12-9-1983

Lots of Talk About LD50

Marjorie Sun

Lots of Talk About LD_{50}

Marjorie Sun

When animal rights groups protest the use of animals in experiments, one of their favorite targets is a test known as the LD_{50}. Since the late 1920's, scientists have killed millions of animals to conduct the test, which was designed to help judge the acute toxicity of drugs, pesticides, and other chemicals. But animal rights groups and scientists in general agree that the test is now outdated and has limited value. Even so, according to animal rights activists, industry continues to perform the test to meet federal requirements, unnecessarily killing millions of animals a year. The animal rights groups have raised such a ruckus that last month 16 congressmen wrote a joint letter to several federal regulatory agencies expressing concern about the test. About the same time, the Food and Drug Administration, with several other agencies, hosted a daylong workshop on the topic, which revealed that there is considerable confusion about how often the test is actually used and about federal requirements concerning the test.

LD_{50} refers to the dose of substance that kills 50 percent of a batch of test animals. This information has helped scientists and federal regulators determine what safety precautions should be taken in the manufacture, transport, use, and disposal of various substances. But in recent years there has been growing scientific agreement that the LD_{50} gives only a rough idea about a substance's toxicity and that other, newer tests provide much more information. Moreover, LD_{50} tests require a large number of animals, anywhere from 50 to 120, which are usually rodents. David Rall, director of the National Institute of Environmental Health Sciences and the National Toxicology Program, has called the LD_{50} "an anachronism."

It is not clear how many laboratories among industry, academia, and government actually conduct the traditional LD_{50} test. Henry Spira, the leading opponent of the test and head of the Coalition to Abolish the LD_{50}, alleges that 4 million animals a year are killed to conduct the test. But when asked recently about the basis for that figure, Spira said that he generated it after "talking with scientists from industry and academia" and acknowledged that "there are no good numbers on how many animals are used." At the FDA meeting, representatives from the cosmetics and pharmaceutical trade associations said they did not have any solid estimates either, but it was their impression that use of the traditional test has decreased overall. They contend companies are relying on a modified version of the LD_{50}, in which only 10 animals are used, and on other types of tests. A small and informal survey conducted by Bristol-Myers scientist Thomas E. Hickey showed that some 50 manufacturers of chemicals, cosmetics, and drugs use about 155,000 animals annually. But a company spokeswoman cautioned against extrapolating the figure to a nationwide estimate. The Office of Technology Assessment has just begun a study on the use of animals in experiments, including the LD_{50}, but its findings will not be completed for another year. Until then it is difficult to judge how many animals are used for the test.

According to Hickey's survey and the Pharmaceutical Manufacturers Association, drug companies perform the tests in the belief that they are complying with federal regulations. But at the recent meeting, officials from FDA declared repeatedly that the agency does not require the LD_{50} to meet safety standards. The FDA "does not have any regulation specifying the need for LD_{50} testing," stated Gary Flamm of the FDA's Bureau of Food. "The LD_{50} test is of limited value and we would prefer other testing" to meet FDA's rules on acute toxicity. The only agencies that do mandate the test, in a modified form, are the Environmental Protection Agency (EPA) and the Department of Transportation.

Raymond Stoll of Sandoz Pharmaceuticals, who represented the Pharmaceutical Manufacturers Association at the meeting, said later "there is considerable confusion" about FDA's requirements for acute toxicity testing. "The meeting was the first time FDA stated its position clearly," he said. “The misunderstanding is so widespread that the agency is planning to publish a notice in the *Federal Register* sometime early next year to clarify its position.

Although EPA requires manufacturers of pesticides and toxic substances to test their products using the LD_{50} method, officials stressed that the agency is only interested in a rough estimate. A test using fewer animals than the traditional procedure "is often adequate," said William Burnham of EPA's Office of Toxic Substances. The agency, he said, supports the development of in vitro tests, but, as yet, no alternatives to animal testing are acceptable.

A hapless official from the Department of Transportation’s Office of Hazardous Substances said his office has been besieged with more than 1000 letters in the past year, protesting the agency's alleged requirement for LD_{50} testing. In fact, the department does not require the traditional test, but a modified version of it that generally requires only ten animals. With the information, the department determines how a substance such as a chemical should be shipped. Department scientist George Cushmac added that by the time a manufacturer applies for permission to ship, it has usually already conducted a pared-down version of the LD_{50} test for EPA. The EPA data can be recycled to the transportation department, voiding the need for additional testing, he said.

Representatives from animal rights groups were out in force at the meeting, seeking reassurances from the agencies that they would discourage the use of LD_{50} testing. Spira said he was pleased to bear that FDA does not require LD_{50} testing and that the meeting helped to clear up the confusion. It is hard to know what the hullabaloo is all about.

Recommended Citation:

Sun, M. (1983). Lots of talk about LD50. *Science*, *222*(4628), 1106-1106.