors reads as follows: "CAUTION. Eye irritants. When oxidation haircolors are mixed with developers (hydrogen peroxide), the mixture may cause severe irritation and possible permanent eye injury."

The notice for Clairol's semipermanent hair color simply states: "CAUTION, eye irritants."

Clairol's bleach powders: "CAUTION, eye irritant. When the bleach powders are mixed with hydrogen peroxide, the mixture may cause severe irritation and possible permanent eye injury...Flush with plenty of water immediately. Remove contact lenses if used. Get medical attention IMMEDIATELY."

Clairol's Metalex hair dye remover is called an "eye irritant" and Clairol's aerosol hair sprays are described as "potential eye irritants."

It is clear that companies market products in spite of Draize test results. Many have asked why the Draize test is done at all. In fact, the Draize is used for reasons related to legal liability rather than scientific testing.

In 1968, the court case of Harris vs Belton illustrated the use of testing from a liability standpoint. The plaintiff was a black woman who used a skin-lightening cream. Artra Skin Tone

Cream promised a "lighter, lovelier skin beauty for you...a complexion fresh and bright as springtime."

Unfortunately, the product caused the plaintiff's skin to be burned, scarred, and darkened. She sued for damages. A small but significant number of other users of the product also had adverse reactions.

The court ruled that the law does not prohibit the manufacture and sale of dangerous products, but simply provides that the customer be warned of potential adverse effects. The Artra product was labeled as potentially damaging for some users, and, on that basis, the court ruled that the company was not responsible for damages to the plaintiff.

The Draize appears to be used mainly as a method to decide when to label. Obviously, all cosmetic and household products should be appropriately labeled based on the knowledge of the potential effects of their ingredients. Draize testing is certainly not necessary in order to establish potential risk. A similar general purpose label can be found on over-the-counter medications: "Keep this and all medications out of the reach of children."

Even if it were used as a safety screen, the Draize is entirely inadequate as a measure of safety. This World War II-vintage test is well-known for its failures. Not long ago, I attended a meeting with representatives of industry, the Food and Drug Administration, and others concerned about the Draize test. It was generally acknowledged in that meeting that the Draize was far from a good measure of human reactions to substances. Manufacturers cling to it apparently because it is an easily performed test that has acted as a standard of practice for purposes of guarding against litigation.

In 1948, the Draize test was four years old. In that year, researchers found that a concentrated solution of histamine phosphate caused only a slight and transient reaction in the rabbit eye, which failed to predict the harsh reaction of even much more dilute solutions in the human eye. A 1:200 dilution caused only a slight and brief reaction in the rabbit eye, while even a 1:50,000 dilution had a potent effect in the human eye. This was one of the early failures of the Draize test. But there have been many more.

0.5% selenium sulfide caused no reaction in the Draize test. But in humans it caused irritation and inflammation of the eye. 2.5% cresol caused only a mild reaction in rabbits, but in the human can cause swelling of the eye, opacification of the cornea, and congestion of the conjunctivae. Certain detergents caused no reactions in the rabbit eye, even at high concentrations. In humans, these same detergents caused pain and altered vision. A male hairdressing formulation passed the Draize test, only to cause numerous reports of irritation to the human eye. A 5% soap solution produced almost no effect in rabbits, but caused corneal

damage in humans. Ozone at levels of 2-37 ppm were not injurious to rabbits but did cause irritation in the human eye.

Why so many differences between the rabbit test and human experience? There are many structural differences between the rabbit eye and the human eye. The pH of human tears (7.1 to 7.3) is much lower than that of rabbits (8.2). A one-point difference on the pH scale means a ten-fold difference in the acidity of tears. The rabbit's cornea is about 30 percent thinner than the human cornea. The "third eyelid" (nictitating membrane) which rabbits have (and humans do not) may change the animal's response to substances by clearing them away, or perhaps by trapping them against the cornea. Rabbits blink and tear at rates very different from the human. All these change the way different species react to substances.

Moreover, the Draize test is so subjective that different technicians can obtain vastly different results. Scientists at Carnegie-Mellon University distributed test substances to 24 different laboratories for Draize testing. They wrote:

"Certain laboratories consistently recorded unusually severe scores...for the materials tested...Other laboratories reported consistently nonirritating scores...Certain materials were rated as the most irritating tested by some laboratories and, contrariwise, as the least irritating by others...Thus, the tests which have been used...to decide the degree of eye or skin irritation produce quite variable results among the various laboratories as well as within certain laboratories. To use these tests, or minor variations of them, to obtain consistency in classifying the material as an eye or skin irritant or nonirritant, therefore, is not deemed practical."

They went on to recommend:

"...it is suggested that the rabbit eye and skin procedures currently recommended by the federal agencies for use in delineation of irritancy of materials should not be recommended as standard procedures in any new regulations."

What are the alternatives?

The Noxell Corporation, makers of Noxzema, Cover Girl, and other cosmetic products recently accepted an alternative to the Draize test called the agarose diffusion method. This method has long been established for testing the safety of synthetic materials in medical devices which come in contact with human tissues. Heart valves, intravenous lines, artificial joints and other products have been tested for irritancy with this method for about 25 years. The method was adapted for testing cosmetic products by Richard F. Wallin and R. Douglas Hume of North American Science Associates in Northwood, Ohio, and Edward M. Jackson of Noxell. The test is included in the U.S. Pharmacopeia, an indication of its official acceptance.

In the test, a thin layer of cells is placed along the bottom of a flask. Small amounts of the materials to be tested are placed on top of the cell layer. A thin cushion of agarose, a polysaccharide derivative of the sea plant agar, allows the test material to be held near the cells without crushing them. If the test material is an irritant, a zone of killed cells will be seen around it.

In their 1987 report, Wallin, Hume and Jackson found an 81 percent correlation between the agarose diffusion method and the Draize test for 16 products. The discrepancy was that the agarose method was slightly more sensitive than the Draize: two substances which passed the Draize showed some potential for danger on the agarose method. In addition, one chemical which failed the Draize appeared to be non-irritating on the agarose method.

In their next report, the authors tested 22 cosmetic products and found a 100 percent correlation with the Draize. Regarding the broad applicability of the test, they stated:

"To date, we have tested virtually every type of aqueous and nonaqueous cosmetic product formulation type by using actual finished cosmetic products as test materials. These products were emulsions (oil/water and water/oil; pigmented and nonpigmented), solutions, suspensions (both water-based and hydrocarbon-based), gels, and physical mixtures (both powder and wax mixtures)."

The new method costs less than the Draize. The agarose diffusion test costs $50-$100 per product compared to $500-$700 per product for the Draize. The agarose diffusion test can be run in 24 hours, in contrast to the Draize, which takes a minimum of three days and may take as long as 21 days to complete. The test does not require laboratory modifications or special technician training. The same laboratories that are currently using the Draize test could begin using the agarose diffusion method. As a result, there would be no loss of jobs or market share.

The chorioallantoic membrane (CAM) test, developed by Dr. Joseph Leighton and his colleagues at the Medical College of Pennsylvania uses the membrane found under the shell of a chicken egg. This membrane contains blood vessels and epithelial cells and reacts very much like the human eye. Validation studies conducted by Colgate Palmolive showed a high correlation between the CAM test and Draize results.

The tetrahymena method, developed by Jerald Silverman of the Ohio State University, uses protozoans to measure irritancy. These single-celled organisms reduce their movement when exposed to substances that can be irritating to cells. In a validation test using 21 chemicals, an 86% correlation with the Draize was achieved. The discrepancy was that the tetrahymena method was, in general, slightly more sensitive than the Draize. In other

words, a few products that may appear non-irritating on the Draize may not pass the tetrahymena method. This, of course, is desirable for a safety test. It should be a bit over cautious.

Avon has accepted the Eytex System, developed by the National Testing Corporation, as its alternative to the Draize. This testing package uses a complex mixture of chemicals which simulate the structures of the human eye. If the test material turns cloudy when exposed to a substance, the potential for irritancy is indicated. The test has been run on hundreds of compounds with a high rate of accuracy.

Sophisticated cell culture methods can be used in several different ways to assess the irritancy of substances. The uridine uptake inhibition assay, the cell growth/protein accumulation assay, and several other methods can be performed by laboratories in standardized testing kits available from Clonetics Corporation and other firms. Validation tests of these testing methods have been very favorable.

It is important to remember that the Draize test itself has never been validated and is inherently flawed, resulting in the numerous errors noted above. One could certainly never suggest that this test from the 1940's represents the state of the art in toxicology. Pregnancy was once detected using a rabbit test. But no longer. Now, modern methods are employed that are quicker and cheaper. The same march of technology must retire the Draize test.

Because of these problems, many companies chosen to never use the Draize at all. They rely on what might be called selective formulation. They choose many of their ingredients from the Food and Drug Administration's GRAS (Generally Recognized as Safe) list, which contains numerous ingredients which are known to be non-toxic. If they intend to use a potentially irritating or poisonous ingredient, they choose from the thousands of ingredients which have a history of human use. The great advantage of this method is that, in the event of accidental ingestion, the treating physician will have a basis on which to provide treatment. Animal safety testing gives no information about antidotes. Nexxus, Paul Mitchell, and Elizabeth Taylor's new Passion perfume are among the products which have never been Draize tested. These companies make excellent products and good profits without this antiquated test.

Banning cruel animal toxicity tests will not hinder research into cancer or heart disease or birth defects. But it will make the consumer and the voter a bit more secure in the notion that their legislators are doing what they can to modernize testing methods.

Some manufacturers have fought this ban because they fear encroachment on animal testing. Would these same people oppose safeguards against drunk driving on the grounds that it would lead to total prohibition of alcohol use? Would they have fought

child labor laws on the grounds that keeping young children out of factories might lead to a massive prohibition on jobs for minors? Whether manufacturers will acknowledge it publicly or not, they will tell you privately that the Draize test is both cruel and badly flawed. It is long past time that this relic of a by-gone era was retired.

A further provision of this bill would allow students the right not to participate in animal laboratory exercises. Just as no medical student would be forced to perform an abortion if they objected to that procedure, fundamental beliefs concerning killing animals should be respected as well. This policy is already in place at nearly all medical schools, according to a survey published in the Journal of Medical Education, September, 1988. Tufts University veterinary school has recently established a track for students who wish a similar provision. There is little reason to believe that any teaching institution would have difficulty in respecting these beliefs.

References:

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