“GLP Forum” addresses topics of interest associated with good laboratory practices. We intend this column to be a useful resource for daily work applications. The key objective for the column: Useful information.

Reader comments, questions, and suggestions are needed to help us fulfill our objective for this column. Please send your comments and suggestions to column coordinator Steven Kuwahara at stevekuwahara@yahoo.com or to journal coordinating editor Susan Haigney at shaigney@advanstar.com.

KEY POINTS
The following key points are discussed in this article:

• Good laboratory practice (GLP) animal studies are regulated by GLP regulations (1) and US Department of Agriculture (USDA) regulations (2). USDA regulations are national regulations just like the US Food and Drug Administration regulations
• An institutional animal care and use committee (IACUC) is required for institutions conducting animal studies. The IACUC performs functions similar to those performed by the Institutional Review Board (IRB) in clinical trials, except that the IACUC acts on behalf of animals used in studies or tests
• Responsibility for establishing the IACUC lies with test facility management, such as the chief executive officer of the research facility or the highest ranking executive with direct responsibility for the research facility
• The IACUC must have at least three members. A large test facility with many different types of tests or animals may want a larger committee to distribute the workload and allow for the creation of sub-committees that specialize in certain types of research or testing or in certain types of animals
• At least one member must be a Doctor of Veterinary Medicine (DVM) with expertise with laboratory animals
• The public or independent member is frequently chosen from local community leaders and has no background in experimental animal science so that the individual will be a better representative of the general community
• The public member should be an individual who is literate and easy to educate about procedures and practices in the facility
• Remuneration for the public member typically includes compensation for expenses and payment for time served at the same level as that for the company members on the IACUC. If pay is refused, donations may be made to the church or other organization of the public member
• Training of the members of the IACUC is as important as their selection
• Although the effort of selecting and training the members of a good IACUC may seem high, not expending this effort may prove very costly.

INTRODUCTION
When conducting non-clinical studies on medicinal products, it is important to remember that the GLP regulations (1) are not the only US rules pertaining to the use of animals in research and testing. The US Department of Agriculture (USDA) also has regulations that have an impact on the care and treatment of animals that are used for these purposes. While most of the USDA regulations are aimed at animals that are raised for use as pets or for commercial purposes, some of the regulations apply to all animals, including those used in research and testing by pharmaceutical companies, university and hospital laboratories, or contract organizations. These rules apply to anyone employing animals in any kind of study in the United States. Some of the more naive workers in pharmaceutical organizations and university laboratories take the position that USDA regulations do not apply to them because their work is being regulated by the US Food and Drug Administration. The fact is that USDA regulations (2) are national regulations just like the FDA regulations.

Another frequently heard objection is the claim that the USDA regulations only apply to commercial or research establishments and not to testing laboratories. This is not an acceptable objection because the definition given in 9 CFR 1.1 states the following:

“Research facility means any school (except an elementary or secondary school), institution, 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 funds under a grant, award, loan, or contract from a department, agency, or instrumentality of the United States for the purpose of carrying out research, tests, or experiments: Provided, that the Administrator may exempt, by regulation, any such school, institution, organization, or person that does not use or intend to use live dogs or cats, except those schools, institutions, organizations, or persons, which use substantial numbers (as determined by the Administrator) of live animals the principal function of which schools, institutions, organizations, or persons, is biomedical research or testing, when in the judgment of the Administrator, any such exemption does not vitiate the purpose of the Act.”

Note that this definition does appear to contain an exemption for laboratories that conduct biomedical research or testing, but this exemption must be by regulation. If a laboratory has not received such an exemption from the administrator of the USDA, it should consider itself to be regulated under the Animal Welfare Act.

NEED FOR THE INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)
One of the requirements that is often ignored in pharmaceutical start-up companies and university laboratories is the need for an Institutional Animal Care and Use Committee (IACUC). Subpart C of Title 9 of the Code of Federal Regulations (9 CFR) applies to research facilities, and 9 CFR 2.31 refers to the composition and responsibilities of the IACUC. The IACUC performs functions similar to those performed by the Institutional Review Board (IRB) in clinical trials, except that the IACUC acts on behalf of animals used in studies or tests. The basic requirements under 9 CFR 2.31 are also found in 7 USC 2143(b) wherein the term IACUC is not used, but the committee that is described has the same responsibilities as the IACUC (3). The responsibility for establishing the IACUC lies with test facility
management. The 9 CFR 2.31(a) states, “The Chief Executive Officer of the research facility shall appoint an Institutional Animal Care and Use Committee (IACUC), qualified through the experience and expertise of its members to assess the research facility’s animal program, facilities, and procedures. Except as specifically authorized by law or these regulations, nothing in this part shall be deemed to permit the Committee or IACUC to prescribe methods or set standards for the design, performance, or conduct of actual research or experimentation by a research facility.”

Note that this regulation clearly states that the IACUC does not set standards or methods for the experimental work within the facility. The only methods or standards that it may establish are those required under this regulation. Note also that the responsibility for setting up the IACUC rests with the chief executive officer of the research facility. In a large organization, this may not be the chief executive officer of the company but the highest ranking executive with direct responsibility for the activities of the research facility.

Membership of the IACUC

The regulations have specific requirements for the composition of the IACUC. 9 CFR 2.31(b)(1 & 2) places the responsibility for appointing a committee with at least three members on the shoulders of the chief executive officer of the research facility. They read as follows:

“(b) IACUC membership.

(1) The members of each Committee shall be appointed by the Chief Executive Officer of the research facility;

(2) The Committee shall be composed of a Chairman and at least two additional members…”

These requirements do not prevent the appointment of more than three individuals to the committee. In fact a large test facility with many different types of tests or animals may want a larger committee to distribute the work load and allow for the creation of sub-committees that specialize in certain types of research or testing or in certain types of animals. In fact as given in 9 CFR 2.31(a), the actions of the committee are qualified by the experience and expertise of its members. Therefore, the members of the committee should have the necessary experience and expertise to properly perform their expected functions. It may be necessary to appoint sub-committees to bring specific experience and expertise to bear on a particular problem. It may also be necessary to hire consultants to provide specialized expertise or to perform specialized training.

IACUC Membership Requirements

Requirements are given in 9 CFR 2.31(b)(3) for the individuals who will form the IACUC. It states the following, “(3) Of the members of the Committee: (i) At least one shall be a Doctor of Veterinary Medicine, with training or experience in laboratory animal science and medicine, who has direct or delegated program responsibility for activities involving animals at the research facility…”

This requirement for a Doctor of Veterinary Medicine (DVM) places a requirement on the background of the DVM. The DVM must have training or experience with laboratory animals. A local DVM with a practice covering household pets or only large farm animals may not be acceptable unless there is some evidence that the DVM has worked with laboratory animals. Also, many companies and contract testing facilities require that their DVMs be board certified in veterinary pathology. This is because of the need for necropsies on animals that die during a study and for histopathological studies on tissues from treated animals.

Selecting The Public Member

Requirements for selecting the public member for the IACUC are stated in 9 CFR 2.31(b)(3). The regulation states, “(3)(ii) At least one shall not be affiliated in any way with the facility other than as a member of the Committee, and shall not be a member of the immediate family of a person who is affiliated with the facility. The Secretary intends that such person will provide representation for general community interests in the proper care and treatment of animals…”

This person, often known as the public or independent member, is frequently chosen from local community leaders. The usual practice is to choose someone who has no background in experimental animal science, so that the individual will be a better representative of the general community. At the same time, it is best not to choose an animal rights activist as they are
also biased and do not really represent the attitudes of the community as a whole.

Because of the need to review documents related to the work of the research facility, the public member should be an individual who is literate and easy to educate about procedures and practices in the facility. These individuals are often found among the respected school teachers and ministers of the community. When interviewing potential members it is best to determine their attitudes toward science and the pharmaceutical industry. Individuals who are curious about the activities of the pharmaceutical industry will take an interest in the work of an IACUC. However, those who appear to be willing to accept any kind of work proposed by company personnel will not be helpful. If there should be a later review of a controversial study, it will be very important to be able to show that the public member carefully considered the implications of the work and did not simply act as a “rubber stamp.”

**Public Member Remuneration**

The subject of remuneration can be a difficult issue with respect to the public member. The company members and the DVM will be receiving pay for their service on the IACUC, and the public member should also be paid. The normal practice is to compensate the public member for expenses such as mileage and parking and pay them for their time at the same level as that for the company members on the IACUC. The remuneration should be done in the form of a consultant’s fee so that the public member will not become an employee of the company. Some public members, such as ministers, will refuse any pay beyond reimbursement of expenses. This is good as it helps to support the independence of the public member. Many companies will still compensate the member by making donations to the church or other organization to compensate them for their loss of the public member’s services.

If the activities of the IACUC become extensive or intensive, the public member may need to devote a large amount of time to service on the IACUC or on its behalf, and it is only proper that their compensation should increase proportionally. However, the compensation should not become so large as to appear coercive. This is why the level of compensation should be tied to the amounts received by corresponding company members of the IACUC. Also, by establishing the public member as a consultant, the company can avoid the possibility that the public member might be considered to be a direct employee.

**IACUC LIMITATIONS**

The regulation, 9 CFR 2.31(b)(4), states, “If the Committee consists of more than three members, not more than three members shall be from the same administrative unit of the facility.”

This part of the regulation limits the choice of company members for a large IACUC. The term “administrative unit” is defined in 9 CFR 1.1 as: “Administrative unit means the organizational or management unit at the departmental level of a research facility.” Of course this then raises the question of “What is the departmental level?” given the amorphous structure of many modern organizations. It is probably best to consider this on the level of functional units, headed by a single functional manager. Frequently, the chair of the IACUC will be the head of the test facility, and if the DVM is also employed by the test facility, only one more member of the test facility can be appointed to the IACUC.

However, other company members such as personnel from research and development (R&D), quality assurance, or regulatory affairs departments could be appointed. This is actually helpful for large and active IACUCs by diffusing the requirements for time commitments. It is important to remember the requirement for experience or expertise to qualify the person for service on the committee. Also, additional, non-company DVMs and additional public members may be added to the IACUC.

When assigning work to the IACUC or to its members, it is very important to avoid even the appearance of a conflict of interest. This is why the chair of
the IACUC is usually assigned to the supervisor of a test facility or research group. There have been problems with IRBs where lower ranking faculty members have been assigned to review proposals submitted by senior faculty or other individuals of high standing. In some cases IACUCs have been known to create a subcommittee reporting directly to its chairperson in order to exclude members who had potential conflicts. As far as the public is concerned, all company employees on the IACUC will have potential conflicts of interests as they will be expected to favor work proposed by other company employees. This is where the actions of the public member will be critical as this person must act to balance the assumed favoritism toward the company.

Training IACUC Members
The training of the members of the IACUC is as important as their selection. While the DVM must have prior training or experience with laboratory animal care and medicine, it is not wise to assume that the other members, including the chairperson, will be well versed in the subject of animal welfare. If the work is done in a GLP test facility, familiarity with the GLP regulations will also be important. The training should involve non-company personnel at least some of the time. It is important to avoid inbred thinking and to remember that regulations and attitudes change over time. The initial training on the regulations and company practices could be done by company personnel, but follow-up training, especially on the ethics of animal experimentation, should involve external sources.

FINAL THOUGHTS
Although the effort of selecting and training the members of a good IACUC may seem high, the company should realize that a poor response to an animal welfare issue could be very costly. Bad public relations and the attention of unreasoning animal rights activists could easily create expenses that will exceed the cost of creating a strong IACUC. A carefully selected and well trained IACUC can defend the company’s actions by showing that the company carefully considered its actions before it performed the acts that are in question.

REFERENCES
3. Section 2143. Standards and certification process for humane handling, care, treatment, and transportation of animals, United States Code, Title 7, Chapter 54 – “Transportation, Sale, and Handling of Certain Animals,” Section 2143(b)–Research Facility Committee; establishment, membership, functions, etc., 7 USC 2143(b).

ARTICLE ACRONYM LISTING
CFR Code of Federal Regulations
DVM Doctor of Veterinary Medicine
FDA US Food and Drug Administration
GLP Good Laboratory Practice
IACUC Institutional Animal Care and Use Committee
IRB Institutional Review Board
USDA US Department of Agriculture

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