

# Who's responsible for Offsite Animals?

The number of institutions housing animals at places *other* than their main facility is on the rise. These “offsite” locations include contract laboratories, collaborating universities and other types of research facilities. The explosion in the use of transgenic animals with concurrent space constraints, the globalization of science (exemplified by international corporations), and the rapid pace of research, are just a few of the factors driving this trend. In the months and years ahead, it's likely that the number of institutions sharing animals or housing animals offsite will continue to escalate at an even faster rate.

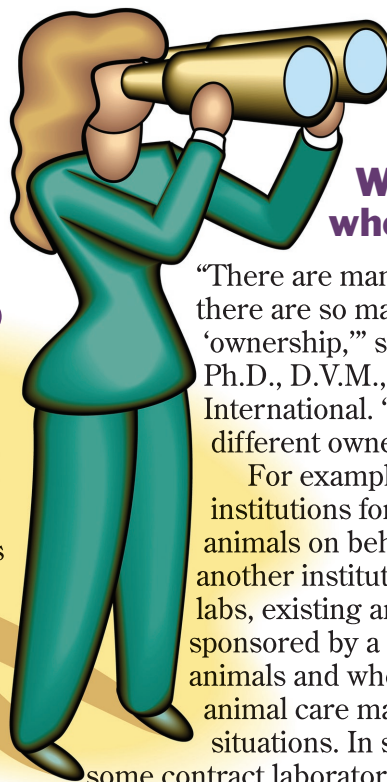
In many cases, keeping animals offsite offers scientific and logistical advantages. But it has also posed some perplexing issues for institutions. Who actually *owns* these offsite animals? Who is ultimately responsible for their well-being? And if the offsite animals are housed at an institution that is *not* accredited by AAALAC International, are there implications for the accredited program?

## What's at stake?

Collaboration among institutions—and sharing animals in the process—improves science. It also helps reduce the overall number of animals used. But this type of collaboration may also make oversight more difficult—especially for institutions that haven't considered their oversight role or other involvement with animals at remote locations.

“Today everybody is sharing animals,” says Dennis M. Stark, D.V.M., Ph.D., Executive Director of Veterinary Sciences for Bristol-Myers Squibb and an AAALAC Council member. “This is not just an industry issue, it's an issue everywhere, including academia.”

“This is an issue that's going to get more challenging as more and more animals are being shuffled back and forth,” says Laretta W. Gerrity, D.V.M., Director of Animal Resources Program at the University of Alabama-Birmingham & VAMC, a former member of AAALAC's Council on Accreditation who is now an ad hoc Consultant to AAALAC. “The question is, ‘who's in charge of those animals when they are at each of those places?’”



## Who's the owner and who's responsible?

“There are many challenges in this area because there are so many gray areas regarding ‘ownership,’” says Kathryn A. Bayne, M.S., Ph.D., D.V.M., Associate Director of AAALAC International. “I receive calls every week posing different ownership scenarios.”

For example, animals may be sent to other institutions for studies. Institutions may buy animals on behalf of a study sponsored by another institution. Or in the case of contract labs, existing animals may be used for a study sponsored by a client. Who legally owns the animals and who is responsible for oversight and animal care may be different in each of these situations. In some instances, such as with some contract laboratories, the contractor requires the sponsoring institution to own the animals. In other cases, the parent institution requires the offsite organization to own the animals.

Gerrity notes that issues of ownership and responsibility may be especially challenging when dealing with primates. For example, if the original owner of a primate is conducting a long-term study and doesn't need the animal for a while, it may loan the animal to another institution to be held, or perhaps used for blood draws or other minor procedures. For a number of reasons—e.g. applying the 3 Rs and the scarcity of some nonhuman primate species—the original institution may wish to retain ownership. The responsibility for decisions regarding the health and welfare of the animal on a day-to-day basis should be determined.

Indeed, in any partnership or contract situation, the issue of who owns the animals—and who will provide oversight and care—should be clearly defined and agreed upon in advance. But there are a number of ways to do this and many variables that will affect final decisions.

## Ownership and proprietary rights to the data

In addition to issues of ownership and responsibility, some institutions—pharmaceutical companies in particular—are working through possible legal issues surrounding animal ownership. Some lawyers representing these companies feel strongly that animals transferred to non-company (or “host”) facilities must remain the property of the parent company. They also want the animals to be labeled with the company's name while residing at the host facility. They believe these measures will help protect future patent rights.

Stark explains that while pharmaceutical companies are eager to have research generated at collaborating institutions, legally owning the animals is risky. He says such agreements between his own institution and collaborating institutions are covered by a ‘materials transfer agreement’ that all parties sign. It defines who owns the animals, what standards of IACUC review are expected, what husbandry and veterinary care will be maintained, and how the animals will be identified.

“Some legal opinions note that in order to retain proprietary rights to data involving transferred animals, the source institution must retain ownership of the animals,” Stark says. “But some of us in the veterinary community feel the institution sponsoring the study should be able to retain ownership of the proprietary information generated from the animals, even if the offsite facility assumes ownership of the animals. The partner facility should be willing to take on the responsibility of providing care and doing it right.”

But while some legal departments are saying they want to own the offsite animals, others are saying they wouldn’t own them under any circumstances.

Stark informally polled his colleagues—industry veterinarians, most of whom work for pharmaceutical companies—on the subject. Among those who responded, the majority indicated that their company would *not* own animals held at other institutions or contract research organizations. Stark notes that if he had polled the company lawyers instead of the veterinarians, he may have gotten a different response.

“The veterinary community is pushing for legal departments to *not require* that the parent company maintain ownership,” Bayne observes. But she notes that many lawyers continue to feel that their patent rights may be threatened if they cede ownership to the offsite or contract facilities. “A lot of these feelings are likely due to the complexities of international intellectual property laws,” Bayne adds.

For the foreseeable future, negotiations on this topic between the animal care community and legal departments are likely to continue.

## Complying with rules and guidelines

Whether your institution owns the animals at the host facility or not, your institution will, in most cases, be subject to certain rules or guidelines. *Which* rules or guidelines apply depends on the organizations to which you are accountable—the USDA, AAALAC International, OLAW (the Office of Laboratory Animal Welfare), plus state and local regulations.

“A lot of times, when people get into trouble it’s when the institutions don’t understand the rules,” says Gerrity. “It’s not a case of people disregarding them.”

Each of the three organizations—USDA, AAALAC International and OLAW—have slightly different views on the issue of offsite animals ...

## The USDA perspective: responsibility follows ownership

According to the USDA, in most cases responsibility for offsite animals is assigned to the institution that owns the animals. But if more than one facility is involved with a particular research study, USDA places responsibility for the animals being used not only with the institution that is involved in their housing and care, but also with any institution that is involved in the planning and execution of the study itself.

If an institution merely owns the animals being used in a study—but has no input or is not involved in the planning, review, approval, or conduct of the study—then USDA would not hold that institution responsible for those animals. (In fact, if that was the only involvement with animals this institution had, it would not even be required to be registered since it does not meet the regulatory definition of a research facility.) If the owning institution has any say in how those animals were to be used, however, the USDA would then hold them responsible. USDA representatives say the organization has encountered this type of situation several times in recent years, primarily with regard to transgenic animals.

“It’s important to note that to the USDA, ownership encompasses more than just ‘sign on the dotted line’ ownership,” Gerrity says. “They also want to know who is in *control* of the animals.” She adds that in making this determination, USDA will look at considerations such as: Who wrote the protocol? Whose IACUC is doing the review? Who is conducting the hands-on procedures? Who houses the animals? And who provides the daily care?

Some believe that the USDA is starting to take a closer look at animals in offsite facilities.

“I think over the last three or four years we’ve seen more USDA inspectors paying increased attention to animals at contract facilities,” notes James F. Taylor, D.V.M., M.S., Director of the Office of Animal Care and Use at the National Institutes of Health (NIH), and member of AAALAC’s Council on Accreditation. This means that institutions will need to make sure that offsite facilities using regulated animals (animals other than rats, mice and birds) are registered with the USDA if they are located in the United States. And the parent institution needs to be able to clearly document ownership and who is responsible for monitoring their care.

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## Ownership and AAALAC's perspective

Like USDA, AAALAC International follows ownership in terms of defining who is responsible for animals at an offsite facility. If an accredited institution

does not own the animals—if they just own the data that results from the studies conducted using those animals—AAALAC does not *require* oversight by the accredited program. However, they should ensure that they are partnering with reputable organizations.

Bayne says AAALAC site visitors typically see two scenarios ...

### AAALAC's Rules of Accreditation regarding contract facilities

“Institutions may have contractual arrangements for certain aspects of their animal care activities with other animal care agencies/facilities. In some situations, an accreditable unit may issue a comprehensive contract whereby the contractor provides most or all specified facilities, services, personnel, animals, etc., and the animals are owned by the contractor. In this situation, AAALAC International accreditation does not extend to the contracted facilities and their associated animal care programs. However, the accredited unit may have a more limited contract in which the accredited unit owns the animals. In this latter situation, AAALAC International considers those facilities to be an integral part of the institution's animal care program. The services and facilities provided by the contractual arrangement must be included in the application and annual reports, and the facilities will be visited as a part of the institution's original and periodic site visits to determine compliance with AAALAC International standards. Contractual agreements made by AAALAC International accredited institutions or applicants must provide for the inspection of the contracted facilities by AAALAC International site visit teams. If the contract facility is separately accredited by AAALAC International and is currently fully accredited, it will not be necessary to visit that facility during the site visit.”

### If the offsite facility is also accredited ...

“The first scenario is that the parent institution—institution A—has arranged to have research using animals conducted at institution B, and B is also accredited by AAALAC,” Bayne says. “This is an easier scenario to handle.”

During the site visit of the parent institution, the AAALAC evaluators will *not* visit institution B, because B is already on its own AAALAC site visit schedule. “However, this does not mean that institution A should abdicate all responsibility for those animals,” Bayne adds. “We would still expect some level of involvement by institution A's IACUC.”

Although there is nothing in writing and no regulations that require it, AAALAC generally *recommends* that institution A get copies of institution B's IACUC meeting minutes and semiannual reviews *as they relate to A's animals*.

“Institution B may want to keep a lot of information private, but A certainly has a right to see information that pertains to its own animals,” says Bayne.

In sum, if AAALAC is site visiting institution A, and offsite facility B is also AAALAC accredited, AAALAC will *not* visit B during A's site visit. But, AAALAC will expect A's IACUC to maintain awareness of—and appropriate involvement in—the work being done on the animals it owns.

### If the offsite facility is not accredited ...

From AAALAC's perspective, the alternative scenario—when the satellite facility is not AAALAC accredited—is more difficult.

“When institution A owns the animals, and offsite facility B is *not* accredited, A must describe B's animal care and use program and facilities in its own AAALAC Program Description and annual report,” Bayne says. “In this situation, institution B *will* be included in the site visit—specifically, those areas that are related to the animals owned by A. This includes all housing, support and procedure areas.” Even if B is geographically far away, AAALAC will evaluate it as part of A's site-visit process.

But what level of oversight does AAALAC expect the parent institution's IACUC to have over the animals it owns at another institution?

“When the contract or offsite facility is not accredited, we suggest that the parent institution ramp up the intensity of its oversight,” Bayne says. She notes that AAALAC typically recommends that this oversight include a facility inspection as part of the IACUC's semiannual review, along with other forms of long-distance monitoring.

“There's a risk in partnering with non-accredited facilities,” Bayne adds. “The parent institution may be jeopardized because they are linked with that offsite facility. If something happens at the offsite facility—even if it involves animals not owned by the parent institution,

and even if the report is not factual—the negative public perception can spill over to the parent institution.”

This is likely the reason why some institutions, the NIH Intramural Research Program for example, will only contract with other AAALAC-accredited institutions.

“We have many animals placed at other institutions—and the other institutions are all accredited,” says Taylor. “We will only partner with accredited programs—this is one of our own ground rules.”

He adds that his office *does not* expect their animal care and use committees to do site visits of those satellite facilities. “They may choose to do it, but we haven’t made it a policy that they must,” Taylor says. “We do say, however, that they need to have some form of oversight—whether it’s handled by the veterinarian or the project officer—there needs to be someone who can verify that our expectations are being met. But we leave it to the committees to decide how they will do this.”

AAALAC’s own Rules of Accreditation offer some guidelines (see the sidebar on page 8 for details).

## Follow the funding: OLAW’s perspective

OLAW, the Office of Laboratory Animal Welfare, has oversight responsibility for all PHS-funded activities involving animals. Its jurisdiction is based on the source of support, not ownership. Dr. Nelson Garnett, Director of OLAW, emphasizes that, “It’s imperative that PHS-supported institutions that subcontract, collaborate or have other such agreements with other institutions, clearly define respective responsibilities.” The PHS Policy requires that all awardees and performance sites hold an approved Animal Welfare Assurance.\* When an awardee institution does not have an Assurance (and cannot obtain one because it does not have an animal care and use program or an IACUC), OLAW negotiates an Interinstitutional Agreement Assurance of Compliance whereby the awardee institution will rely on the program of an Assured institution.

Assured institutions that wish to subcontract or use performance sites that are *not* Assured also have the option to amend their Assurance to cover the nonassured entity. This effectively subjugates the performance site to the Assured institution and makes the Assured institution responsible for the performance site. Garnett adds, “the Assured institution must then treat the performance site as though it were another component of the institution’s program, with responsibility for occupational health, training, IACUC review, semiannual inspections, and the reporting and other requirements of the PHS Policy.” (OLAW guidance on this is found in NIH Guide notice OD-01-017.)

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*\*Public Health Service (PHS) states that as a condition of receipt of support for research involving laboratory animals, awardee institutions must provide a written Animal Welfare Assurance of Compliance (Assurance) to OLAW describing the means they will employ to comply with the PHS Policy.*

## PHS Policy on satellite facilities

### PHS defines a satellite facility this way ...

“Animal Facility: Any and all buildings, rooms, areas, enclosures, or vehicles, including satellite facilities, used for animal confinement, transport, maintenance, breeding, or experiments inclusive of surgical manipulation. A satellite facility is any containment outside of a core facility or centrally designated or managed area in which animals are housed for more than 24 hours. “

### It also says that a function of the IACUC is to inspect satellite facilities ...

“Functions of the Institutional Animal Care and Use Committee:

As an agent of the institution, the IACUC shall with respect to PHS-conducted or supported activities:

1. review at least once every six months the institution’s program for humane care and use of animals, using the *Guide* as a basis for evaluation;
2. inspect at least once every six months all of the institution’s animal facilities (including satellite facilities) using the *Guide* as a basis for evaluation ...”

### PHS Policy is applied to satellite facilities in this way ...

“This Policy is applicable to all PHS-conducted or supported activities involving animals, whether the activities are performed at a PHS agency, an awardee institution, or any other institution and conducted in the United States, the Commonwealth of Puerto Rico, or any territory or possession of the United States. Institutions in foreign countries receiving PHS support for activities involving animals shall comply with this Policy, or provide evidence to the PHS that acceptable standards for the humane care and use of the animals in PHS-conducted or supported activities will be met. No PHS support for an activity involving animals will be provided to an individual unless that individual is affiliated with or sponsored by an institution which can and does assume responsibility for compliance with this Policy, unless the individual makes other arrangements with the PHS. ...”



“OLAW says that the awardee institution has responsibility for ensuring that all terms and conditions of award, including the PHS animal welfare policy, are met.” Gerrity says. Her institution has investigators in other countries and at other U.S. institutions performing

subcontracted research on behalf of the university.

According to OLAW, Gerrity’s institution maintains some responsibility for those animals because her institution is the PHS awardee institution.

## What can institutions do to ensure proper oversight?

### Think through the issue of responsibility

“Remember that if your institution receives PHS funding, even if you subcontract or conduct research at a performance site, you have a legal responsibility for the federal funding your institution receives,” Garnett says. Part of that responsibility is met by simply ensuring that all performance sites are covered by an appropriate PHS Assurance.

“The IACUC needs to establish its realm of responsibility,” Gerrity says. “IACUC members need to have it clear in their minds what they are responsible for.”

Gerrity’s institution has defined responsibility a bit broader than others. “But our IACUC has said, ‘this is how we’ve defined responsibility for ourselves, based on our interpretation of AAALAC, OLAW, and USDA.’” Gerrity says. “We *voluntarily* set a higher level of oversight—this was not required, it was our choice.”

At the start of any arrangement, IACUCs must answer questions about which committee will have final say in care and use issues. “Determine which committee has priority of review up front,” Stark says. “Is it the person who gave the animal to you and still owns it—or the person using it?”

### Develop clear criteria

Defining the boundaries of responsibility includes setting criteria for determining the IACUC’s role in overseeing animals and studies at offsite facilities. “You have to develop criteria to identify those offsite studies that will require IACUC oversight,” Gerrity says.

For example, some questions to help determine the institution’s role in oversight might include: Will the animals be used for research, teaching and testing? Will they be cared for and used at a site registered with the USDA? Does the site have an approved PHS Animal Welfare Assurance on file with OLAW? Is the program AAALAC accredited?

Many times IACUCs will need to make judgment calls

on what they will track and when. Gerrity sometimes uses what she calls an “off-the-shelf” test to determine the level of oversight needed. If her university has an investigator using antibodies produced at a contract lab, she asks if those antibodies are being produced specifically for that study. If they are, the institution will assume responsibility for overseeing the animals involved in the production of the antibodies. But if those antibodies would be produced anyway (i.e. for use at other institutions), her IACUC labels it a commercial product and leaves the oversight up to the producing site. This approach is consistent with OLAW guidance on custom antibody production contained in a March 8, 1995, OPRR Report (<http://grants2.nih.gov/grants/olaw/references/dc95-3.htm>).\*

Gerrity also suggests that IACUCs clearly think through all issues surrounding ownership and responsibility, including questions about who will pay per diem charges and who will determine treatment for the animals.

“You also need to think about what would happen to the animals if the principal investigator leaves,” Gerrity says. “Will the research continue because it’s a well-developed program and there are lots of people responsible for it? Or will it stop because that one investigator is driving the research and animal use?”

Other decisions include determining which institution has the authority to euthanize the animals (should it become necessary), deciding if the offsite institution will provide their written procedures for their IACUC, veterinary care, husbandry, etc., to the source institution, and also what will happen to animals in the event of a disaster.

*\*OPRR Report 95-02 states “In the case that standard reagent antibodies (e.g. mouse-antihuman) are produced by a commercial supplier using their own resources and offering them for general sale, for example, through a catalogue, the institution may consider the antibodies to be ‘off-the-shelf’ reagents, and the supplier is not required to file an Assurance with OPRR. If, on the other hand, a supplier or contractor produces custom antibodies using antigen(s) provided by or at the request of a principal investigator, the antibodies are considered “customized” and the vendor or subcontractor must file an Assurance with OPRR.”*

### Create detailed agreements

As a member of AAALAC’s Council on Accreditation, Stark has visited several institutions that keep animals at other facilities but have no formal agreement with them.

“While these institutions haven’t faced any problems yet, it would be wise for them to outline the specifics of their arrangements—whose committee is ultimately responsible, what type of animal care and use procedures will be allowed, and so on—so that there’s something in writing,” Stark says. “Then if there’s a problem, it’s covered. Even though the USDA doesn’t require it, you really should do some formal assessment of how things will be handled.”

This can be accomplished by developing a simple contract or letter of agreement that outlines these details and is signed before the animals are shipped out.

“A good contract is going to have reasonable detail on how animal husbandry, veterinary care, and so on, are going to be handled,” Taylor adds.

“Put it in writing,” says Garnett, “that way everyone is clear on who is responsible for what.”

### **Ask for verification of oversight and information on their program—then follow up on a regular basis**

Most institutions know to check the USDA, OLAW and AAALAC accreditation status at offsite facilities where animals will be used. But what else can be done to verify that your animals will receive proper care and use?

Along with developing clear criteria for determining responsibility and oversight, Gerrity suggests that the IACUC also decide what information it wants to request from the offsite facility.

“Ask about their USDA registration, OLAW Assurance, AAALAC accreditation and the IACUC’s semiannual reviews.” She notes that some institutions may be reluctant to share their internal reviews. But as Bayne noted earlier, it is reasonable (and good practice) to ask to see those internal reports that relate directly to your institution’s animals.

“On one occasion, we ran into an institution that only conducted an internal review of protocols every three years,” Gerrity says. “In that case we had to say, ‘sorry we need you to conduct an annual review or we’ll have to take our study elsewhere.’”

Talking to others that have worked with the offsite facility is another good way to find out about their program.

Taylor adds, “My personal feeling is that I like to see institutions find some proactive way of making sure that the partner is doing things the way they should. It’s like any other contractual arrangement—you should have some kind of auditing process to verify that what you’re paying for is what you’re getting.”

Garnett suggests, “Ask for documentation. If the awardee institution is relying on the IACUC review and inspection at another institution, then it’s prudent to obtain evidence that there is appropriate oversight as required by PHS Policy.”

### **Decide how protocols will be reviewed and approved**

Determining how protocols will be reviewed and approved is another decision that needs to be made up front. For AAALAC-accredited institutions, this decision is likely to depend on whether or not the offsite institution is accredited, and its past performance.

If an offsite animal care and use program is *not* accredited, the parent institution can decide whether or not it will accept the protocol being used by the offsite program. In some situations, the IACUC may fully accept

## **Suggested checklist for working with contract and offsite facilities ...**

- Get your IACUC to establish its “realm of responsibility”—when and how it will assume oversight of offsite animals.
- Establish who owns the animals.
- Create detailed agreements (perhaps a contract or letter) when working with offsite programs. Make it clear who owns the animals, whose IACUC is responsible, and who will make the day-to-day decisions about animal care.
- Check your compliance with OLAW and USDA (as necessary), and review AAALAC’s Rules of Accreditation as they relate to offsite animals.
- Ask for information that will verify the quality of the other institution’s animal care and use program. Check their USDA registration, PHS Assurance, AAALAC accreditation status, and internal reviews. Talk to other institutions that have partnered with them in the past.
- Decide how protocols involving offsite animals will be reviewed and approved. A dual review is not required, but some choose to do it—it’s up to the IACUC to decide.
- Consider periodic visits to the site to monitor care and quality.
- Call the AAALAC office if you have additional questions or concerns!

### **Web resources:**

- [www.aaalac.org/rules.htm](http://www.aaalac.org/rules.htm)
- <http://grants1.nih.gov/grants/olaw/olaw.htm>
- [www.aphis.usda.gov](http://www.aphis.usda.gov)

their protocol and find it to be in complete compliance. But Bayne notes that because of slight differences in the animal study proposal forms, some institutions choose to perform a dual review of protocols—the parent institution reviews it, then the IACUC at the offsite program also reviews it.

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