In U.S., Few Alternatives To Testing On Animals
Panel Has Produced 4 Options in 10 Years

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Each year, American doctors inject more than 3 million doses of Botox to temporarily smooth their patients’ wrinkles and frown lines. But before each batch is shipped, the manufacturer puts it through one of the oldest and most controversial animal tests available.

To check the potency of its product under federal safety rules, Allergan Inc. injects mice with Botox until it finds a dose at which half of the animals die -- a rough gauge of potential harm to humans.

Animal protection groups consider "lethal dose 50," as the test is known, to be "the poster child for everything that's wrong with animal testing," said Martin Stephens, vice president for animal research issues at the Humane Society of the United States. "It's as bad as it gets, poisoning animals to death."

Allergan officials say they have no choice. Without a federally approved safety test that does not use animals, a company spokeswoman says, lethal dose 50 "is by default the required test."

The controversy over the Botox test highlights the slow pace of government efforts to replace or reduce the large numbers of animals used by pharmaceutical companies, chemical manufacturers and consumer firms to ensure that their products are safe for people. A decade after Congress created a panel to spur the development of non-animal tests, only four such tests have been approved out of 185 reviews, according to the panel's records.

Several of the panel's original backers now consider the system broken. As a result, critics say, hundreds of thousands of mice, rabbits, hamsters and dogs continue to suffer and die unnecessarily in tests for pesticides, household cleaners, sunscreens and other products.

"We were thrilled when the legislation was passed," said Sara Amundson, a former official with the Doris Day Animal League who was involved in creating the panel. "It's shocking to look back and see how little we have accomplished."
The federal panel is known as the Interagency Coordinating Committee on the Validation of Alternative Methods, or ICCVAM. Representatives of 15 federal agencies make up the committee.

Instead of acting as an advocate for companies and nonprofits proposing non-animal tests, the panel has become an obstacle, animal welfare groups say. They point to Europe, where a similar panel has approved 34 alternatives to animal tests and has another 170 in its pipeline. Critics say the U.S. panel is slow and favors older animal tests that have never gone through the same rigorous scientific review.

The executive director of the U.S. panel, William S. Stokes, said in a statement that his group "has successfully reviewed over 185 test methods" and that the four alternatives it has endorsed "have significantly reduced the number of animals required for safety assessments, and provided for improved welfare of animals used in safety evaluations." One alternative has saved "at least 36,000 animals annually," Stokes said.

Members of the panel also contend that it is unfair to compare Europe and the United States because the laws, rules and expectations are different. Europe has legislation mandating the use of non-animal tests. The United States only recommends their use.

Nevertheless, some U.S. company officials and scientists said they have delayed or abandoned their proposals for non-animal tests because panel reviews are protracted and expensive. Others consider panel members biased in favor of animal tests that in some cases date back to the 1920s.

"One should ask why after years of existence they have reviewed so few tests," said Neil Wilcox, a former Food and Drug Administration official involved in the creation of the committee.

"The fundamental reason, in my opinion, is that the ICCVAM process has become recognized as an obstacle to getting tests validated as opposed to helping having tests validated," said Wilcox, now director of regulatory and scientific affairs for Kimberly-Clark Corp.

An e-mail exchange last summer between the panel's chair and other government scientists reinforced the suspicions of animal advocates that panel members are resistant to newer tests. In the exchange, copies of which were obtained by The Washington Post, the scientists discussed two recent papers by a prominent European researcher favoring an alternative approach known as evidence-based toxicology. One scientist asked what they could do "to combat these papers." The chair, Marilyn L. Wind, responded: "What I see is them trying to build a case to not use animals for testing."

Jessica Sandler of the group People for the Ethical Treatment of Animals called the e-mail "disturbing. Why are they using phrases like 'to combat these papers'? That has no place in there."

Wind declined to discuss the exchange but said in an e-mail to The Post that the panel "has a proven track record" of advancing animal safety. Stokes stressed that panel members work closely with their European counterparts.

In February, at its 10-year anniversary celebration, the panel released a five-year plan, with a goal of assuming a greater leadership role in promoting research, development . . . and regulatory acceptance of alternative test methods."
Wilcox, of Kimberly-Clark, was not impressed. "The five-year plan is not a strategy," he said. "It's a reiteration of what they're doing. It's certainly not a vision."

'A New World'

For more than half a century, companies have tested chemicals, drugs and cosmetics on animals to prove that their products are safe. Poisons are fed to rats and mice to determine what dose may be harmful to humans. Chemical compounds are dripped on the skin and eyes of rabbits to check for irritation. Vaccines are given to mice before being made available to the public.

Animal welfare groups contend that millions of animals are used in such tests each year. But no one knows for sure. Unlike rules covering animals used in medical research, there are no federal reporting requirements for mice and rats, which account for most of the animals used in product testing.

Some scientists argue that animals provide the most reliable way to gauge the effects of toxins and drugs on humans. Others contend that newer tests take advantage of advances in biology and computer science, offering a potentially richer array of safety data.

"The reason we use animal tests is because we have a comfort level with the process . . . not because it is the correct process, not because it gives us any real new information we need to make decisions," said Melvin E. Andersen, director of the division of computational systems biology at the Hamner Institutes for Health Sciences near Raleigh, N.C. "Animal tests are no longer the gold standard," he said. "It is a marvelously new world."

Allergan officials say that in recent years they have reduced their use of animals by one-third but declined to disclose the number, citing company confidentiality.

Many firms say they have stopped using the lethal-dose method in favor of a test that uses fewer animals. But Allergan officials say that, for assessing potency, their only choice is the lethal dose test.

In 2005, the Humane Society requested that ICCVAM review non-animal alternatives to the Botox test. A panel of scientists gathered in 2006 and produced a draft report of the meeting in August 2007. But nearly a year later, the Humane Society's Stephens said he is still waiting for a final report and for direction from the federal group on what additional research is needed.

"It's great that ICCVAM held its workshop and drew some attention," said Stephens, a former member of the federal panel's scientific advisory committee. "But that alone won't get us to the finish line. We need to move beyond the animal methods and figure out which one or two of the replacements are the most promising."

Scientists who have gone before ICCVAM contend the process is unduly cumbersome, with multiple layers of review and panels that include scientists who are not familiar with regulatory issues or are not experts on non-animal tests.
"The big problem with the peer review panel was that many of them were chosen for their knowledge of the general field but didn't have a real understanding of what they were there to do," said Kristie Stoick, scientific and policy adviser to the Physicians Committee for Responsible Medicine.

Stoick closely followed a panel that recently reviewed a series of alternatives for a rabbit test used to measure bacteria levels in blood products and other materials. The panel rejected the alternatives, which have been used in Europe for years. Stoick said that several of the panel's observations and recommendations "seemed nonsensical, irrelevant or inappropriate. Too often it seems that panelists have unreasonable expectations regarding every minute detail of the alternative methods, without a clear understanding of the limitations of the current animal-based methods."

That view was echoed by Catherine Willett, director of science policy for People for the Ethical Treatment of Animals. "People just assume de facto that animal tests are relevant to humans without scientific evidence," she said. "It's not fair to make non-animal tests go through this [approval] process but not make the others."

One result of the delays is that some companies use non-animal tests in-house but are still required to perform animal tests to meet regulatory requirements.

"Companies are putting infinitely more money into the development of alternatives and are much more aware of . . . new in vitro methods than government regulators," said Rodger Curren, president of the nonprofit Institute for In Vitro Sciences in Gaithersburg, which works with consumer products companies to develop non-animal tests.

"But the regulators say, 'You still have to prove to me that it's safe using an animal.' "

The European Plan

Europe began moving away from animal testing more than 20 years ago. The European Commission voted in 1986 to require the use of alternative tests wherever possible. It later banned animal testing for cosmetics and passed other rules affecting chemical makers.

The European Center for the Evaluation of Alternative Methods, or ECVAM, was created in 1991. It has more than 60 employees and a budget of $25 million, about 10 times the size of its American counterpart. Another important difference: The European panel researches and develops non-animal tests, while the U.S. committee does not.

"Some animal tests haven't changed in 60 years," said Thomas Hartung, head of the European group. "The tests are frozen in time. This is not science. Science is always moving ahead."

Hartung, who helped write the papers discussed in last summer's e-mail, said he was not surprised by the response from some U.S. scientists: "When you say something new, there is resistance to change."