

Animal Welfare

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The Issue

Animal welfare is a scientific, regulatory, business, ethical and public relations issue. Since the time of Selye the effect of animal stress on experimentation has been recognized by scientists. The Animal Welfare Act, first enacted in 1965 and amended several times since, now mandates USDA regulation of the conduct of animal research in a manner which prevents interference with research. The Food and Drug Administration has reviewed the conduct of animal research through the Good Laboratory Practice (GLP) regulations and assures compliance with USDA regulations. There have been significant advances in cell and tissue culture technique making it possible to use non animal tests as adjuncts or replacements for animal studies. The scientific community also has developed a peer review process of animal research administered by the American Association for the Accreditation of Laboratory Animal Care (AAALAC).

The business impact of the animal welfare issue has been most noticeable in the cosmetic industry where banning the use of animals for testing is used to promote sales. Ethically, veterinarians have always been interested in the relief of animal suffering as expressed in their oath and with conferences and panels developed to study issues such as euthanasia and pain. The public has concern for the use of animals in research as noted in the popular press, letters to legislators, and by a small group who have followed civil disobedience to make their point. The issue of animal rights became more meaningful when the results of a nationwide poll conducted by the Los Angeles Times indicated that 47%

of those polled believe that animals are just like humans. Animal welfare is not an issue that we either want to or can ignore.

Alternatives

The biological screening of a large number of compounds in animals can no longer be scientifically or competitively justified. The selection of the most promising compounds is accomplished by computer modeling, structure activity databases, review of the literature, receptor binding assays and tissue culture. These tests act as adjuncts to animal testing but do not totally replace animal testing because final testing must occur prior to use in animals or man. There are very few alternatives that totally replace animals, but one example is the use of diagnostic test kits for pregnancy diagnosis instead of either the frog or rabbit bioassays. The limulus test for pyrogens which uses the blood of the limulus instead of rabbits is also a replacement test. In toxicology there has been a considerable effort to discover and validate non-whole-animal assays. It is expected that any type of replacement evaluation for specific toxicological effects will involve a panel of tests. Important scientific data are available from assays such as the neutral red assay which provide a measurable endpoint, tissue cultures and slices, toxicokinetic models and structure activity relationships and databases. These sources are presently not satisfactory substitutes for animal studies especially those required to be conducted in the animal health field on the end use species. However, alternative tests can be valuable in selecting compounds least likely to be toxic from a series of compounds intended for eventual animal use. In this manner alternative tests can be used like the Ames test to eliminate

compounds from further testing but not to guarantee safety.

The Regulators

USDA

The USDA presently regulates all facilities that use animals in research, tests or experiments, but their definition of animals presently excludes rats and mice. The regulations require the registration of research facilities and the licensing of dealers and exhibitors. The USDA has promulgated standards for animal husbandry, animal health, facilities, transportation, handling, exercise of dogs and a physical environment to promote the psychological well-being of primates. Records also must be maintained primarily to determine the source of all animals used in research. In 1985 the USDA required that an Institutional Animal Care and Use Committee (IACUC) be established in each research facility. These Committees must consist of at least three individuals and must include a person not affiliated with the research facility in any way and a doctor of veterinary medicine. The Committee must conduct semiannual inspections of all animal study areas and animal facilities. Every six months a review of the program for the humane care and use of animals also must be conducted. The IACUC must review all proposed activities relating to the care and use of animals regulated by the USDA under the Animal Welfare Act. Specific requirements for review are included in the regulations. The USDA conducts unannounced inspections of facilities. Each research facility must submit an annual report including the numbers of animals used in research and an affidavit that the provisions of the Animal Welfare Act are being followed.

AAALAC

AAALAC is a voluntary accrediting group that inspects facilities every three years and requires yearly reports from the facility. Inspections are conducted by a least one member of the AAALAC Council and one other person. The facility must submit a description of their facilities and

program prior to the site visit. The inspection team report is reviewed by the Council on Accreditation which makes the final decision on accreditation. Facilities may be awarded full accreditation with recommendations for improvement, various forms of temporary accreditation based on correction of deficiencies or have their accreditation revoked. AAALAC relies primarily on the Guide for the Care and Use of Laboratory Animals as its primary standard for evaluating programs but other publications are used.

FDA

The FDA considers IACUC activities within the scope of the GLPs because Standard Operating Procedures (SOPs) are required for all study activities. They consider it essential for each facility to have an SOP for their IACUC, and the Quality Assurance Unit (QAU) should inspect IACUC activities. They also have determined that it is inappropriate for QAU personnel to serve as chairman or as a voting member on the IACUC. It is considered to be a conflict of interest because QAU is responsible for monitoring procedures used in the IACUC.

Regulatory Differences

These agencies and organizations that monitor animal research are not consistent in the species, facilities or activities considered. The USDA regulates farm animals only if used in non-agricultural research and does not regulate mice and rats. The FDA is involved with any species used to support safety and efficacy submissions by the company requesting drug approval. The USDA registers research facilities based on physical location and level of control by the business entity. NIH and AAALAC include all species of animals used in research, testing or teaching. NIH only regulates those groups receiving Public Health Service funds, and AAALAC only those that voluntarily seek accreditation. NIH considers contract facilities to be the responsibility of the primary organization as long as federal funds are used by the grant recipient to pay for the services of the contractor. The USDA views

contractors as separate research facilities because they register facilities based on control from a parent corporation. AAALAC will only consider contractors if the animals are owned by the accredited facility or if someone from the accredited facility participates in activities conducted at the contractor's facility. This would not include monitoring studies by quality assurance personnel. How the various agencies view the relationship of contracting facilities to the contractor determines which IACUC must review the protocol. Companies, regardless of which IACUC reviews protocols, are legally and morally responsible to assure a review is conducted. Contracting sensitive or questionable studies does not relieve the company of public criticism; in fact, if a contracting facility comes under public scrutiny for any activity conducted, all of its clients are often subject to the same public criticism.

IACUC Review

If any animals in a study are subject to pain or distress the IACUC must assure anesthetics or analgesics are used or that the investigator has justified the reason for not using them and has determined that no alternative test could be used. In toxicology studies it is often not possible to predict if the animals will experience pain or distress and the question arises as to when the animals will be euthanatized. The USDA also requires animals in pain to be euthanatized at the end of the experiment. IACUC's will commonly question the need of having death as an endpoint of an experiment. Most toxicology studies do have some criteria for moribund animal euthanasia in order to obtain viable tissue and body fluids for analysis. Mutually agreeable criteria for moribund animals are best developed prior to study submission.

Public Opinion

The public has expressed its opinions in the marketplace. This frequently has been seen on environmental issues with those companies considered to be "green" and in political issues such as

doing business with South Africa. The cosmetic industry is an example of where animal rights issues have had a marketing impact. The publication, "Personal Care with Principle", published by the National Antivivisection Society lists those companies which market household and cosmetic products that are "cruelty free" and don't use animals in testing. Companies such as the Body Shop have flourished primarily by promoting their products as cruelty free. Many cosmetic companies have publicly stated they will no longer test products in animals. L'Oreal, the world's largest cosmetic, company just recently announced its ban. Animal welfare issues have resulted in stock holder resolutions at over a dozen major companies including Proctor and Gamble and IBM. The issue of animal rights have been mixed with some politically correct issues. The Physicians Committee for Responsible Medicine, which is an animal rights organization, arranged press conferences with Dr. Spock who denounced the use of cows milk for babies. This same group also has promoted the use of meat-free diets to prevent athero-sclerosis. The use of bovine growth hormone as a biotechnology product has been criticized because of the possible threat to human health and the economic effect on the farmer, but the animal rights concern is that humans are altering animals for their benefit. The animal rights groups have a potpourri of issues from pet napping to vegetarianism that they offer to the public; at least one of the issues is designed to hit a responsive cord in every person. This educational program begins in the formative years with school programs, including a comic book called PETA kids.

The Challenge

Acquiescence to demands to refrain from animal research is not a valid choice for veterinary medicine and pharmaceutical research as it was for the cosmetic industry. Veterinary medicine, unlike the cosmetic industry, is dependent upon new and novel treatments and medications that can only be discovered and determined to be a safe utilizing

animal experiments. It is hard to understand why veterinarians would oppose animal research. Is it possible that we have failed to educate them about how veterinary drugs are discovered and brought to the clinics? Do we include this as part of the veterinary curriculum or even as part of a visit to a pharmaceutical company? The elimination of animal testing for development of therapies that benefit many animals is one of the hardest concepts for animal rights groups to convince the public. Why are we not telling this to the public? A recent publication distributed by the Foundation of Biomedical Research called "Research Helping Animals" tells this story very effectively. We need to make this message available to the youth of today if we are ever to be given the opportunity to continue to benefit animals. We must also continue to strive to reduce animal research wherever possible and to conduct it in the most humane manner possible. As an industry and as researchers we must remember that animal research is not a right but a privilege that we must not abuse.