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The cost of self-imposed regulatory burden in animal research

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ABSTRACT **U.S. federal regulations and standards governing the care and use of research animals enacted in the mid- to late 1980s, while having positive effects on the welfare and quality of the animals, have resulted in dramatic increases in overall research costs. In addition to the expenses of housing and caring for animals according to the standards, establishing the requisite internal compliance bureaucracies has markedly driven up costs, in both institutional monetary expenditures and lost research effort. However, many institutions are increasing these costs even further through additional self-imposed regulatory burden, typically characterized by overly complex compliance organizations and unnecessary policies and procedures. We discuss the sources of this self-imposed burden and recommend strategies for avoiding it while preserving an appropriate focus on animal well-being and research success.—Thulin, J. D., Bradfield, J. F., Bergdall, V. K., Conour, L. A., Grady, A. W., Hickman, D. L., Norton, J. N., Wallace, J. M. The cost of self-imposed regulatory burden in animal research. *FASEB J.* 28, 000–000 (2014). www.fasebj.org**

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Twenty-six years ago in the wake of the then recently enacted U.S. federal legislation requiring significant enhancements in the oversight, care, and use of research animals, the late Arthur C. Guyton opined, "While medical research using animals has not been killed outright, it is slowly bleeding to death. And regulations being proposed will only hasten its demise" (1). Guyton's chief complaint was that regulatory standards would increase the costs of using animals in research to a point that would be unsustainable. Since then, the specific federal regulations and standards about which Guyton was concerned, and newer ones, have become reality, and a whole generation of biomedical scientists have come of age under the ensuing regulatory landscape. As we reach the third anniversary of the latest iteration of standards, the 8th edition of the *Guide for the Care and Use of Laboratory Animals* (*Guide*; ref. 2), it seems fitting to take a fresh look at the benefits and costs not only of the regulatory requirements, but also of the strategies adopted by institutions to achieve compliance. Could it be that we have become too focused on the letter at the expense of the spirit of the regulations and of science? We, as laboratory animal veterinarians who have nearly 200 collective years of experience in providing, overseeing, and evaluating research animal care and use, believe many institutions have done just that. Furthermore, we believe that this is a commonly held sentiment among our peers.

The overall improvements in research animal health and well-being during the past quarter century are indisputable. The prevalence of devastating diseases, such as mouse hepatitis virus and rodent mycoplasmosis, that were once rampant in many animal colonies has been markedly reduced, and in many cases, once-common diseases have been totally eradicated. The potential pain and distress associated with experimental procedures have been mitigated through the better use of anesthetics, analgesics, procedural refinements, prompt veterinary medical attention, and implementation of humane endpoints. Opportunities for animals to exhibit species-typical behaviors have increased through a greater awareness of the animals' psychological and behavioral needs. Improved husbandry and housing systems have permitted effective maintenance

Abbreviations: AV, attending veterinarian; COI conflict of interest; IACUC, institutional animal care and use committee; IO, institutional official

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of fragile animal models, such as humanized severe combined immunodeficiency (SCID) mice. Explicit considerations for enhancing animal well-being have been integrated into experimental design, protocol review, and animal management programs. These are but a few examples of the tangible benefits stemming from the systematic consideration of animal well-being engendered by the regulatory standards. Notably, the improved health and well-being of the animals have, in turn, benefitted research outcomes, simply by fostering animal welfare and better quality in animal subjects.

These improvements, however, have come at considerable cost. As Guyton predicted, the costs of virtually every phase of animal research have skyrocketed. The cost of animals has greatly increased because of the need for purpose-bred, pathogen-free models. Animal holding facilities that meet rigorous quality standards for the conduct of contemporary science, as well as regulatory expectations, are among the most sophisticated and expensive areas in the construction and maintenance of laboratory buildings. Animal program staffing, including veterinary, administrative, and compliance personnel, have added significant operational costs to animal care and use programs. Of particular concern to researchers is the additional time needed to ensure compliance, both before and after receiving permissions from the institutional animal care and use committee (IACUC). This includes time needed for preparation and submission of protocol forms, correspondence with IACUC support staff and IACUC reviewers, preparation and submission of amendments and progress reports, animal use recordkeeping, attendance at orientations and other training sessions, hosting laboratory regulatory audits, and so on. It is no wonder that many researchers feel that they spend far more time gaining and maintaining approvals to do research than actually conducting research.

Regardless of what the regulated community thinks about the considerable cost of animal research, one thing is clear: the laws, regulations, and guidelines are here to stay. They will not be rescinded, and if history tells us anything, these requirements are likely to become even more stringent. Furthermore, the research community must recognize that societal expectations mandate regulation and oversight of animals in research. That said, our system of oversight in the United States, which is based on self-regulation to ensure that we are good stewards of the research animals in our care, does permit a degree of leeway not available in some other countries.

Can anything be done to ease the burden of compliance, whether it be lowered costs or reduction in the time and effort associated with the regulatory requirements? The short answer is yes. Despite recent warnings from the scientific community (3), the solution might be surprising. Enforcement of the animal welfare laws and regulations in the United States relies heavily on internal oversight at the institutional level through requisite organizational entities—namely, an institutional official (IO), an IACUC, and an attending veterinarian (AV). Although the roles and responsibilities of each of these entities are reasonably well defined, the regulatory standards are largely silent on matters of procedure for achieving and ensuring compliance. Furthermore, the *Guide* (2), one of the principal standards, repeatedly emphasizes the importance of professional judgment in interpretation and application of the standards. As such, there remains a great deal of flexibility in how oversight of the animal care and use program is exercised and compliance ensured. It is at the level of the institution's choices for compliance strategies, not the regulatory requirements themselves, where there may be the greatest opportunity for reduction of the regulatory burden.

Effective internal oversight incorporates two key foundational elements: the responsibility and integrity of scientists and the development of an institutional culture that promotes ethical actions, individually and collectively, in the pursuit of success. Yet many institutions concentrate on policing activities intended to enforce and assure conformance with the rules. In doing so, they may take self-policing to an extreme and do far more than is required legally. Doing more than is minimally required can be, and often is, good, particularly if it results in tangible benefits to the animals and the research. However, many institutions have become so risk averse that they elect to build overly complex organizational infrastructures and processes under the guise of improved compliance, best practices, or both, without rigorous consideration as to the benefit to animal well-being, research, or even institutional risk. More is not always better.

Unfortunately, the well-intentioned drive for best practice in compliance has, in many cases, resulted in compliance bureaucracies that are far removed from both the researchers and the animals. Ostensibly under the authority of the IACUC, these compliance organizations may operate with impunity and have no tolerance for even the most trivial issue, even when the issue involves no negative effect on animal well-being or represents no explicit regulatory noncompliance. Policies and procedures proliferate, forms get longer and more complicated, prerequisites for protocol approval become more onerous, inspections and monitoring become more frequent, and, of course, staffing grows because of the workload related to a perceived need to be "ultracompliant." Beyond a certain point, the compliance efforts yield smaller and smaller benefits while simultaneously adding cost and burden (**Fig. 1**). Yet, because the efforts are made in the name of compliance, researchers seem to have little recourse. As far as we know, Guyton did not predict just how zealously institutions would embrace and pursue compliance, even to the point of overcompliance.

Beyond the unnecessary burden placed directly on the researchers, unfettered compliance efforts can add unnecessary burden and cost to oversight of the animal care and use program, which ultimately affects the research enterprise at the institution. Many contend that the tripartite organizational approach for oversight

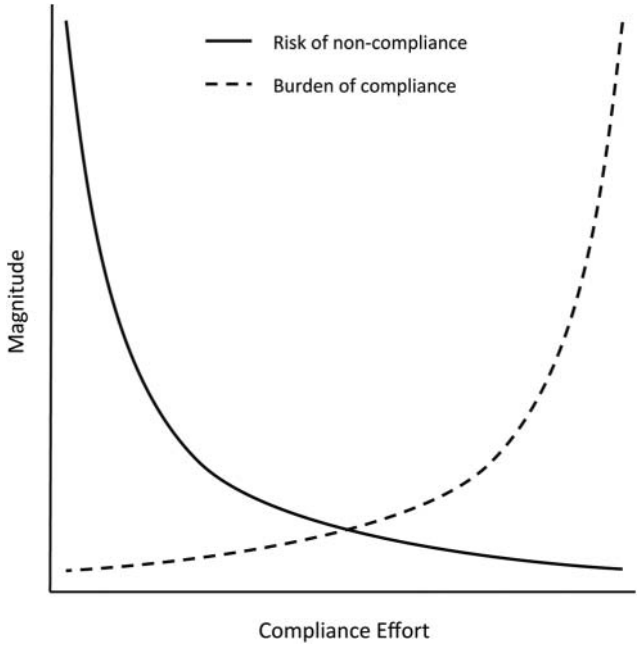

Figure 1. The relationship of overall compliance effort (*x* axis) to the magnitude of noncompliance risk and compliance burden (*y* axis). With little or no compliance effort, the risk of noncompliance is high, whereas the compliance burden is low. As the effort increases, risk decreases and burden increases. However, there most likely is a point, perhaps at the theoretical intersection of the two curves, when the amount of risk reduction to be gained combined with the amount of added burden does not support increasing the effort.

(IO, IACUC, and AV) was specified by the regulations to foster a cooperative approach and create a system of checks and balances. In past decades, the primary concern of scientists, as articulated by Guyton (4), was the newly found consolidation of authority in a potentially overzealous AV. However, the scientific community has expressed little concern about the potential consequences of an overzealous IACUC for which checks are lacking.

The IACUC is the central component for the compliance apparatus and, in contemporary programs, is often staffed by compliance specialists working on behalf of the IACUC but with considerable autonomy. When given too much independence, these spin-off compliance groups sometimes insulate the IACUC members from decision-making processes, minimize the influence of the AV, subjugate both the researchers and AV, and adopt an exaggerated interpretation of conflict of interest (COI). A risk here is in creating increasingly fragmented and disconnected organizational structures for animal program oversight. In such ensiled organizations, cooperation among the organizational silos can wane and dissonance can rise. Unnecessary duplication of effort develops, convenience and efficiency decrease, and institutional costs increase further. Moreover, the IACUC, IACUC support staff, and AV may end up operating in opposition to one another instead of in cooperation, and the investigator may be caught in the middle. This unnecessarily fragmented approach to oversight increases costs, places further strain on research activities by siphoning resources that could be used elsewhere, and is unlikely to improve animal welfare.

It should be recognized that some institutions have built their compliance machines in the wake of severe and systemic noncompliance identified by regulatory or accrediting agencies. A more robust approach to compliance in these cases is understandable. All institutions want to meet the standards and regulations and uphold animal welfare, while avoiding fines and suspensions of funding. However, many other institutions have reorganized based on a small or rare flaw in the program and then may have overcompensated by adopting a solution that inadvertently added layers of unneeded bureaucracy across the entire animal care and use program. Unfortunately, this seems to have become a trend across many institutions rather than isolated, local developments.

Are there strategies that institutions can use to protect themselves from an excessive self-imposed compliance burden? The key lies in the recognition of just how much flexibility is afforded under the current regulatory framework. Following are several examples of where this flexibility might be found:

1) "Should" is not the same as "must." The *Guide* (2) is replete with "shoulds" and relatively spare with "musts." We do not suggest that it would be acceptable for an institution to base their animal care and use program solely on the *Guide* "musts." Nevertheless, institutions clearly have the freedom to consider their own approach to each "should."

2) There is more than one acceptable organizational approach. As indicated above, the regulations are largely silent on how the standards are to be achieved. The only required organizational entities are the IO, IACUC, and AV. Beyond the establishment of these, the institution is free to organize as it sees fit. It is acceptable to consider efficiency in tasking individuals and organizational entities (*e.g.*, IACUC office, compliance office, and animal resource unit) with compliance-related activities, such as postapproval monitoring and even protocol review processes. Regardless of the specific structure chosen, however, institutions and individual investigators should insist on seamless integration and cooperation among the animal care and use program entities, specifically the IACUC, IACUC support apparatus, and AV/animal resource.

3) A "best practice" is relative and contextual. What is best practice at one institution may not be—and often is not—at another. This is an overused term that many would say justifies almost any proposed policy or method. After all, who can reasonably argue with the insinuation that if we do it any other way, we'll be settling for less than the best? Institutions should be wary of proposed one-size-fits-all solutions.

4) The potential for COI does not trump every other consideration. The mere fact that our regulatory framework is predicated on self-enforcement by the institu-

tion means that there will be potential or perceived COI. Indeed, it is a chief concern of some extremist groups that IACUCs composed of scientists, AVs, and other representatives of the institution have an inherent COI, since they have a vested interest in the institution's research program and reputation. In this light, most IACUC members, AVs, and IOs all have conflicts, and completely eliminating all appearance of or potential for COI is not possible. The value of extraordinary efforts aimed at rooting out all potential for COI within the program therefore has to be questioned. Under these circumstances, COI is something to be managed through integrity, transparency, clarity, sound judgment, and timely communication. This approach does not preclude considerations of efficiency and cost, among others.

5) Outcomes are paramount. Yet while outcomes are of utmost importance, there typically are no universal measures that indicate success. The institution, perhaps primarily through its IO, should feel comfortable in challenging the IACUC and AV with such questions as, "Is this (requirement/policy/procedure) required by the regulations and standards?" Or, "Does this (requirement/policy/procedure) maintain or improve animal welfare while supporting the integrity of the science?" And, "If so, can that benefit be measured against the costs?" The answers to such questions require IACUCs and AVs to be expert on the content of the *Guide* and regulations, to ensure that the program meets standards, promotes ethics and welfare, and fosters efficient, high-quality science.

6) Institutions should consider the costs of risk aversion. Although most animal programs appropriately strive for "perfection," mistakes are inevitable. In a cooperative environment, a sound program can preempt mistakes and deal effectively with them when they occur without building a bureaucratic fortress. Institutional concern about public perception and oversight agencies is appropriate as long as that concern does not develop into an overly burdensome expectation that more is always better.

The regulatory standards implemented in the mid- to late 1980s had a tremendous effect on animal-based research in the United States. On the one hand, the regulations have facilitated significant improvements in the health and well-being of laboratory animals and the quality of research models. On the other, they have increased the cost of doing research. Compounding the situation, many institutions have adopted suffocating approaches to achieving compliance. The compliance thrust has lead to increasingly complex organizations and processes. Too often, "best practice" in compliance has eclipsed animal welfare and research considerations, resulting in an increased burden on investigators and programmatic dysfunction. The compliance operations that have been installed and touted in a growing number of animal care and use programs run the risk of becoming disproportionally intense and sapping institutional resources for small or negligible benefits. Institutions should be mindful of the flexibility inherent in the regulatory guidelines, better understand how to evaluate both compliance and performance outcomes, and recognize that overcompliance for the sake of better compliance can become burdensome and negatively affect the scientific endeavors of the institution. FJ

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