Wire-Bottom Versus Solid-Bottom Rodent Caging Issues Important to Scientists and Laboratory Animal Science Specialists

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Recent emphasis in the National Research Council's *Guide for the Care and Use of Laboratory Animals* and by the Association for Assessment and Accreditation of Laboratory Animal Care, International, related to the availability of bedding in rodent cages raises regulatory and accreditation issues in the toxicology-laboratory setting. This article reviews the results of a recent survey of 12 United States-based pharmaceutical and contract toxicology laboratories. The perceived benefits and issues related to the use of wire-bottom and bedded caging for rodent studies are presented. The 1999 survey showed that more than 80% of the rodents in surveyed toxicology facilities were housed in wire-bottom cages. Long-term budget expenses related to supplies and waste disposal are assessed. Considerable short-term and long-term costs to programs would be associated with a change from wire-bottom to solid-bottom caging. A review of the past and recent literature related to animal preferences and cage-associated animal lesions is included. The importance of IACUC review of caging chosen by the investigative staff is emphasized.

Increasingly, concerns of animal welfare, environmental issues, productivity, cost containment, and improved research and safety testing are influencing the care and use of laboratory animals. In its 1996 edition, the *Guide for the Care and Use of Laboratory Animals* (1) noted the following related to rodent housing, which affects all of the previously noted concerns: "Rodents are often housed on wire flooring, which enhances sanitation of the cage by enabling urine and feces to pass through to a collection tray. However, some evidence suggests that solid-bottom caging, with bedding, is preferred by rodents. Solid-bottom caging, with bedding, is therefore recommended for rodents." The *Guide* continues, "IACUC review of this aspect of the animal care program should ensure that caging enhances animal well-being consistent with good sanitation and the requirements of the research project."

A review of the literature cited in the *Guide* and articles related to the well-being and preferences of rodents revealed a number of interesting associations. The *Guide* cites three references to substantiate rodent preferences for bedded cages (2-4). Although such references do exist, none of those cited in the *Guide* address animal-preference studies; rather, they document lesions associated with wire-bottom housing of rodents.

These three references and others (5, 6) provide evidence of a variety of pathologic changes associated with rodents held in wire-bottom caging. Some microscopic changes to nerve tissue have been documented to occur within weeks of caging rodents on wire-bottom cages (4). Other more obvious lesions required longer periods of housing on wire-bottom caging (2, 3, 5). Some of these same lesions developed independently of animal housing on wire-or solid-bottom caging (3, 5).

Preference testing between solid-bottom caging with bedding and wire-mesh caging has been evaluated in numerous studies (7-12). Only one of these studies reports rodent preference for wire-bottom caging (12). All indicate a preference for housing which includes bedding as part of the environment, especially when animals are resting. Awake, active animals reportedly use wire-bottom sections of caging systems that have both bedded-solid and wire-bottom options. No differences in body-weight gain, water consumption, physiologic data, or ease of handling by technical staff have been reported associated with either caging type (8, 10-12). Differences in caging materials and the presence or absence of bedding have been shown to affect thermoregulation of rats and metabolic responses (13).

With the preceding information as background, a survey of rodent-caging use in the United States was conducted among pharmaceutical and contract toxicology laboratories. The investigator preferences in caging type for rodent housing were documented. The perceived value of either wire- or solid-bottom caging to the scientific study was assessed, and the implications of conversion from wire-bottom caging to solid-bottom caging with bedding were evaluated.

Materials and Methods

The survey. A 1999 survey of four questions (Fig. 1) was distributed to 14 pharmaceutical and 5 contract toxicology laboratories. The survey was specifically directed to the head of toxicology, not the head of laboratory animal science, as the toxicology department was the group actually choosing the caging for their research. Nine of the 14 companies and three of the five contract laboratories that were contacted responded to the survey.

1. On a typical day, what percentage of your company wide Safety and Toxicology study rodents are housed in suspended wire _____%; bedded solid bottom cages _____%

2. What advantages do you see to housing your study rodents in:

   a. solid bottom bedded cages-

   b. suspended wire bottom cages –

3. What disadvantages do you see to housing your study rodents in:

   c. solid bottom bedded cages-

   d. suspended wire bottom cages –

4. Please provide any other comments or insights related to this issue which you feel should be considered before standards, policies or guidelines are changed to address the recommendation in the current Guide.

Figure 1. Content of the survey distributed to toxicology laboratories.

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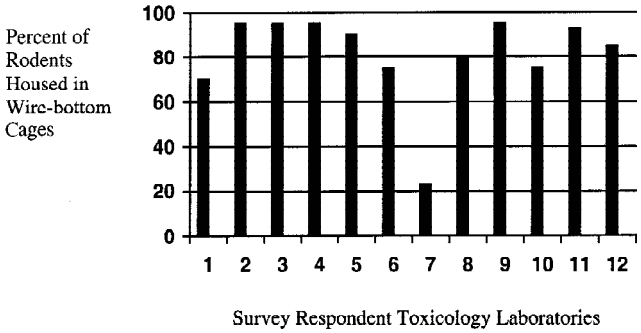

Figure 2. Current rodent caging use in 12 surveyed toxicology programs.

Replacement analysis. The multifaceted factors affecting the use of any type of caging, beyond those that affect the validity of the science and study needs, are important to the laboratory-animal-science community. These factors include capital purchase costs, replacement and supply costs, labor expenses, waste disposal, occupational health risks to staff, available space, animal health, and the well-being of the laboratory animals. These factors are raised in the Results or Discussion sections of this report. Where data are provided, they are based on estimates provided by cited references or from analysis of operational records at the author's institution.

Estimated cage-replacement costs were developed internally in 2000 by using catalog descriptions and current prices (14). These results then were interpolated and expanded from the published research and development expenditures of 15 United States-based pharmaceutical companies (15).

Results

Figure 2 summarizes the response data to the first survey question. The typical surveyed facility houses its rodent population on wire-bottom caging approximately 80% of the time.

The survey respondent data, although extremely subjective, reflect scientific or other perceived value of specific caging choices. Both perceived advantages and disadvantages of a particular caging are summarized below in an order based on the frequency of survey responses.

Toxicologists prefer wire-bottom caging because of ease of sanitation; better animal health assessment; serviceability of the equipment; labor savings; controlled exposure to drug and drug metabolites; more accurate feed consumption data; reduced staff allergies; elimination of bedding ingestion as an experimental variable; better air circulation and ammonia control; denser cage census; reduced fecal and urine exposure; no significant watering-based accidents; and existing baseline data.

Preferences of toxicologists for solid-bottom bedded cages were based on: reduction of limb lesions; improved thermoregulation; better health assessment capabilities; easier group housing; reduced lighting exposure; potential use within an isolator; and global pressure.

The statement in the *Guide* that "Solid-bottom caging, with bedding, is therefore recommended for rodents" prompted an analysis of the costs of conversion from wire-bottom caging to solid-bottom bedded caging. By using a single toxicology program's caging needs as an "index case," the capital cost of replacement was estimated at $1.17 million (Table 1). It was then assumed that the extent of needed replacement caging for the other pharmaceutical toxicology laboratories would be proportional to the research/development budgets of the individual companies. The total replacement capital costs to the major United States-based pharmaceutical-company toxicology programs is estimated to be greater than $16 million (Table 2). This capital replacement cost does not include toxicology facilities operated in the United States by foreign-based pharmaceutical companies. The figure also does not include replacement costs for contract toxicology laboratories, university-based programs, or nontoxicology facilities using wire-bottom caging.

Additional long-term costs for labor, supplies, waste disposal, and animal health and well being are addressed in the Discussion of this report.

Table 1. Caging[a] replacement analysis of solid-bottom replacement for wire-bottom cages at one toxicology facility (Company A)

Mouse cages (9,333)	$457,333
Racks for mouse cages (78)	$80,808
Rat cages (12,150)	$607,500
Racks for rat cages (72)	$26,325
Total replacement costs for this toxicology program	$1,171,966

[a]Lab Products model #10017 mouse cage in rack model #H2776; model #18783 rat cage in double-faced rack model #H2766.

Table 2. Estimated research/development (R&D) budget ratios and replacement solid-bottom caging costs for existing wire-bottom cages for 15 United States-based pharmaceutical companies

Company	Ratio of R&D Budgets[a]	Cost of Cage Replacement[b]
A	1.00	$1,171,966
B	0.78	$908,144
C	0.08	$92,895
D	1.50	$1,229,932
E	0.42	$492,716
F	0.20	$234,096
G	1.10	$1,292,358
H	1.44	$1,686,234
I	1.16	$1,353,297
J	0.80	$938,613
K	2.34	$2,744,496
L	1.22	$1,432,816
M	0.77	$904,428
N	0.98	$1,148,928
O	0.64	$748,363
		Total $16,379,282

[a]R&D budget of each Company B through O/R&D budget of Company A ("index case")
[b]Ratio of R&D budgets x Cost of cage replacement for Company A

Discussion

Numerous factors traditionally are involved in the selection of caging types for scientific studies involving animals. These factors include experimental, biologic, economic, animal-welfare, and regulatory aspects based both on objective data and/or subjective reasoning.

Caging choice must be compatible with the study objective, or there is no reason to perform the study. Several such science-based concerns were raised by the respondents to the survey, including: control of exposure to drug and drug metabolites in feces and urine; elimination of bedding ingestion, a common problem when gastrointestinal upset is a drug response; and the need to conduct certain isolator studies. Sometimes a single factor is key to a caging preference of a study director. Examples include a strict requirement for absolute fasting of large numbers of study animals; the need for housing an infectious study in an isolator; and a requirement for maximized air and volatile test agent circulation during an inhalation study.

Biologic factors are closely linked with experimental requirements in many cases. Limb lesions and injuries can cause the premature termination of a study or affect data, such as weight gain. The fact that differences in caging environment have been shown to affect at least some aspects of thermoregulation raises the concern of some toxicologists about changes in baseline data,

be it developed in solid-bottom bedded or wire-bottom caging.

The cost of capital replacements with solid-bottom caging at only 15 programs using wire-bottom caging is considerable (Table 2). The overall economic effect in the United States when all universities, private laboratories, contract laboratories and non-United-States-owned but United States-based research facilities are included would be much greater.

Beyond the capital expenses, other important long-term economic factors are involved in a potential change to a standard of bedded caging. One can expect markedly increased ongoing maintenance costs to be associated with the use of solid-bottom bedding caging. The per-diem rates for maintaining animals are related to differences in ease of animal observation, costs of cleaning cages, frequency of cage changes, cage set-up time, and cost of supplies (16). The cost of commercially prepared paper-based bedding (Omega-Dri, Harlan, Indianapolis, Ind.) needed in one rat cage is approximately \$0.80 for 1,100 cm^3 of bedding. The fee for landfill disposal of this same bedding is approximately \$0.03 (in New Jersey) and has an unfavorable environmental impact. More than 90% of solid-bottom cage capital costs are for the plastic cages, not the racks holding the cages (Table 1). The useful life of such polycarbonate plastic caging is dependent on chemical exposure, wash temperature, autoclaving, cleaning frequency, and other factors. On average, such polycarbonate caging will require replacement every 2.5 years (17).

Depending on the frequency of cage washing, available cage-wash systems, contact or noncontact bedding changes, the type of water and feeding systems, and numerous other variables, labor expenses vary from facility to facility. Typical cage-wash and cage-change schedules are more intensive for bedded solid-bottom cages than for suspended wire-bottom caging (1). Therefore, labor costs and potential staff health risk exposure are higher for the solid-bottom caging systems.

The welfare and comfort of laboratory animals is likewise a key part of the caging-choice issue. If caging is inappropriate and leads to animal stress, research results are not likely to be valid. Subjective evaluation of rodent cage type leads many people to assume bedded caging preferred by the animal is better for the animal. Yet, no objective data are available to support such assumptions.

Many reported cage-type comparative studies provide animals with a choice of wire-bottom and bedded areas (7, 11). Overwhelmingly, the rodents prefer to rest and sleep in bedding or on solid floors; however, no significant differences in weight gain, water intake, or physiological data have been reported for such animals (8-10). When provided a choice between wire-bottom and bedded areas, awake rodents spend much time exploring and living in the wire-bottom section. Group-housed rats were shown to actually play longer and engage in more species-typical rank-indicating behaviors when held on wire-bottom cages (10, 12). Sanitation issues related to use of wire-bottom cages and contact-bedding cages also can be a consideration when diarrhea or polyuria are drug-induced. Significant differences in foot lesions of rats held on wire greater than 1 year are an obvious welfare concern that must be addressed (5).

Conscientious and informed scientists and laboratory-animal-science specialists comply with regulatory guidelines. The *Guide* notes that solid-bottom caging with bedding is "recommended," but it also notes the Institutional Animal Care and Use Committee "should ensure" caging enhances animal well-being consistent with good sanitation and the requirements of the research project.

Basically, we are left with some flexibility and no compelling scientific evidence that wire-bottom caging is inappropriate for rodent housing of less than 1-year duration. The inclusion of a resting area in wire-bottom caging, although not proven, might address the latter time restriction if foot lesions are eliminated with its use. Use of a nontoxic, plastic or aluminum open-ended box has served this function at our facilities (Fig. 3).

Figure 3. Rodents using a plastic resting box while housed on wire-bottom caging.

The issue of rodent caging is quite complex, as are most areas of science and animal welfare. The mere preference of an animal for one type of caging does not automatically mean that caging is best for all animals in most situations. Most of the available animal-preference data for choosing one housing type over another are species-, strain-, sex-, and age-dependent. Unfortunately, many physical differences such as wire gauge, wire shape, mesh size, or bedding type have not been addressed in the literature reporting animal-preference data.

The effort to enrich the environment for laboratory animals has been reviewed recently (18). That review's summary indicated a complex multitude of factors affecting the usefulness of techniques to enhance the well-being of animals maintained in a research and testing environment. In light of the projected initial and subsequent costs of converting to bedded caging and the dearth of objective data related to positive or negative effects of caging type, one should proceed with caution. New research funding to address this question would be insignificant in comparison to just 5 years of capital and supply costs for research institutions involved in a conversion from wire-bottom to bedded caging. Publicly or privately funded research followed by a professional forum for discussion seems most prudent.

At this time, the decisions that Institutional Animal Care and Use Committees make when addressing the rodent cage-type issue must vary from institution to institution and protocol to protocol. What is most important is that these committees carefully review the scientists' rationale for caging type and make judgment calls that they can defend on grounds of experimental, animal-welfare, and regulatory needs at their institution.

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