Academy Explores Use of Laboratory Animals

The National Research Council (NRC) has issued a report on the use of laboratory animals in research that is designed to serve as a "carefully reasoned statement" in the face of the rising tide of animal rights activism. Its conclusion is that "animal experiments are still critically important to further improvements in medicine and biomedical science." The report, which cost $315,000, was initiated by the NRC in 1985. The research council is the operating arm of the National Academy of Sciences' complex.

The NRC's Committee on the Use of Laboratory Animals in Biomedical and Behavioral Research, chaired by Norman Hackerman of Rice University, acknowledged that animals pay a high price for human benefits, but concluded that "humans are morally obliged to each other to improve the human condition." It also affirmed that "scientists are ethically obliged to ensure the well-being of animals used in research and to minimize their pain and suffering."

In a brief discussion of animal activism, the committee observed that "the use of the term 'rights' in connection with animals departs from its customary usage or common meaning," in which rights refer to moral and legal relationships among humans. "Our society does, however, acknowledge that living things have inherent value." The comprehensive report adds that American society is influenced by the Judeo-Christian notion that humans have dominance over animals, but that concept "also insists that dominance be attended by responsibility."

The report describes benefits derived from animal research in polio, AIDS, organ transplantation, cardiovascular and kidney research, and research on behavior, pain, and memory. It also notes the benefits of animal research for animal health and wildlife management. Continued work on the development of alternatives to animal use is strongly encouraged, but the panel said alternatives will not eliminate the need for animals in the foreseeable future because certain studies simply require animal use.

With regard to other controversial issues, the committee found "no convincing evidence" of any widespread abuse or neglect of research animals. It also defended the use of pound animals (about 200,000 a year) in research. The committee did not address one of the main criticisms of the Animal Welfare Act—that it has not been interpreted to apply to rats and mice. At a press conference, panel member and theologian James M. Wall, editor of *The Christian Century*, said they did not find enough "public sentiment" to warrant recommending such coverage.

The panel had hoped to be able to report on an updated survey of animal use by the Institute of Laboratory Animal Resources (ILAR), but this has been postponed by contractual difficulties, so the estimate of animals used in research, testing, and education, continues to be the 1983 ILAR estimate of 17 to 22 million.

The report recommends that no new laws or regulations be adopted until current ones have been "fully implemented and their impact has been assessed." It also calls for standardization of rules followed by federal agencies, more money for the Department of Agriculture's (USDA) laboratory inspection duties (an increase from $6.2 million to a recommended $10 million), and the appropriation of more money to enable researchers to comply with animal research guidelines.

One panel member, Christine Stevens of the Animal Welfare Institute of Washington, D.C., refused to sign the report. In an angry statement at the end of the report, Stevens wrote: "The report refuses to face the widespread, ingrained problem of unnecessary suffering" among laboratory animals and does not "make so much as a passing reference to the serious problem of poor research using excessive numbers of animals." She also wrote: "I was shocked by the attitude of Committee members who asserted that we have no moral obligation to animals. . . . "

The report says all animals get adequate pain-relieving drugs in painful experiments, but Stevens says in 1987, more than 130,000 were exempted from this requirement. She also said the committee falsely claimed that all serious violations of animal care standards have been punished. (Study director John Burris says the committee took data from the last ILAR survey, covering 1968 to 1978, and that it felt pain control for animals was "adequate" given the needs of research.)

Also submitting a separate statement was Arthur C. Guyton of the University of Mississippi School of Medicine, who said the report "fails to make clear how seriously the Animal Rights Movement and increasing government regulation are impeding essential medical research."

He expressed particular concern over the future of large animal research, noting that one-fifth of the states have already forbidden the use of pound animals. These restrictions, combined with new regulations, mean that the cost of using a dog or cat approaches $1000 a year, not counting the costs of research, he said. Other measures that Guyton said were costly and unnecessary include the imposition of "a very costly layer of veterinarian regulators," requirements for expensive operating suites for surgery on rabbits or larger animals, and "very arbitrary regulations for specific cage sizes."

■ CONSTANCE HOLDEN

Much Work but Slow Going on Alternatives to Draize Test

Since animal welfare activists started to call for an end to the Draize eye irritation test in the late 1970s, there has been a dramatic reduction in the use of the 44-year-old test that uses laboratory rabbits. Research is now being conducted on dozens of possible substitutes. But at a September meeting in Washington organized by the Soap and Detergent Association, speakers said that total elimination of the test will take a long time. And there is no evidence that any single non-whole animal test will ever be developed to substitute for the versatile Draize.

The use of the Draize test has been reduced by perhaps more than 50% in this decade as much of the testing has been found to be redundant or, in the case of substances of known irritability, unnecessary. Tests have also been modified: some now use three instead of the six rabbits usually required. Since rabbit eyes are much more sensitive than human ones, Procter & Gamble has developed a "low volume" test which dilutes the materials to one-tenth the strength customarily used. Local anesthesia is also sometimes used.

"An alternative test cannot be required to be a valid predictor for all chemicals and products," noted Gary Flamm of the Food and Drug Administration (FDA). The Draize test is used to establish safety and determine ocular toxicity for a tremendous variety of products including drugs, cosmet-

ics, household products, agricultural and industrial chemicals, and chemical warfare agents. The test can simultaneously evaluate effects of a substance on various parts of the eye, identify corrosiveness, irritation, swelling, opacity, initial pain response, speed of healing, and possible systemic effects.

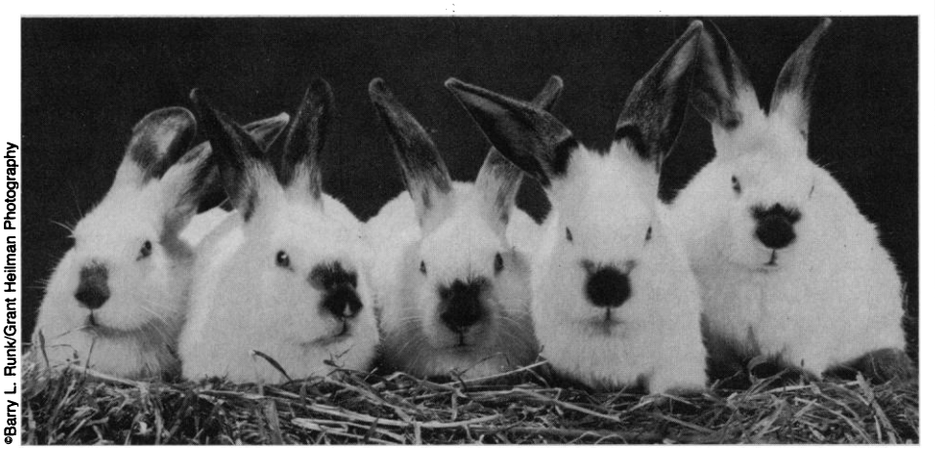
A multitude of in vitro alternatives involving cell, tissue, and organ systems are now under investigation. For example:

- Chorioallantoic membranes, the membranes covering live chick embryos, which can register tissue injury, cell toxicity, and inflammatory and immune responses. There have been problems correlating the results with the Draize test because they do not take alkalinity into account.
- Whole eyes from mice, rabbits, or cows. These are of limited use since inflammatory and healing responses cannot be triggered.
- Corneal cells from mice and rabbits to detect cell injury. Some cells are destroyed and their ability to grow back indicates whether healing will take place.
- Various tests with mammalian skin cells where uptake and release of certain chemicals indicate cell toxicity.
- Assay using a multicellular aquatic organism, tetrahymena (also used to assay teratogenicity), which registers an inflammatory response.

The biggest problem is the validation of alternative tests. "It will not be possible any time soon to validate new tests," said Keith Booman of the detergent association. New data will be needed that can be compared with the existing database, so new tests "will have to be supplemented by animal test results." Booman added there is no possibility of establishing a "gold standard" in the form of a material that can be tested across the board. The job is so large, he said, that if use of the Draize test were to be foreclosed, the period required to validate tests would be extended by years. Much cooperation between various laboratories will be needed to assess the variability of new tests.

As for possible regulatory obstacles to the adoption of new tests, the three federal agencies involved—the FDA, the Environmental Protection Agency (EPA), and the Consumer Product Safety Commission (CPSC)—have shown some willingness to be flexible about the kinds of tests used to provide safety data. The CPSC has said that if the *p*H factor of a new product is over 5, it will assume that the product is an irritant for which labeling is required and will not require corroborative testing. The Federal Insecticide, Fungicide and Rodenticide Act, administered by EPA, requires in vivo testing to get a new product registered, but the act allows much discretion on waiving data requirements. The EPA also announced recently that it will accept guidelines recently put out by Organization for Economic Cooperation and Development which permit the use of only three animals in Draize tests. It appears that no change in federal laws would be required. "There are really no legal barriers to the implementation of alternatives—just scientific ones," said Washington lawyer James C. Lamb.

There has been a good deal of cooperation among the various parties, much of it owing to the tireless efforts of New York activist Henry Spira, who launched the Coalition to End the Draize Test in 1978. Flamm of the FDA said he was "impressed with the increased intensity of commitment" on the part of industry. Speakers agreed on the need to establish time frames for various phases of test development, and the need for "harmonization" of test data so they can be shared among industries. There was general agreement that government, industry and academia will have to cooperate on the development and validation of alternative tests. Said Spira, "This is almost like a Manhattan Project." ■ CONSTANCE HOLDEN



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California bunnies. *Advances in toxicity testing and reduced use of the Draize test by the cosmetics industry means that fewer rabbits are used in research.*

CBO Cautions Congress on SSC

The Superconducting Super Collider could cost far more than what the Department of Energy (DOE) has estimated, warns the Congressional Budget Office (CBO) in a report scheduled to be delivered to the Senate Budget Committee later this month.

The report, requested by retiring committee chairman Lawton Chiles (D–FL), is generally positive about the potential contribution the SSC could make to high energy physics. It stresses, however, that while project costs have not escalated significantly to date, recent experience with accelerators suggest that outlays could be higher than the $4.4-billion (constant 1988 dollars) estimate provided to Congress.

The statement is based on a simple analysis of cost increases three of four accelerator projects built in the 1980s. The report's author, analyst Philip Webre, observes in *Risks and Benefits of Building the Superconducting Super Collider* that the "unweighted average cost increase in constant dollar terms was 46%." If this were to happen with the SSC, CBO estimates that the cost could rise to $6.3 billion.

The report cites several areas where the higher costs could be incurred:

- Difficulties in developing detectors could boost their costs by $200 to $400 million, CBO says. DOE has said the detectors can be built for around $719 million.
- Superconducting magnets could cost $270 million more than the $1.4 billion allotted, if economies of scale from mass production are not achieved.

The draft report also observes that the SSC would account for a substantial fraction of the federal basic research budget while it is under construction. As a result, funding growth in other basic research programs could be limited. The author also seems to question whether other science disciplines are being treated equitably, noting that in 1988 high energy physics received 6.6% of all federal basic research money even though physicists account for about 2% of "active scientists."

Despite these cost factors, the report's author also states that the SSC appears to be the most scientifically sound machine for the United States to pursue at this time. Cheaper options, he says, such as participating in Europe's Large Hadron Collider or building an advanced electron-positron linear collider, may not be as rewarding. What Congress must decide, notes Webre, is how fast it wants high energy physics to advance. ■ MARK CRAWFORD