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I. Introduction

Federal regulation of animal use in biomedical research and laboratory testing is a subject which receives periodic attention by lawmakers and the interested public. We are nearing the end of a current cycle in which significant changes have been made in the major systems of regulation. There have been recent amendments to the Animal Welfare Act (AWA),[1] and to the Public Health Service (PHS) policies regulating animal use by PHS grantees.[2] Attention should now focus upon methods to promote the use of alternatives to testing of animals, especially in the field of toxicological testing, and upon ways to increase the effectiveness of self-regulation.

The federal system of regulation is quite extensive, and efforts to consider ideal systems must take into account the reality of what already exists. The basic premise by proponents of animal testing is that testing is necessary and provides a social benefit which exceeds the "costs," particularly when there is adequate assurance of humane care for the animals. Further amendment of the current system will invaria-

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1. 7 U.S.C. §§ 2131-2156 (1982 & Supp. II 1984). The AWA was amended by the Food Security Act of 1985, Pub. L. No. 99-198, 99 Stat. 1354 (codified as amended at 7 U.S.C. §§ 2131-2157 (Supp. III 1985)).

2. *See infra* note 55 and accompanying text.

bly impose additional "costs," (any change in a regulatory program involves both direct and indirect costs associated with adapting to the change) which may not be justified by the incremental benefit.

This article describes and analyzes the major federal systems of regulation of animal use in research and testing. These include the Animal Welfare Act, the PHS policies followed in PHS-funded research activities, and federal regulations applicable to animal testing of products regulated by the United States Food and Drug Administration (FDA) and Environmental Protection Agency (EPA). State laws and regulations are beyond the scope of this article. In addition the article discusses three avenues of improvement in animal welfare regulation: use of alternative methods to animal testing; increased enforcement of the existing regulations; and increased use of self-regulatory programs.

II. Animal Welfare Act

The Animal Welfare Act (AWA) establishes the federal legislative framework for the regulation of animal testing.[3] Administered by the United States Department of Agriculture (USDA), the statute was first passed in 1966,[4] was amended in 1970,[5] and again in 1976.[6] Further amendments to the AWA were passed by the 99th Congress as part of the Food Security Act of 1985,[7] and became effective on December 24, 1986. The AWA is essentially comprised of three components: licensing/registration requirements; standards which govern the handling of laboratory animals; and the authority to inspect, investigate, and enforce violations of the AWA.

A. *Licensing/Registration Requirements*

The regulatory system that Congress has established re-

3. 7 U.S.C. §§ 2131-2157 (1982 & Supp. III 1985).

4. Laboratory Animal Welfare Act, Pub. L. No. 89-544, 80 Stat. 350 (1966).

5. Animal Welfare Act of 1970, Pub. L. No. 91-579, 84 Stat. 1560.

6. Animal Welfare Act Amendments of 1976, Pub. L. No. 94-279, 90 Stat. 417.

7. Food Security Act of 1985, Pub. L. No. 99-198, 99 Stat. 1354 (codified as amended at 7 U.S.C. §§ 2131-2157 (Supp. III 1985)).

quires licensing of animal dealers and exhibitors.[8] Research facilities, as well as handlers, carriers, and unlicensed exhibitors are not required to obtain a license per se. but are required to register with the USDA.[9] The regulation of laboratory animals used in research or testing is accomplished primarily by the AWA's regulation of research facilities, which are defined as

> any school (except an elementary or secondary school), institution, or organization, or person that uses or intends to use live animals in research, tests, or experiments, and that (1) purchases or transports live animals in commerce, or (2) receives [federal] funds . . . for the purpose of carrying out research, tests, or experiments. . . .[10]

The AWA also imposes commercial record keeping requirements upon dealers, exhibitors, research facilities, intermediate handlers, and carriers.[11]

B. *Standards for Care and Handling of Animals*

The AWA directs the USDA to promulgate standards "to govern the humane handling, care, treatment, and transportation of animals by dealers, research facilities, and exhibitors."[12] The standards are required to include "minimum requirements with respect to handling, housing, feeding, watering, sanitation, ventilation, shelter from extremes of weather and temperatures," and to assure "adequate veterinary care, including the appropriate use of anesthetic, analgesic, or tranquilizing drugs, when such use would be proper in the opinion of the attending veterinarian of such research fa-

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8. 7 U.S.C. §§ 2133, 2134 (1982).

9. 7 U.S.C. § 2136 (1982). *See* 9 C.F.R. §§ 2.25-.28 (1986). Although federal research laboratories do not come within the definition of research facilities and are not subject to registration and other provisions applicable to research facilities, they are required to comply with humane standards issued by USDA, 7 U.S.C. § 2144 (1982).

10. 7 U.S.C. § 2132(e) (1982). A 1985 General Accounting Office (GAO) report indicates that in 1983 there were 3379 research sites subject to AWA regulations. *See infra* note 119.

11. 7 U.S.C. § 2140 (1982).

12. *Id.* § 2143(a).

cilities."[13] In addition, the statute provides for separation by species when the USDA "finds such separation necessary for the humane handling, care, or treatment of animals."[14] These provisions were significantly expanded in the 1985 amendments, which are discussed below.[15]

The statute also expressly states that it does not authorize USDA to regulate the design or performance of "actual research or experimentation by a research facility."[16] However, each research facility is required, at least annually, to show "that professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, during experimentation are being followed by the research facility. . . ."[17] The AWA also requires all federal laboratory animal facilities to comply with the humane standards and other requirements established by USDA for research facilities.[18]

C. *Enforcement of the AWA*

The AWA authorizes the USDA to undertake investigations or inspections to determine whether those subject to the statute are violating any provision of the AWA or any regulation or standard promulgated under the statute.[19] In addition, the USDA "shall, at all reasonable times, have access to the places of business and the facilities, animals, and those records required to be kept . . . of any such dealer, exhibitor, intermediate handler, carrier, research facility, or operator of an auction sale."[20] Criminal penalties can be imposed for activity interfering with the performance of official duties under the AWA.[21]

The AWA also provides authority for assessment of civil

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13. *Id.*
14. *Id.*
15. *See infra* notes 26-34 and accompanying text.
16. 7 U.S.C. § 2143(a) (1982).
17. *Id.*
18. *Id.* § 2144.
19. *Id.* § 2146(a).
20. *Id.*
21. *Id.* § 2146(b).

penalties and issuance of cease and desist orders with respect to any violation of the statute or any rule, regulation, or standard promulgated by USDA.[22] Due process procedures require that before a penalty can be assessed or a cease and desist order issued, the aggrieved party must have notice and an opportunity for an administrative hearing. An unfavorable administrative decision may be appealed to the appropriate United States Court of Appeals.[23] Criminal penalties of imprisonment up to one year, a fine of not more than one thousand dollars, or both, may be imposed upon conviction for a knowing violation of any statutory provision.[24]

D. *The 1985 Amendments to the Animal Welfare Act*

The 1985 amendments to the AWA represent the culmination of a legislative effort over the past several years to improve the Animal Welfare Act.[25] The amendments expand

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22. 7 U.S.C. § 2149(b) (1982). Civil penalties of up to $1,000.00 may be assessed for each violation; each additional day the violation continues constitutes a separate offense. *Id.* A knowing failure to obey a cease and desist order is subject to a civil penalty of $500.00 for each offense; each additional day the failure to obey continues constitutes a separate offense. *Id.* The 1985 amendments to the AWA increased the monetary amounts which may be assessed: civil penalties are increased to $2,500.00 for a violation; and imposition of a $1,500.00 fine may be assessed for a knowing failure to obey a cease and desist order, 7 U.S.C. § 2149(b) (Supp. III 1985).

23. 7 U.S.C. § 2149(c) (1982).

24. *Id.* § 2149(d). Fines have been increased to $2,500.00 under the 1985 legislation, 7 U.S.C. § 2149(d) (Supp. III 1985).

25. In July, 1983 several congressional hearings were held in the Senate to discuss a bill which would amend the Animal Welfare Act to ensure the proper treatment of laboratory animals. S. 657, 98th Cong., 1st Sess., 129 Cong. Rec. 2013 (1983). Senator Dole introduced the bill, which was co-sponsored by Senators Melcher, Randolph, Heinz, Percy, and Stevens. The bill was subsequently referred to the Committee on Agriculture, Nutrition, and Forestry. A similar bill was introduced in the House of Representatives by Congressman Brown in May, 1984, co-sponsored by Congressman Foley. H.R. 5725, 98th Cong., 2d Sess., 130 Cong. Rec. 2453 (1984). The House bill was subsequently referred to the Committee on Agriculture. No further action was taken on those bills during that legislative year.

On June 4, 1985 Senator Dole and Congressman Brown reintroduced the animal welfare legislation in their respective houses of Congress. S. 1233, 99th Cong., 1st Sess., 131 Cong. Rec. 7394 (1985); H.R. 2653, 99th Cong., 1st Sess., 131 Cong. Rec. 3808 (1985).

The omnibus agriculture report which was presented to the Senate, S. Rep. No. 145, 99th Cong., 1st Sess., *reprinted in* 1985 U.S. Code Cong. & Ad. News 1676, did

and make more explicit the statutory requirements for humane standards to minimize animal pain and distress associated with experimental procedures.[26] New USDA standards required by the amendments will expressly direct the principal investigator to consider alternatives to any procedure likely to produce pain or distress in an experimental animal.[27] For any research facility practice which could cause pain to animals, the amendments require the USDA to issue revised standards for: (1) consultation with a doctor of veterinary medicine in planning the procedures; (2) the use of tranquilizers, analgesics, and anesthetics; (3) pre-surgical and post-surgical care; (4) prohibition on the use of paralytics without anesthesia; and (5) the withholding of tranquilizers, anesthesia, analgesia, or euthanasia when scientifically necessary for only

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not contain the AWA animal welfare legislation. However, on October 28, 1985 the animal welfare provisions were added to the bill as amendments. S. 1714, 99th Cong., 1st Sess., 131 Cong. Rec. 14,246-50 (1985). The House Report, H.R. 271, 99th Cong., 1st Sess., *reprinted in* 1985 U.S. Code Cong. & Ad. News 1103, did not contain such legislation. The Senate amendment was incorporated into the House Conference Report, H.R. Conf. Rep. No. 447, 99th Cong., 1st Sess. 592-98 *reprinted in* 1985 U.S. Code Cong. & Ad. News 1103, 2518-24, and became law as part of the Food Security Act of 1985. 7 U.S.C. §§ 2131-2157 (Supp. III 1985).

26. 7 U.S.C. § 2143(a)(3)(A) (Supp. III 1985).

27. *Id.* § 2143(a)(3)(B). The language seems to indicate that alternatives only need to be considered by regulated facilities when pain and distress are likely to be inflicted upon a experimental animal. The legislative history indicates that the issue of alternatives should not be construed so narrowly. The House Conference Report in discussing the Senate's findings declared that:

> methods of testing that do not use animals are being and continue to be developed which are faster, less expensive, and more accurate than traditional animal experiments . . . and further opportunities exist for the development of these methods of testing; measures which eliminate or minimize the unnecessary duplication of experiments on animals can result in more productive use of Federal funds. . . .

H.R. Conf. Rep. No. 447, 99th Cong., 1st Sess. 592 *reprinted in* 1985 U.S. Code Cong. & Ad. News 1103, 2518. The Congressional intent to seek alternatives is manifested by the statement, "[t]he Conference intends that the adequacy of efforts to develop techniques that reduce or eliminate the use of animals be a matter of continuing concern and attention." *Id.* at 2519. Thus, on a broader scale the Congress has acknowledged that alternative methods are being pursued which could cover a broader range of activities. In addition the possibility that federal funding may restrict the type of experiments a facility may undertake could further encourage the development of alternatives.

the necessary period of time.[28] The revised standards will also restrict the use of an animal in more than one major operative experiment. [29]

Under the new legislation, research facilities must show, upon inspection and in reports at least annually, that professionally acceptable standards governing care and treatment of animals are being followed.[30] The facility must provide the USDA information on its procedures likely to produce pain or distress and assurances demonstrating that the principal investigator considered alternatives.[31] The research facility must also provide assurances satisfactory to USDA that the facility is adhering to the other USDA standards including those described in the new legislation.[32] If the facility deviates from any humane standard, an explanation must be given.[33] It may be presumed that these more stringent requirements for inspections and annual reports will be amplified in regulations to be issued by USDA, enhancing USDA's effectiveness in enforcing the AWA.

Another major change instituted by the 1985 legislation is the requirement that each research facility establish at least one institutional animal committee to assess animal care, treatment, and practices in experimental research at the research facility, and to represent societal concerns regarding the welfare of animal subjects used at the facility.[34] The committee will be required to inspect, "at least semiannually all animal study areas and animal facilities," and review research practices and animal conditions, to assure that pain and distress to animals is minimized in compliance with statutory re-

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28. 7 U.S.C. § 2143(a)(3)(C)(Supp. III 1985).

29. *Id.* § 2143(a)(3)(D). Only in instances of scientific necessity or other special circumstances can the USDA allow the reuse of an animal. *Id.*

30. *Id.* § 2143(a)(7)(A).

31. *Id.* § 2143(a)(7)(B)(i).

32. *Id.* § 2143(a)(7)(B)(ii).

33. *Id.* § 2143(a)(7)(B)(iii).

34. *Id.* § 2143(b)(1). This new statutory requirement is based on a similar provision in Section B of the Public Health Service (PHS) policies for PHS-funded research. *See infra* note 55. Similar committee requirements are imposed on federal research facilities by the Food Security Act of 1985, 7 U.S.C. § 2144 (Supp. III 1985).

quirements.[35] The committee will also file with the facility an inspection certification report of each inspection which includes reports of any violations of standards or assurances, reports of deficient conditions for animal care or treatment, any deviations from approved protocols that adversely affect animal welfare, and any corrections made after notification to the facility.[36] These inspection certification reports must remain on file for at least three years at the research facility and be available to USDA inspectors and any federal agencies which fund animal research at the facility.[37] The institutional animal committee is required to notify the administrative representative of the research facility of any deficiencies or deviations it discovers, and if the deficiencies or deviations remain uncorrected, the committee is directed to notify the USDA's Animal and Plant Health Inspection Service (APHIS), and the federal funding agency.[38]

The 1985 legislation also provides increased opportunities to improve the welfare of laboratory animals through education. The USDA is directed to establish an information service at the National Agricultural Library to provide information "which could prevent unintended duplication of animal experimentation."[39] In addition, information "on approved methods of animal experimentation, including methods which

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35. 7 U.S.C. § 2143(b)(3) (Supp. III 1985). The requirement for inspections extends to the USDA which is required to inspect each research facility at least once each year. The USDA also is required to conduct follow up inspections as may be necessary until all deficiencies or deviations from standards are corrected. *Id.* § 2146.

36. *Id.* § 2143(b)(4)(A)(ii).

These reports are not readily accessible to the public, in fact the release of any confidential information by a member of an institutional animal committee is unlawful, including information pertaining to "trade secrets, processes, operations, style of work, or apparatus . . . [or] the identity, confidential statistical data, amount or source of any income, profits, losses, or expenditures," of the research facility. *Id.* § 2157. This provision is totally new, added by the 1985 amendments.

37. *Id.* § 2143(b)(4)(B).

38. *Id.* § 2143(b)(4)(C). APHIS is the agency which administers the AWA. *See infra* notes 41-55 and accompanying text.

39. 7 U.S.C. § 2143(e)(2) (Supp. III 1985). Furthermore the amendments require the training of scientists, animal technicians, and other personnel involved with animal care and treatment at a research facility, including instruction on research or testing methods that minimize or eliminate the use of animals, or limit animal pain or distress. *Id.* § 2143(c).

could . . . reduce or replace animal use [and] minimize pain and distress to animals, such as anesthetic and analgesic procedures," will be provided by the National Agricultural Library in cooperation with the National Library of Medicine.[40]

E. *Administration of the AWA*

The Animal Welfare Act (AWA) is administered by the Animal and Plant Health Inspection Service (APHIS), within the USDA regulations implementing the AWA are codified in Title 9 of the Code of Federal Regulations (CFR).[41] USDA regulations define "animal" to include any live or dead dog, cat, monkey (nonhuman primate mammal), guinea pig, hamster, rabbit, or any other warm-blooded animal used for research, testing, experimentation or exhibition purposes, but exclude birds, rats, and mice.[42] The regulations implement the licensing provisions for dealers, exhibitors and operators of an auction sale and the registration provisions for research facilities, carriers, and intermediate handlers. Unlike licensing, registration is accomplished without need for prior demonstration of compliance with the humane standards.[43] However, the registrant, including any research facility, is required to acknowledge receipt of a copy of the standards and to agree to comply with them.[44]

Research facilities are required by USDA regulation to submit an annual report showing that professionally acceptable standards governing the care, treatment, and use of animals were followed during the previous year.[45] The annual re-

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40. *Id.* § 2143(e)(2). Congress apparently intended, through establishment of the information service at the National Agricultural Library, that all investigators be provided ready access to methods of research and testing involving fewer or no animals or reduced pain or distress. H.R. Conf. Rep. No. 447, 99th Cong., 1st Sess. 596 *reprinted in* 1985 U.S. Code Cong. & Ad. News 1103, 2522.

41. 9 C.F.R. §§ 1.1-167.10 (1986).

42. *Id.* § 1.1(n).

43. *Id.* § 2.3. Licensing applicants are expressly required to demonstrate compliance with the standards prior to the issuance of the license, but registration applicants are not subject to a similar regulatory requirements. *See infra* note 44.

44. 9 C.F.R. § 2.26 (1986).

45. *Id.* § 2.28. Federal agency laboratories which use live animals in research, tests, or experiments are also required to submit annual reports under the USDA

port sets forth the common names and numbers of animals involved in research which is divided into three categories: (1) research involving no pain, distress, or use of pain-relieving drugs; (2) research involving pain or distress and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used; and (3) research involving pain or distress and for which the use of anesthetic, analgesic, or tranquilizing drugs would adversely affect the procedures, results, or interpretation of the research.[46] In the latter case, the report must include a brief statement explaining the reasons why drugs were not used. [47] The annual report also must currently include a certification by the attending veterinarian or an institutional animal committee, that the "type and amount of anesthetic, analgesic, and tranquilizing drugs used on animals during an actual research, testing, or experimentation was appropriate to relieve pain and distress of the subject animals."[48]

The USDA regulations establish detailed standards for the humane handling, care, treatment, and transportation of animals, with which dealers, exhibitors, and research facilities are required to comply.[49] Separate standards have been published for dogs and cats, guinea pigs and hamsters, rabbits, nonhuman primates, marine mammals, and other warm-blooded animals.[50] Each set of specifications includes facility and operating standards, animal health and husbandry standards, and transportation standards.[51]

The USDA standards are not intended to interfere with

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regulations. *See infra* note 46.

46. 9 C.F.R. §§ 2.28(a)(2)-(4) (1986).

47. *Id.* § 2.28(a)(4).

48. *Id.* § 2.28(a)(5). These current requirements will be affected by the 1985 amendments. *See supra*, note 31. USDA regulations also require research facilities to maintain specified records concerning live dogs or cats in its possession or under its control, 9 C.F.R. § 2.76 (1986).

49. *See generally* 9 C.F.R. §§ 3.1-.142 (1986).

50. *See generally* 9 C.F.R. §§ 3.1-.17 (Dogs and Cats), §§ 3.25-.41 (Guinea Pigs and Hamsters), §§ 3.50-.66 (Rabbits), §§ 3.75-.91 (Nonhuman Primates), §§ 3.100-.118 (Marine Mammals), §§ 3.125-.142 (Other Warm-blooded Animals) (1986).

51. *See, e.g.*, 9 C.F.R. §§ 3.1-.4 (Facilities and Operating Standards), §§ 3.5-.10 (Animal Health and Husbandry Standards), §§ 3.11-.17 (Transportation Standards) (1986), which are illustrative.

the type of research a research facility undertakes, the protocol for such research, or the method of performance of research. Rather, the standards are intended to establish basic minimum criteria for human handling, care, and treatment of animals within the context of such research as is being done by that facility. For example, the standards include provisions for adequate veterinary care, which includes the use of anesthetic, analgesic, or tranquilizing drugs.[52] The regulations, however, specify only that the use of these drugs shall be in accordance with currently accepted veterinary medical practice "consistent with the protocol or design of the experiment."[53] Additionally, it "shall be incumbent upon each research facility through its animal care committee and/or attending veterinarian to provide guidelines and consultation to research personnel with respect to the type and amount of tranquilizers, anesthetics, or analgesics recommended as being appropriate for each species of animal used by that institution."[54] The standards therefore permit a relatively wide degree of discretion regarding the use of such drugs in research facilities.

III. Public Health Service/National Institutes of Health Policies

A second major source of laboratory animal protection lies in the policies of the Public Health Service (PHS) regarding research funded by that agency.[55] In addition, the National Institute of Health (NIH), a component of PHS, has sponsored a guide for the care and use of laboratory animals

52. In each of the sections of applicable regulations in 9 C.F.R. §§ 3.1-.142 (1986), a provision for veterinary care is included. *See, e.g.*, 9 C.F.R. § 3.10(1) (1986).

53. 9 C.F.R. § 3.10(c) (1986).

54. *Id.* § 3.10(c)(2).

55. Public Health Service, Public Health Service Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions (1985), *reprinted in* National Institutes of Health, Dep't of Health and Human Services, Pub. No. 23, NIH Guide for Grants and Contracts: Special Edition, Laboratory Animal (June 1985) [hereinafter cited as PHS Animal Policy].

The Public Health Service (PHS) is comprised of the Alcohol, Drug Abuse, and Mental Health Administration, the Centers for Disease Control, the Food and Drug Administration, and the National Institutes of Health. *Id.* § III H.

(NIH Guide),[56] which was initially published in 1963 and thus antedates the Animal Welfare Act. Since 1971 PHS grantees have been required under the PHS policy to provide assurance of compliance with the principles in the NIH Guide.

A. *The Public Health Service Policy*

The PHS requirements are set forth in the Public Health Service Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions (PHS Animal Policy), which was most recently revised in 1985.[57] The PHS Animal Policy incorporates two primary elements for the assurance of laboratory animal welfare: (1) an Institutional Program for Animal Care and Use;[58] and (2) Institutional Animal Care and Use Committees.[59] PHS policies apply to all animal research supported by PHS, with animal being defined as "any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes."[60] Unlike the USDA regulations, rats and mice are not excluded.[61]

Each institution receiving PHS funds for research involving animals must submit detailed information in an Animal Welfare Assurance (Assurance) regarding the institution's program for the care and use of animals.[62] The Assurance

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56. National Institutes of Health, Dep't of Health and Human Services, Guide for the Care and Use of Laboratory Animals, Pub. No. 23, Guide for Grants and Contracts: Special Edition, Laboratory Animal Welfare (Supp. June 1985) [hereinafter cited as NIH Guide].

57. PHS Animal Policy, *supra* note 55. The revised policy became effective December 31, 1985.

58. PHS Animal Policy, *supra* note 55, at IV.A.1.

59. *Id.* at IV.A.3.

60. *Id.* at III.A.

61. *See* 9 C.F.R. § 2.3 (1986).

62. Each PHS awarding unit may not make an award "unless the institution submitting the application or proposal is on the list of institutions that have an approved Assurance on file with OPRR [NIH Office for Protection from Research Risks]. . ." PHS Animal Policy, *supra* note 55, at V.B. In the event an institution is not listed, "the awarding unit will ask OPRR to negotiate an Assurance with the institution before an award is made." *Id.*

An Animal Welfare Assurance must contain the following:

a. a list of every branch and major component of the institution, as well

must identify an institutional official who is ultimately responsible for the institution's program for the care and use of animals, and a veterinarian qualified in laboratory animal medicine who will participate in the program.[63] Institutions also must designate clear lines of authority and responsibility for those involved in animal care and use in PHS-supported activities.[64] The Assurances submitted by the institution are evaluated by the NIH Office for Protection from Research Risks (OPRR) to determine the adequacy of the proposed program. OPRR may approve or disapprove the Assurance or negotiate a revised Assurance with the institution.[65] The Assurance must fully describe the institution's program for the care and use of animals, using the NIH Guide as a basis for developing and implementing the institution's program.[66]

Each PHS-funded institution must appoint an Institutional Animal Care and Use Committee (IACUC), composed of members qualified to oversee the institution's animal program, facilities, and procedures.[67] The revised policy more clearly defines the role and responsibility of institutional animal care and use committees. It requires that institutional

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as a list of every branch and major component of any other institution which is to be included under the Assurance;

b. the lines of authority and responsibility for administering the program and ensuring compliance with this policy;

c. the qualifications, authority and responsibility of the veterinarian(s) who will participate in the program;

d. the membership list of the Institutional Animal Care and Use Committee(s)[1] (IACUC) established in accordance with the requirements set forth in IV.A.3.;

e. the procedures which the IACUC will follow to fulfill the requirements set forth in IV.B.;

f. the health program for personnel who work in laboratory animal facilities or have frequent contact with animals;

g. the gross square footage of each animal facility (including satellite facilities), the species housed therein and the average daily inventory, by species, of animals in each facility; and

h. any other pertinent information requested by OPRR.

Id. at IV.A.1.

63. *Id.* at IV.A.1.b.-c.

64. *Id.*

65. *Id.* at IV.A.

66. *Id.* at IV.A.1.

67. *Id.* at IV.A.3.a.

animal care and use committees have five members, who must include at least: a veterinarian who has program responsibilities for animals at the institution and has training or experience in laboratory animal science and medicine; a practicing scientist experienced in research involving animals; a member whose concerns are in the non-scientific area, and an individual unaffiliated with the institution.[68]

The IACUC reviews then approves or disapproves those sections of funding applications or proposals related to the care and use of animals, determining whether the proposed activities are in accordance with PHS policy, including policies on procedures which involve pain or distress to animals.[69] In addition, the IACUC confirms that the activity will be conducted in accordance with the AWA (if applicable) and that the activity is consistent with the NIH Guide unless acceptable justification for a departure is presented.[70]

The IACUC must review at least annually an institution's program, and inspect, at least annually, all of that institution's animal facilities.[71] The IACUC makes recommendations to the responsible institutional official concerning improvements to the institution's animal program.[72] If deficiencies are found the IACUC report must contain a reasonable and specific plan and schedule for correcting each deficiency. The failure of an IACUC to conduct an annual evaluation and submit the required report to the institutional official can result in PHS withdrawal of its approval of the institution's Assurance.[73]

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68. *Id.* at IV.A.3.b. An individual who meets more than one of the requirements in the categories may be counted toward fulfilling the policy's requirements. However, no committee may consist of less than five members. *Id.* at I.V.A.3.c.

69. *Id.* at IV.C.1.

70. *Id.* The IACUC also has the authority to suspend an activity previously approved if it determines that the activity is not being conducted in accordance with applicable provisions of the AWA, the NIH Guide, the institution's Assurance, or the PHS Animal Policy. *Id.* at IV.C.6.

71. *Id.* at IV.B.1.-2.

72. *Id.* at IV.B.4.

73. *Id.* at IV.B.5.-6. *See also id.* at IV.C.6.-7.

B. *The National Institutes of Health Guide*

Substantive standards for animal care and use in PHS supported research activities are contained in the NIH Guide. Prepared by a committee of the National Research Council,[74] and revised in 1985, the NIH Guide is widely accepted by scientific institutions as a primary reference on animal care and use. The NIH Guide includes sections on institutional policies, laboratory animal husbandry, veterinary care, physical plant, and special considerations. [75] Standards within the veterinary care section provide guidance for the exercise of preventive medicine, diagnosis, treatment, and control of disease, anesthesia, analgesia, surgery, post-surgical care, and euthanasia.[76] The NIH Guide acknowledges the responsibility of scientists to develop and use "scientifically valid adjunctive or alternative methods to animal experimentation."[77] However, the NIH Guide also indicates that it is not intended to "limit an investigator's freedom-indeed, obligation-to plan and conduct animal experiments in accord with scientific and humane principles."[78] The standards in the NIH Guide provide much of the scientific basis for the USDA standards issued under the Animal Welfare Act.

C. *The Health Research Extension Act of 1985*

Prior to 1985, PHS policies were implemented under the general authority of the Public Health Service. The Health Research Extension Act of 1985 (HREA),[79] however, provides specific statutory authority for the establishment of guidelines

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74. Within the National Research Council, the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources promulgates the NIH Guide. The committee functions to coordinate, compile and disseminate information on the care and use of laboratory animals.

75. NIH Guide, *supra* note 56.

76. NIH Guide, *supra* note 56, at 34-39.

77. *Id.* at 1.

78. *Id.* at 1-2. One purpose then of the NIH Guide is to encourage scientists to seek improved methods of animal research without mandating how that result will be reached.

79. Health Research Extension Act of 1985, Pub. L. No. 99-158, 99 Stat. 820 (codified as amended at 42 U.S.C. §§ 281-289h (Supp. III 1985)).

for the proper care of animals to be used in biomedical and behavioral research. Under this statute, new guidelines shall require "the appropriate use of tranquilizers, analgesics, anesthetics, paralytics, and euthanasia for animals in such research; and . . . appropriate presurgical and post surgical veterinary medical and nursing care for animals in such research."[80] The legislation also provides a statutory basis for the animal care committees already required under the PHS Animal Policy.[81] The committees will be required to review the care and treatment of animals at least semi-annually with certification to the director of NIH and reports of violations that remain uncorrected after notification to the institution.[82]

The 1985 statute also provides express authority for the requirement of an Animal Welfare Assurance.[83] Each grant application must include a "statement of the reasons for the use of animals in the research to be conducted with funds provided under such grant or contract."[84] The legislation directs NIH to suspend or revoke grants or contracts if NIH determines that the conditions of animal care, treatment, or use do not meet applicable guidelines and the facility has been notified and given a reasonable opportunity to take corrective action.[85] The rationale for the requirement to state the reasons for the proposed use of animals in the research project is to "allow peer review committees to consider possible alternatives to or duplication of research."[86]

The HREA requires NIH to establish a plan for research into alternative methods of biomedical research and experimentation to reduce the use or number of animals or the pain and distress produced in current methods.[87] NIH is also di-

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80. 42 U.S.C. § 289d(a)(2) (Supp. III 1985).

81. *Id.* § 289d(b)(1). Unlike the current PHS policy, the new statute provides that the committee shall be comprised of no fewer than three members. *Id.* § 289d(b)(2).

82. *Id.* § 289d(b)(3).

83. *Id.* § 289d(c).

84. *Id.* § 289d(c)(2).

85. *Id.* § 289d(d).

86. H.R. Conf. Rep. No. 309, 99th Cong., 1st Sess. 86, *reprinted in* 1985 U.S. Code Cong. & Ad. News 731, 747.

87. Health Research Extension Act of 1985, Pub. L. No. 99-158, 99 Stat. 820,

rected to plan the development of methods which have been established to be valid and reliable, and to take such actions as may be appropriate to disseminate information concerning the valid and reliable alternative methods to scientists and others involved with research or experimentation involving animals.[88]

IV. Federal Regulatory Agencies/Good Laboratory Practices

Laboratory animal welfare is also of concern to federal regulatory agencies which require, in various contexts, submission of toxicological test data. The regulatory programs of the Food and Drug Administration (FDA) mandate in many instances that sponsors of regulated products develop data to support the safety of the product.[89] In order to establish standards for assuring the reliability of this data, FDA issued in 1978 Good Laboratory Practice (GLP) regulations for nonclinical laboratory studies.[90] The FDA's GLP regulations include provisions on animal care facilities, animal supply facilities, and animal care.[91] Requirements for animal care facilities include: standards for the number of animal rooms needed to

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Section 4 *reprinted in* 42 U.S.C. § 289 (Supp. III 1985)(The requirement for the plan was not codified as part of the statute, but appears directly following § 289).

88. *Id.* The conference report of the bill points out that alternative "methods would, in certain instances, provide more accurate research results and reduce the costs of research while concurrently reducing the number of laboratory animals required and reducing the pain and distress to animals involved in such research." H.R. Conf. Rep. No. 309, 99th Cong., 1st Sess. 88, *reprinted in* 1985 U.S. Code Cong. & Ad. News 731, 749.

89. An applicant seeking FDA approval of a new drug is required to submit data and study results demonstrating that the drug is safe and effective for use. 21 U.S.C. § 355(b) (1982 & Supp. III 1985). Before human safety studies are undertaken, FDA regulations require submission of adequate information, typically in the form of animal data, to show that an investigational drug may be safely tested in humans. *See* 21 C.F.R. § 312.1(a)(2) (1986). Sponsors of food additive petitions seeking approval of a new food additive also are required to submit data establishing that the additive may be safely used. 21 U.S.C. § 348(b) (1982). Many instances in which nonclinical laboratory studies involving animal testing may be included in an application to FDA are set forth at 21 C.F.R. § 58.3(e) (1986).

90. 21 C.F.R. §§ 58.1-.219 (1986).

91. *Id.* §§ 58.41-.51.

assure separation or isolation of animals;[92] separate areas for diagnosis, treatment and control of laboratory animal diseases;[93] and facilities for collection and disposal of waste.[94] The facilities requirements are, however, directed more toward assuring the ability to carry out scientifically valid tests than to the humane care and treatment of animals.

The FDA's GLP regulations also include standards for animal care.[95] These standards are intended to assure that the validity of an experiment is maintained and thus are written to address conditions that might interfere with the purpose or conduct of the study. They nevertheless serve to provide some protection to laboratory animals.

A test facility may be disqualified upon a finding of violation of a GLP regulation if the non-compliance adversely affects the validity of the study and other lesser regulatory actions would not be adequate to achieve compliance with the GLP regulations.[96] If a testing facility has been disqualified, non-clinical laboratory studies begun after the disqualification date will not be considered in support of an FDA submission unless the facility has been reinstated.[97] In addition, FDA submissions which contain or rely on any non-clinical laboratory study conducted by the facility prior to the date of disqualification may be examined and the study presumed to be unacceptable, unless the submitter can establish that the study was not affected by the circumstances that led to the disqualification.[98] The FDA regulations also provide for the agency to refuse to consider any particular non-clinical laboratory study if it finds that the study was not conducted in accordance with the GLP regulations, without disqualifying the testing facility as a whole.[99]

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92. *Id.* § 58.43(a)-(b).

93. *Id.* § 58.43(c).

94. *Id.* § 58.43(d).

95. *Id.* § 58.90.

96. *Id.* § 58.202.

97. *Id.* § 58.210(b). A determination under this section does not relieve the applicant of any obligation incurred under any other applicable regulation which requires submission of results of a study to the FDA. *Id.* at § 58.200(b).

98. *Id.* § 58.210(a).

99. *Id.* § 58.215(b).

The Environmental Protection Agency (EPA) also regulates test laboratory activities under its authority arising under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA),[100] and the Toxic Substances Control Act (TSCA). [101] FIFRA, which requires registration of pesticides, generates a substantial amount of toxicological test data.[102] Under FIFRA, EPA has issued regulations modeled closely on the FDA's GLP standards.[103] Animal test data is also generated in the testing of chemical substances under TSCA, and regulated under TSCA's GLP regulations, which are again similar to those promulgated by the FDA.[104]

V. The Future for Animal Regulatory Measures

As the foregoing analysis indicates, the use of laboratory animals in research and testing is far from unregulated. The Animal Welfare Act, as well as other federal regulations and policies, provides a comprehensive system of regulation which appears to include the appropriate elements of a workable regulatory system. Improvements in animal welfare regulation then do not lie in major modifications of the existing system, but rather in facilitating the use of alternatives to animal testing when appropriate alternatives are available, and in increasing the effectiveness of self-regulation by research and testing facilities.

A. *Increased Attention to Alternative Models*

Although substantial progress has been made over the

100. 7 U.S.C. §§ 136-136y (1982 & Supp. III 1985).

101. 15 U.S.C. §§ 2601-2629 (1982 & Supp. III 1985).

102. 7 U.S.C. § 136a (1982 & Supp. III 1985).

103. 40 C.F.R. §§ 160.1-.130 (1985). EPA's FIFRA good laboratory practice standards authorize the agency to refuse to consider as reliable, for purposes of supporting a pesticide registration, any data from a study not conducted in accordance with its regulations. *Id.* § 160.17(a).

104. 40 C.F.R. §§ 792.1-.130 (1985). Noncompliance with TSCA's good laboratory standards is considered a violation of section 15 of TSCA. *Id.* § 792.17(a). In addition, EPA may consider any non-complying study as unreliable for purposes of showing that a substance poses no risk of injury to health or the environment. *Id.* at § 792.17(b).

years in establishing and improving standards for the care and treatment of laboratory animals, an increased awareness and effort is being developed to promote the use of alternatives to animal testing. As described above, the 1985 amendments to the AWA; the HREA; and the revised PHS/NIH policy guidelines all include provisions to encourage the development of alternative methods to animal testing.

The National Research Council[105] recently issued a report prepared at the request of the National Institute of Health concerning models for biomedical research.[106] The report noted that a substantial amount of work has already been done on the use of alternative systems for toxicity testing.[107] The National Research Council report concluded: "[b]iological models or model systems derived from or consisting of nonmammalian organisms, or cell and tissue culture systems derived from vertebrates, can reduce the use of mammals, especially in the early stages of some investigations."[108] However, the authors also found that, "[f]or several aspects of human biology, mammals provide the best, and in some cases the only, biological models. In some instances, primates are the only animals that can serve as models for a specific purpose."[109]

Toxicology is a possible fertile area for use of models other than animal systems. The National Research Council has recommended that:

> The NIH should explore the possibility of creating a clearing-house to encourage the use of non-mammalian model systems for testing the effects of exposures to chemicals of interest to environmental toxicologists. Such a clearinghouse function might, for example, encourage NIH-supported researchers studying nonmammalian sys-

105. The National Research Council is a research arm of the National Academy of Sciences.

106. National Resource Council, Models for Biomedical Research: A New Perspective (1985).

107. *Id.* at 52.

108. *Id.* at 73.

109. *Id.* at 75.

> tems to test chemicals of potential concern as identified by the National Toxicology Program.[110]

The Congress endorsed the findings of this report, which can be found in the legislative history of the 1985 NIH legislation.[111]

Regulatory agencies are aware of the need to consider alternatives to animal testing. In a 1984 internal FDA report, the agency concluded:

> There are many alternative tests being studied and developed throughout the Agency. Although most require more research for validation, some *in vitro* studies are useful as screening tools to provide guidance to determine if additional animal studies are required or can be omitted. Immunochemical and biochemical techniques are being substituted for animals to determine the potency and purity of some biological products. There is excellent potential for developing acceptable alternatives to the use of animals or their reduction in test numbers for some purposes.[112]

However, it is clear that FDA scientists do not foresee that animal testing will be eliminated in the foreseeable future. As the executive summary indicates, "[w]hile much progress is being made on the development of certain alternative test procedures, animals will remain essential to medical and health research, safety determinations, and risk assessment for the foreseeable future."[113]

The Office of Technology Assessment (OTA), a research arm of Congress, recently issued a comprehensive report analyzing the "scientific, regulatory, economic, legal, and ethical considerations involved in alternative technologies in biomedical and behavioral research, toxicity testing, and educa-

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110. *Id.* at 76-77.

111. H. R. Rep. No. 158, 98th Cong., 1st Sess. 43, *reprinted in* 1985 U.S. Code Cong. & Ad. News 672, 714.

112. FDA Agency Steering Committee on Animal Welfare Issues, Final Report to the Acting Commissioner ii (1984).

113. *Id.* at i.

tion."[114] The OTA report noted:

> Government regulatory practices can be read as promoting animal testing, although the laws and practices appear flexible enough to accept alternatives when such tests become scientifically acceptable. To date, regulatory practices have not, in fact, provided a basis for companies to expect that acceptance of alternative methods will be an expedient process. In addition to responding to regulatory requirements, companies conduct animal tests to protect themselves from product liability suits. Here, the necessary tests can exceed government requirements.[115]

The promotion of alternatives to animal research appears to be more of a scientific than legal or regulatory issue. However, it may be possible to encourage use of alternatives by expressly requiring federal agencies to consider, whenever possible, whether an alternative approach put forth by a person submitting toxicology data may be sufficient to achieve the purpose of regulation.

Within federal regulatory agencies, some review of testing guidelines now occurs in keeping requirements up to date, although the purpose of that review is to improve the science rather than to protect animals *per se*.[116] Such a policy could encourage industry to develop alternatives because the barriers to acceptance would be reduced.[117]

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114. Off. of Tech. Assessment, U.S. Cong., Rep. No. OTA-BA-2B, Alternatives to Animal Use in Research, Testing, and Education iii (1986) [hereinafter cited as OTA Report].

115. *Id.* at 12.

116. *Id.* at 21.

117. In pursuing this option:

> it is important to appreciate that the swiftest adoption of alternatives may come about if regulatory agencies avoid mandating specific testing requirements. Requiring specific tests might actually serve as a strong inhibitor to the implementation (and development) of alternative methods. Greater flexibility is achieved when testing requirements are defined at a manner that allows judgment and encourages use of alternative methods. Viewed from this perspective, the adoption of alternatives might be best stimulated by regulatory requirement for evaluation of potential toxic response, such as mutagenicity, rather than a requirement of a specified test for mutagenicity.

Id. at 22.

Use of alternatives to animal testing also presents an enforcement issue. Both the 1985 amendments to the Animal Welfare Act and the Health Research Extension Act of 1985 require animal testing facilities to consider the use of alternatives whenever possible.[118] However, compliance with this requirement depends on both the willingness of facilities to comply and on the ability of the administering agencies (either USDA or PHS) to enforce their requirements in a meaningful way.

The willingness of facilities to use alternatives to animals depends in part on the economic and other incentives to adopt alternative approaches, and on the effectiveness of self-regulatory mechanisms. In many instances, alternatives to animal testing may, at least in the long run, be more cost efficient than animal testing. However, this clearly depends on the development and availability of useable and less costly methodologies.

B. *Enforcement of Animal Welfare Regulation*

The USDA enforces the AWA through a system of inspection and compliance monitoring by area and field offices of APHIS. PHS enforces the Animal Welfare Assurances of its grantees, and FDA and EPA have authority to inspect nonclinical laboratories which they regulate under their GLP requirements. The effectiveness of these enforcement efforts depends on a number of factors, including the frequency and thoroughness of inspection, the ability to follow up on compliance activities directed at deficiencies found during inspection, and the availability or threat of meaningful sanctions in the event that deficiencies are not corrected.

Enforcement issues are a subject of periodic attention. The U.S. General Accounting Office (GAO) issued a 1985 report directed at USDA enforcement activities under the Animal Welfare Program and concluded that a major limitation arises from the funding level for the Animal Welfare Program and its effect on the amount of training given to inspec-

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118. *See supra* notes 27 & 87.

tors and the frequency of inspections.[119] GAO has suggested that "if the Congress decides to continue funding a program, it should consider requiring the Secretary of Agriculture to recover more of the cost of the program from licensees."[120]

PHS, FDA, and EPA activities are even more limited, inasmuch as animal welfare is only one part of the regulatory framework for PHS grants,[121] and the non-clinical laboratory testing FDA and EPA must administrate.[122] The focus of regulation in these areas is much broader and animal welfare is only one part thereof.

It is not reasonable then to expect that given the relatively limited inspection and enforcement which occurs that enforcement activity would focus on the relatively subtle issue of whether alternatives were appropriately considered. Therefore, the best approach to this issue appears to be increased reliance on and improving the effectiveness of self-regulatory efforts, primarily through institutional committees.

C. *Self-regulation*

The key then to improving compliance with animal welfare standards, including consideration of use of alternatives to animal testing, lies in self-regulation. The institutional animal committees currently required under both the AWA and PHS/NIH policies afford an excellent opportunity to increase the effectiveness of self-regulation.[123] In addition, the

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119. General Accounting Office, Pub. No. GAO/RECD-85-8, The Department of Agriculture's Animal Welfare Program, (1985)[hereinafter cited as GAO Report].

The Veterinary Services of APHIS has five regional offices located throughout the country and area offices in most states. However, animal welfare is only a small part of the responsibilities of APHIS veterinary services. *Id.* at 2-3. Indeed, USDA's budget for fiscal 1986 proposed that the Animal Welfare Program be eliminated altogether. *Id.* at 3. It is then unlikely to expect any substantial increases in USDA inspection or enforcement activities in the near future.

120. *Id.* at v.

121. *See* PHS Animal Policy, *supra* note 55.

122. *See generally* 21 C.F.R. §§ 58.1-.219 (1986).

123. There are differences imposed by the different statutes or regulatory policies. The Animal Welfare Act, 7 U.S.C. § 2143(b)(1) (Supp. III 1985), and the Health Research Extension Act, 42 U.S.C. § 289d(b)(2) (Supp. III 1985), require minimum committees of three individuals. The PHS Animal Policy requires five. *See* PHS Animal Policy, *supra* note 68 and accompanying text.

activities of these committees can be tied more closely to formal enforcement activities by the administering federal agencies.

The institutional animal committee can be compared to the institutional review boards (IRB) which have been successfully used for a number of years in the field of protection of human subjects.[124] The IRB system reflects recognition that most effective regulation occurs at the local, self-regulation level, with oversight by the federal agency. IRBs are an integral part of the system for approving human drug research under the jurisdiction of FDA and play a major role in determining particular types of research.[125]

The institutional animal committee can serve the same role (as IRBs) in the animal welfare regulatory area if it is supported by adequate training, by respect on the part of facilities, and by adequate oversight in monitoring by the enforcement agency. As the OTA Report points out, "[t]aken together, the requirements for institutional animal committees contained in the Animal Welfare Act [as amended], the Health Research Extension Act of 1985, and the PHS Policy bring the overwhelming majority of experimental-animal users in the United States under the oversight of a structured, local review committee."[126]

Self-regulation can also include self-use of the NIH Guide and/or accreditation by the American Association for Accreditation of Laboratory Animal Care (AAALAC), a voluntary nonprofit private organization.[127] Accredited institutions in-

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124. An institutional review board (IRB) is a multi-member committee appointed by a local institution to exercise oversight over the institution's activities to the extent those activities impinge upon the welfare of human subjects participating in institutional research. The IRB is intended to function as an independent check on whether a proposed human study contains adequate safeguards for the protection of study subjects and therefore may appropriately be conducted. The IRB also provides continuing review of institutional research activities. For studies which require IRB review, FDA will not consider in a research or marketing permit for a regulated product, any data generated in the study unless the study has been approved by the IRB.

125. *See generally* 21 C.F.R. §§ 56.101-.124 (1986).

126. OTA Report, *supra* note 114, at 45.

127. When a facility has been accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC), the National Institutes of Health

clude hospitals, universities, facilities of the Veterans' Administration (VA), and pharmaceutical manufacturers.[128]

Institutional animal committees might also serve as a conduit for transmittal of information from the federal government to individual investigators, including suggestions for alternative methods as part of its review of animal care and use. As part of a federal implementation effort, the institutional animal committees would both contribute to and draw upon the federal regulatory programs.[129]

VI. Conclusion

The federal system of animal welfare regulation in the biomedical research and testing context is a well-developed system which has undergone substantial recent changes. The recent improvements should have the opportunity to demonstrate their effectiveness before attempting further modifications or wholesale dismantling of the current regulatory programs. From a reality-based standpoint, the keys to improving animal welfare in biomedical research and testing are in the increased availability of alternative methods, which will be used without further legal impetus as they become accepted as scientifically valid, and an increased emphasis on self-assessment and self-regulation, which is in the best interest of the regulated industry as well as the regulatory agencies and public at large.

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accepts the accreditation as assurance that the animal facilities are in compliance with the PHS Animal Policy. *See* NIH Guide, *supra* note 56, Appendix B, Professional and Certifying Laboratory Animal Science Organizations. Institutions which maintain, use, import, or breed laboratory animals for scientific purposes are eligible to apply for accreditation.

As of April, 1985, a total of 483 institutions had received AAALAC accreditation, which require site visits that include interviews, inspection of facilities, and review of policies on records.

128. OTA Report, *supra* note 114, at 16.

129. *Id.* at 21.