

**Subject:** Public comments - in vitro testing methods

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**To:** <niceatm@niehs.nih.gov>

**Conversation:** Public comments - in vitro testing methods

To:

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I am writing in response to the request for public comments regarding the announcement of an independent scientific peer review meeting on the use of in vitro testing methods for estimating starting doses for acute oral systemic toxicity tests, as listed in the Federal Register at the following website:

[http://ntp.niehs.nih.gov/files/NICEATM\\_71\\_FR\\_14229.pdf](http://ntp.niehs.nih.gov/files/NICEATM_71_FR_14229.pdf) .

The use of nonhuman animals in lethal dose testing is unjustified, irresponsible, costly, and needless. The federal government convened an international workshop six years ago to review more effective non-animal cell-based methods, yet the announcement for the upcoming workshop doesn't even mention using cell-based methods to replace the use of animals in lethal dose testing.

The practice of using nonhuman animals to mimic or study human disease is often unreliable, and occasionally leads more scientific investigations astray.

Nonhuman animal studies have not contributed to either the prevention or treatment of cancer:

Ø Irwin Bross, Ph.D., former director of biostatistics at the Roswell Institute for Cancer Research, testified before Congress in 1981 that "[w]hile conflicting [nonhuman] animal results have often delayed and hampered advances in the war on cancer, they have never produced a single substantial advance either in the prevention or treatment of human cancer."

Ø A 1980 editorial in Clinical Oncology asks why so much attention is devoted to the study of [nonhuman] animal tumors when "it is ... hard to find a single common solid human neoplasm [cancer] where

management and expectation of cure have been markedly influenced by the results of laboratory research." D.F.N. Harrison explains that "most cancers behave differently from the artificially produced [nonhuman] animal models," and concluded that "it is in the study of human patients where the relevant answers will be found."

Ø Nonhuman animal tests that attempt to predict which substances cause human cancers have also been shown to be unreliable. A 1981 U.S. Congress Office of Technology Assessment Report on the causes of cancer placed more weight on epidemiological data than on nonhuman animal experiments because its authors argued that nonhuman animal tests "cannot provide reliable risk assessments."

Ø According to a 1977 Nature article, of all the agents known to cause cancer in humans, the vast majority were first identified by observation of human populations.

Nonhuman animal studies have not contributed to the study of neurological diseases:

Ø A 1990 editorial in the journal Stroke noted that of 25 compounds "proven" effective for treating strokes in nonhuman animal models over the last 10 years, none have proven effective for use in humans.

Ø Stephen Kaufman, M.D., reviewed nonhuman animal models of such degenerative neurological diseases as Alzheimer's and Parkinson's and concluded that "[nonhuman] animal models designed to improve our understanding and treatment of these conditions have had little impact, and their future value is highly dubious."

Ø Dennis Maiman, M.D., Ph.D., of the Department of Neurosurgery at the Medical College of Wisconsin noted in the Journal of the American Paraplegia Society in 1988, "In the last two decades at least 22 agents have been found to be therapeutic in experimental [laboratory] spinal cord injury.... Unfortunately, to date none of these has been proven effective in clinical spinal cord injury."

Nonhuman animal studies have not contributed to the study of psychology and addiction:

Ø A review of two clinical psychology journals, Behavior Therapy and the Journal of Consulting and Clinical Psychology, showed that only 0.75 percent of the references were to [nonhuman] animal research studies. Yet in 1986 alone the National Institute of Mental Health funded 350 animal experiments in psychology at a cost of more than

\$30 million.

Ø The Alcohol Studies Center in Scotland stated in 1985 that "[n]othing of clinical relevance has been achieved to date for the vast range of experiments in alcoholism" and that "[nonhuman] animal models of addiction are not relevant to human addiction."

Ø However, in 1995 the National Institute on Alcohol Abuse and Alcoholism spent \$50 million on nearly 300 nonhuman animal experiments dealing with alcohol abuse. In 1995 the National Institute on Drug Abuse spent \$90 million on nonhuman animal experiments involving drug abuse. Yet alcohol and drug abuse treatment centers for human sufferers remain underfunded.

Nonhuman animal studies have proven unreliable in testing therapeutic drugs:

Ø Penicillin kills guinea pigs and hamsters, but is very beneficial for humans.

Ø Thalidomide, a tranquilizer formerly prescribed for pregnant women with morning sickness, caused serious birth defects in more than 10,000 children but does not cause birth defects in numerous species of nonhuman animals.

Ø Acetaminophen (Tylenol), a common human pain reliever, is deadly to cats.

Ø The antibiotic chloramphenicol was thoroughly tested on nonhuman animals before being released for clinical use, but was found to cause an often-fatal blood disease in humans.

Ø Of the 198 drugs that were tested on nonhuman animals in accordance with Food and Drug Administration guidelines between 1976 and 1985, 51.5 percent caused reactions serious enough to result in withdrawal from the market or, more commonly, substantial labeling changes. These reactions included heart failure, respiratory problems, convulsions, kidney and liver failure, and death. A consequence of using inaccurate animal tests is that drugs that pass nonhuman animal trials can be approved for human use and later prove harmful to people; conversely, drugs that fail nonhuman animal tests but might actually be beneficial to humans can be wrongly discarded.

Misleading nonhuman animal tests led to increased risk to humans from delaying our understanding of the effects of smoking and through misleading results in early polio tests:

Ø Nonhuman animal tests designed to induce lung cancer through forced inhalation of tobacco smoke were unsuccessful and cast doubt on human clinical findings, delaying health warnings and possibly costing thousands of lives.

Ø Albert Sabin, M.D., who discovered one of the major polio vaccines, testified before Congress that "the work on the prevention [of polio] was long delayed because of an erroneous conception of the nature of the human disease based on misleading experimental models of the disease in monkeys."

The use of nonhuman animals in health care research can lead to the dangerous transmission of viruses between species:

Ø Some primate viruses, when transmitted to humans, can cause disease and even death. Most scientists now believe that the virus that causes AIDS is a descendent of a virus found in nonhuman primates.

Nonhuman animal studies are not responsible for the genuine advances in human health:

Ø Researchers at Boston and Harvard Universities found that medical measures (drugs and vaccines) accounted for at most between 1 and 3.5 percent of the total decline in mortality in the United States since 1900. The researchers noted that the increase in life expectancy is primarily attributable to the decline in such killer epidemics as tuberculosis, scarlet fever, smallpox, and diphtheria, among others, and that deaths from virtually all of these infectious diseases were declining before (and in most cases long before) specific therapies became available. The decline in mortality from these diseases was most likely due to such factors as improvements in sanitation, hygiene, diet, and standard of living.

Ø The isolation of the AIDS virus, the discovery of penicillin and anesthetics, the identification of human blood types, the need for certain vitamins, and the development of x-rays were made without nonhuman animal experimentation. The identification of risk factors for heart disease--probably the most important discovery for decreasing deaths from heart attacks--was made through human population studies.

Ø John Marley and Anthony Michael wrote in the Medical Journal of Australia in 1991, "Our formal knowledge about the factors that

'cause' disease comes primarily from epidemiological research, in which systematic comparisons are made between selected groups of representative individuals."

Nonhuman animal experimentation squanders precious financial resources:

Ø In 2004, total national health expenditures rose 7.9 percent -- over three times the rate of inflation. Total spending was \$1.9 trillion in 2004, or \$6,280 per person, and is expected to reach \$4 trillion in 2015 according to a 2006 report in Health Affairs. Total health care spending represented 16 percent of the gross domestic product (GDP).

Ø The vast majority of federal health care research funds are channeled through the National Institutes of Health (NIH), whose 2005 budget was approximately \$29 billion, of which about eighty percent goes to actual research projects. According to the NIH, at least 40 percent of its grants currently have a nonhuman animal component. This is an incredible waste of precious financial capital that could be better spent on human clinical and epidemiological studies, prevention initiatives, public health programs, and in vitro tests.

Ø The three leading causes of death in this country today are heart disease, cancer, and stroke--diseases that can very often be prevented. Heart disease and stroke have similar risk factors, including high-fat, meat-based diets; cigarette smoking; high blood pressure; obesity; and sedentary lifestyles. A study presented at the 1975 meeting of the American Public Health Association found the heart disease mortality for lacto-ovo-vegetarians to be only one third that of meat-eaters. Pure vegetarians (vegans) had only one tenth the heart disease rate of meat-eaters.

Ø Cancer may also have a significant preventable component. In 1985 the International Agency for Research on Cancer estimated that as much as 80-90 percent of human cancer is determined by such things as diet, lifestyle (including smoking), and environmental carcinogens.

Ø John Bailer and Elaine Smith from the Harvard School of Public Health and the University of Iowa Medical Center wrote in the New England Journal of Medicine that "thirty-five years of intense effort focused largely on improving treatment [of cancer] must be

judged a qualified failure." They further stated that despite progress against some rare forms of cancer (particularly among patients under 30, accounting for 1-2 percent of total cancer deaths), the overall cancer-related death rate has increased since 1950. They recommended a shift in emphasis from treatment research to prevention research if substantial progress against cancer is to be forthcoming.

Ø The fourth leading cause of death (bronchitis, emphysema, and asthma) also has a very large component that is caused by a preventable factor: cigarette smoking.

Ø In addition, other of the ten leading causes of death--injuries, suicide, AIDS, and homicide--could be reduced through prevention. Clearly, prevention should be a priority for health care funding.

The health of this country could be substantially improved if health care dollars were more appropriately distributed. Nonhuman animal experimentation is currently being inappropriately overfunded at the expense of crucial clinical and epidemiological studies, preventive medicine, public health programs, and in vitro studies.

The citizens of this country don't want any more animals killed in unjustified, irresponsible, costly, needless and immoral lethal dose testing in this country. It is long past time to refine and implement non-animal cell-based methods and to stop poisoning animals to death.

Sincerely,  
Linda Serfass