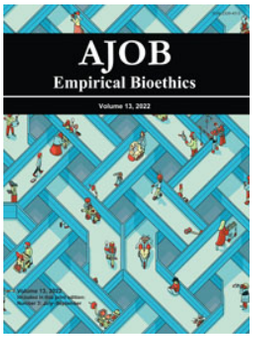

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Mission Creep or Mission Lapse? Scientific Review in Research Oversight

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ABSTRACT

Background: The ethical use both of human and non-human animals in research is predicated on the assumption that it is of a high quality and its projected benefits are more significant than the risks and harms imposed on subjects. Yet questions remain about whether and how IRBs and IACUCs should consider the scientific value of proposed research studies.

Methods: We draw upon 45 interviews with IRB and IACUC members and researchers with oversight experience about their perceptions of their own roles in reviewing the quality and value of scientific protocols. Interview transcripts were memoed to highlight specific findings, which were then used to identify key themes through an iterative process.

Results: IRB and IACUC members expressed broad trust in the need for and value of research, and they often assumed that protocols had social value or that prior review, especially when associated with funding, affirmed both the rigor and merit of those protocols. Some oversight members also took an explicit stance against scientific review by stating that such review is not within the regulatory mandates governing their parts in the oversight system. Yet other interviewees expressed uneasiness about the current paradigm for evaluating the quality and overall value of science, suggesting that IRB and IACUC members perceive gaps in the oversight systems.

Conclusions: These findings reveal many similarities in how IRB and IACUC members understand the roles and limitations of their respective oversight committees. We conclude with a discussion of how the lack of a clear mandate regarding scientific review within US federal regulations may undermine ethical engagement of whether human and animal research is scientifically justified, resulting in a "mission lapse" wherein no organizational body is clearly responsible for ensuring that the research being conducted has the potential to advance science and benefit society.

KEYWORDS

Scientific review; IACUCs; IRBs; research oversight; animal research; human subjects

Introduction

Research oversight in the United States consists of systems to ensure the protection of human subjects, on one hand, and the humane treatment of and care for non-human animals, on the other. Institutional review boards (IRBs) are the organizational body charged with human research oversight while institutional animal care and use committees (IACUCs) oversee animals' involvement in research and educational programs. Although the specific federal mandates for IRBs and IACUCs differ in important ways, the ethical use of both human and non-human animals in research is predicated on the assumption that any science conducted on sentient beings is of a high quality and its projected benefits are more significant than the risks and harms imposed on subjects (DeGrazia and Beauchamp 2019; Emanuel, Wendler, and Grady 2008; Maschke 2008).

Scholarly attention to these research oversight bodies typically focuses on either IRBs or IACUCs, rather than examining them together as part of the broader research enterprise. Drawing upon our research analyzing the nexus between human and animal research (see, e.g., Fisher and Walker 2019), we investigate how responsibility for ensuring the quality and overall value of proposed science is described by IRBs and IACUCs. As we will discuss, the substantial ambiguity that has characterized the regulations from their inception (see Babb 2020; Budda and Pritt 2020) has created problems for determining whether and how IRBs and IACUCs *should* consider the scientific value of proposed research studies. Exploring these and other issues in qualitative interviews with IRB and

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IACUC members, we found variability in how committees approach scientific review. Based on our findings, we argue that regulatory ambiguity facilitates IRBs' and IACUCs' inattention to crucial ethical issues about the scientific rigor and social value of research. The result, as we will illustrate, is that the research oversight system as a whole suffers from a *mission lapse* by lacking clear directives about how IRBs and IACUCs should enact their ethical responsibility to ensure that human and animal involvement in research is justified by its overall quality and potential for scientific advancement or societal benefit.

Research oversight and scientific review

Despite the centrality of the ethical imperative for research to have scientific rigor and social (or scientific) value, the extant literature on the workings of the research oversight system offers few insights into how IRBs and IACUCs address these issues in their review of research protocols. Instead, the literature tends to focus on the administrative and bureaucratic aspects of how these critical bodies conduct their oversight work. This approach to examining IRBs, in particular, is well justified in that empirical studies have documented a vexing degree of variability and inconsistencies in determinations made by different IRBs, as well as legitimate complaints about the inappropriate use of a biomedical framework to review humanities and social science research (Abbott and Grady 2011; Schrag 2010). Additionally, scholars such as Stark (2012) and Babb (2020) have shown the historical contingencies that have created the current IRB system, including a desire among scientists at the National Institutes of Health (NIH) in the 1950s for an oversight system of local review, as well as a later era of hypercompliance after several universities' federal research programs were suspended in the late 1990s and early 2000s. Relative to the amount of literature on IRBs, scholarly attention to the work of IACUCs is scant (Budda and Pritt 2020).[1] Nonetheless, empirical research on IACUCs has also yielded findings that they, like IRBs, lack consistency within and across committees (Plous and Herzog 2001) and that they can become "overzealous" as a result of professional "compliance specialists" reviewing protocols (Haywood and Greene 2008; Thulin et al. 2014).

The US regulations guiding human and nonhuman animal research were designed to allow a fair amount of latitude in how IRBs and IACUCs institutionalize the regulations, but as critics have argued, this has created ambiguity about how each oversight body should evaluate research protocols (Budda and Pritt 2020; Burris and Welsh 2007; Mann and Prentice 2004; Porter and Koski 2008). Human subject research is subject to either the "Common Rule" for most federally funded research (45 CFR 46) and/or the Food & Drug Administration (FDA) regulations for clinical research supporting FDA-regulated products (21 CFR 50/56). Animal research is subject to the Animal Welfare Act (AWA) (9 CFR 2) for specific covered species, as well as separate requirements of the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals for institutions receiving certain federal funds (Haywood and Greene 2008).[2] While human and animal research oversight are typically seen as separate domains, from 1972 to 2000, one single federal agency—the Office for Protection from Research Risks (OPRR)—was charged with overseeing human *and* laboratory animal protections and establishing "assurance" programs between it and any institutions receiving certain federal research grants and using human or animal subjects (Babb 2020). Today, federal assurances for human research are issued by the Office for Human Research Protections (OHRP) whereas the Office for Laboratory Animal Welfare (OLAW) approves federal assurances for animal research funded by the PHS.[3] Overall, the regulations are quite process-oriented, detailing how oversight bodies should do their work rather than providing precedents or rules to guide local review of research (Haywood and Greene 2008; Porter and Koski 2008). This focus has been criticized for creating "compliance bureaucracy" (Babb 2020) or "audit culture" (Stark 2013) in which oversight bodies emphasize documentation of their process instead of a "culture of ethics" in which the rights and welfare of human and animal subjects are prioritized (Burris and Welsh 2007).

The regulations provide minimal guidance to ensure that research overseen by IRBs and IACUCs meets the ethical mandate of having sufficient scientific robustness, on the one hand, and social (or scientific) value, on the other, to justify the use of human or animal subjects. For their part, IRBs are charged with determining that "risks to subjects are minimized: (i) By using procedures which are consistent with sound research design" (Common Rule, 45 CFR 46.111; see also 21 CFR 56.111). Therefore, the regulations explicitly require IRBs in their review of applications to consider research design as it pertains to risk. Additionally, the Belmont principle of beneficence speaks to value by including a directive to achieve a balanced or "fair ratio" of benefits and risk (National Commission 1979), reflected in the regulatory requirement that "risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the

knowledge that may be reasonably expected to result" (Common Rule, 45 CFR 46.111).[4] The federal regulations defining the role of IACUCs instruct them to ensure that the "principal investigator has provided written assurance that the activities do not unnecessarily duplicate previous experiments" (9 CFR 2.31(d)(1)(iii)) and that research proposals contain a "rationale for involving animals, and for the appropriateness of the species and numbers of animals to be used" (9 CFR 2.31(e)(2)). Federally funded animal research should also adhere to the stipulation that "[p]rocedures involving animals should be designed and performed with due consideration of their scientific relevance to human or animal health, the advancement of knowledge, or the good of society" (National Research Council 2011). US IACUCs, however, do not operate under a general mandate to balance known and expected harms to animal subjects against likely benefit, as is specified for human subjects through the principle of beneficence (Ferdowsian et al. 2020; Walker 2006). Also unlike for human subjects, the ethical framework for IACUC review of protocols is primarily tied to the principle of "humane" care and use and the 3Rs (i.e., Reduce, Refine, and Replace animal use) (Russell and Burch 1959; Walker 2016).[5] Thus, while the mission of both IRBs and IACUCs require, in different ways, assurance of the quality and value of the science, neither group is given explicit guidance regarding how to accomplish this key ethical goal as part of their evaluation of research protocols.

Despite the importance of this topic, few empirical studies provide any insights into how IRBs and IACUCs engage in scientific review as part of the routine evaluation of research protocols. One very early study of IRBs found that most committees insufficiently examined the scientific merit of protocols and rejected research protocols only when "scientific flaws [were] glaring" (Goldman and Katz 1982, 200). Based on her ethnographic research, Stark (2012) describes IRB members requiring fundamental changes to study methods for research to receive approval, even though the modifications they requested did not stem from a review of the scientific merit of proposals. Such changes may or may not be protocol improvements per se, and they perhaps even risk *reducing* the scientific value of studies (see also Bledsoe et al. 2007; Cooper and McNair 2014). Empirical studies of IACUCs also suggest a similarly indecisive approach to scientific review in approval of animal studies. For example, Dresser's (1990) early investigation of IACUCs demonstrated that committees actively considered proposals' scientific merit, questioning the extent to which protocols would both produce valid data and benefit society. However, as Dresser observed, "Many [committees] also grappled with the complex and difficult problems of assessing a proposal's merit, but committees appeared less confident and certain about this dimension of their responsibilities" (Dresser 1990, 6). A later survey of IACUCs indicated that committee members believed it appropriate to consider the scientific merit of proposals only when the research would cause greater pain to animal subjects, and a minority viewed scientific review as fully outside the mandate of IACUCs (Graham 2002). Overall, prior empirical research on IRBs and IACUCs suggests that these oversight bodies hold ambivalent views of their role in conducting scientific review.

Materials and methods

As part of a broader study on comparative research ethics in nonhuman animal research and Phase I healthy volunteer trials, we conducted 100 in-depth interviews with IACUC members, animal researchers, IRB members, Phase I investigators, bioethicists, and policymakers. The purpose of this empirical research was to compare how these groups conceptualize (1) the similarities and differences between healthy volunteer and non-human animal research and (2) the ethical, policy, and translational science problems particular to each arena. Despite our project's focus on Phase I clinical trials, IRB, bioethicist, and policymaker informants often reflected much more broadly on clinical research and issues that emerge in the oversight of all biomedical human studies. The Biomedical IRB at the University of North Carolina at Chapel Hill reviewed and approved all study procedures.

In order to recruit participants, we conducted online searches of oversight personnel and researchers at academic institutions, as well as at public and private research and oversight organizations. We also identified potential participants through snowball sampling. As interviews were underway, recruitment efforts were adjusted to have better representation of diverse genders, races, and ethnicities as well as geographic locations in the United States. Recruitment began in September 2018, and interviews were completed in June 2019.

Our interview guides were designed with different topic sections, including views of research oversight generally, issues relating to translational science, research design choices like the selection of research participants or animal models, the risks and benefits involved in Phase I or animal research, and the process of monitoring research in progress. While we did not set out to study scientific review, those who had

participated in research oversight discussed this topic when answering questions from two sections of the interview: their views on research oversight generally and the risks and benefits involved in Phase I or animal research. Questions from these two sections included how interviewees perceived their own roles within the system, important aspects of as well as gaps in the oversight or drug development systems, their approaches to balancing risks or harms and benefits when reviewing research protocols, and, for those involved in animal research oversight, their perspectives on the 3Rs. Interviews were conducted by phone and lasted, on average, 75 minutes. Participants provided informed consent prior to the interview beginning. Interviews were audio recorded and transcribed.

To analyze the interviews, we read transcripts in their entirety and discussed preliminary themes that emerged. We then developed memos to highlight specific findings, including about the strengths and usefulness of oversight systems, the priorities of the oversight systems, experiences with protocol reviews, trust in the oversight systems, and changes that could be made to the oversight systems. Through an iterative process, we used these memos to identify key themes related to scientific review, and the authors identified representative quotes related to these themes in the transcripts.

For this paper, we draw on interviews with those who had prior experience with or were currently involved in research oversight and, therefore, had direct experience conducting scientific review. We reviewed all transcripts, and 45 interviewees had research oversight experience: 10 IRB members, 15 IACUC members, as well as 18 (of 47) animal researchers and 2 (of 12) Phase I investigators. Half of the IRB members worked at central IRBs, and the other half worked in universities (with 40% at private universities and 10% at public). Our sample of Phase I investigators came primarily from the private sector, including the two investigators who had IRB experience. The IACUC members, in contrast, were predominantly associated with academic institutions, with two-thirds at public universities. The institutional affiliations of animal researchers mirrored that of IACUC members, with more than half of our animal researcher informants working at public universities. Table 1 provides demographic data for our sample.

Table 1. Institutional affiliations of interviewees with oversight experience (N = 45).

	Variable	Frequency	Percentage
Interviewee Group	IRB	10	22.2
	IACUC	15	33.3
	Animal Researcher	18	40.0
	Phase I Investigator	2	4.4
Institution Type	Private Academic Institution	11	24.4
	Public Academic Institution	23	51.1
	Institution other than Academic	11	24.4
Gender	Man	24	53.3
	Woman	21	46.7
Age	30–39	7	15.6
	40–49	7	15.6
	50–59	13	28.9
	60–69	14	31.1
	70–79	4	8.9
Race	Asian	1	2.2
	Black or African American	1	2.2
	More than one race	2	4.4
	White	41	91.1
Ethnicity	Hispanic or Latino	1	2.2
	Not Hispanic or Latino	44	97.8
Education^	DVM	14	31.1
	PhD	23	51.1
	Other	11	24.4
Time in the Field	2 – 5 years	2	4.4
	6 – 10 years	8	17.8
	11 – 20 years	9	20.0
	20+ years	26	57.8

^Total is more than 100% because some participants had more than one degree.

Results

Two primary themes emerged from the 45 interviews regarding whether and how IRB and IACUC oversight of research includes review for the quality and value of scientific protocols. First, IRB and IACUC members articulated trust in the research enterprise, which obviated the need for them to engage in scientific review. Second, some IRB and IACUC members voiced unresolved anxiety about whether sufficient scientific review is occurring.

Scientific review and trust in the research enterprise

Given the ambiguity about the manner in which research oversight bodies should be doing scientific review, it may be no surprise that explicit evaluations of the quality of the proposed science was not central to IRB and IACUC members' narratives about their review process. Oversight personnel sometimes even took an explicit stance against review of scientific merit as a key feature of their review process. For example, an IRB member declared, "We sort of leave that to the scientific review committees… because we view our role in the IRB is primarily related to human subjects' protections" (IR03). IACUC members, in particular, often specifically stated that reviewing the quality of the science was deemed out of their board's scope. For instance, an IACUC member said that "although IACUCs are not prohibited from evaluating protocols based on scientific merit, they are not

required to do so. And our [institution's] IACUC has very explicitly decided that we will not review for scientific merit on our committee" (IA06). Another IACUC member described not meddling with the science of protocols, saying, "We try to stay out of the actual experimental design. We don't figure that's our place" (IA04).

In addition to these explicit stances against reviewing for scientific merit, a shared characteristic between IRB and IACUC members was an expressed broad trust in the need for and value of human and animal research. In describing how an IRB should review research protocols, one IRB member avowed, "I think you have to start from… somewhat of an *assumption that this [research] is a noble enough purpose* that we all want to get behind it" (IR07, emphasis added). IRB and IACUC members both claimed that research protocols must have social value for approval, but they also noted that questions about that value typically did not come up in their review. For example, an IRB member explained, "So, if it seemed like somebody was doing a study that just had no benefit and had significant risks, then we likely would not approve it. I can't say I've ever seen that, though, in 20 years. I think just 'cause of the cost of doing research, *most people don't undertake it unless there's a clear benefit for doing it*" (IR01, emphasis added). Thus, IRB and IACUC members often assumed that protocols had social value, indicating trust in the research enterprise.

Supporting assumptions about the value of the research their boards were charged with overseeing, IRB and IACUC members tended to emphasize the distributed nature of scientific review that occurs prior to any research study commencing. In order for responsibility to be divided this way, other parties in the broader research system need to be trusted to conduct scientific review and maintain the quality and value of science. For instance, because many researchers' protocols have been submitted to a funder or federal agency, many IRB and IACUC members believe that the science has already been reviewed by another institutional body prior to their involvement. In this vein, one IRB member underscored IRBs' reliance on prior scientific review as a critical component of the research enterprise:

> I mean, personally I have a lot of *faith in this process and in science* in general. So, we [on IRBs] can't do the same level of background check that's being done at the lab, at the company. We can't do what FDA does… but it's a shared review process, and the burden of responsibility is shared. No one person assumes responsibility, and that's the way that science works in societies, I think. (IR05, emphasis added)

Likewise, another IRB member explained that by the time his board receives a protocol, "it's also been reviewed by the FDA through the granting of an IND or a device exemption. And so we'll try to stay away from reviewing those things… I can't think of anything that would be specifically off limits [to review], but we try to avoid instantly requiring changes" (IR03). The same sentiment of reliance on and trust in prior review processes was echoed in our IACUC interviews. One IACUC chair explained why prior scientific review was tantamount to scientific justification:

> Most of this stuff has been funded also by NIH or some federal agency, and so much of it has already gone through a level of scientific review from that standpoint. *So, much of it would not come to us if it hasn't already been scientifically justified by somebody who's looked at that aspect of it.* (IA03, emphasis added)

Occasionally, our informants made explicit connections between prior scientific review and evidence of the scientific and/or social value of or "need" for the research. For example, an IACUC member asserted that "there is reliability that if something is scientifically funded, that it is scientifically justified. That still doesn't mean that the… IACUC [review] is just a slam dunk, but it does mean that *there is a scientific need or it wouldn't have gotten funded. So that scientific need and that scientific justification is there*" (IA15, emphasis added).

Other IRB and IACUC members revealed a great deal of trust in prior scientific review by emphasizing that other organizational bodies were better positioned to conduct this level of review. These individuals noted that IRBs and IACUCs might not have the right expertise or even sufficient resources for review of both scientific quality and value. One clear example of this perspective came from a Phase I researcher with extensive IRB experience. He claimed:

> IRBs, in general, are not trained to assess the scientific content of the protocol. It would be wonderful if they were, but I was on an IRB for 10 years, and we did not have the expertise to really thoroughly assess the science of each trial we did. To some extent, *we counted on the sponsor and the investigator and the investigator's brochure* to do that… [As for] Why the study is being done, is it being designed correctly, all that kind of stuff, the IRB really doesn't have that expertise to do so. (PI03, emphasis added)

Similarly, an IACUC chair emphasized, "It's not that we don't think it's important; it's just we think other people can do that job better, and so *we leave*

it to the funding agencies or… the PI's department… [to review] *for scientific merit"* (IA06, emphasis added). Thus, for human and animal research, neither IRB nor IACUC members downplay the importance of scientific review for quality and value. However, prior scientific review became a justification for why it may not be part of their regulatory mandates.

In many instances, IRB and IACUC members did not simply reference the broader research enterprise to illustrate their trust in the system. Rather, they appealed to specific organizational actors that further affirmed that they could trust in the scientific merit of the research being proposed. For pharmaceutical industry clinical trials, IRB members identified drug sponsors themselves as the experts responsible for the quality of their science. For instance, one IRB member reported, "Industry sponsors, drug sponsors, in particular, *really know how to do this*. I mean, this is the beginning of the development program; they do these all the time. So, it's vanishingly rare for us to ask for [protocol] changes" (IR04, emphasis added). IRB members also focused their trust on the clinical investigators, particularly those with ample experience conducting research. On this point, an IRB member declared:

> The vast majority of PIs that we review have worked for these same companies that do these research trials for many years. So *they've got a good track record with doing research*. … And because our IRB's been in existence for a little over 20 years and [we] have worked with most of these investigators for a long time, *we kind of have a sense of if there's any issues with the site or an investigator*. (IR01, emphasis added)

IACUC members tended to articulate trust in the investigators specifically. One remarked, "You know, these guys [researchers] are PhDs. *They know what they're doing in terms of the science. I don't really worry about it*" (IA01, emphasis added). Another said that while oversight officials may not trust researchers in every aspect of protocol review, trust is an expected norm when it comes to the quality of their research. She posed the question, "*At what point do we just trust that the scientists know what they're doing* and we're not going to get too involved in the experimental design and the science, and at what point do we try to make sure we have proper oversight of that? Because that's a fine line" (IA15, emphasis added).

Internal critiques of oversight and scientific review

While many interviewees illustrated trust in research oversight systems and the other organizational bodies that provide prior scientific review of protocols, there were nonetheless articulations of uneasiness about the current paradigm for evaluating the quality and overall value of science in both human and animal research. These types of narratives suggest that IRB and IACUC members perceive gaps in the oversight systems.

Although a key part of IRBs' mandate is to conduct risk-benefit assessments to protect human subjects by ensuring risks are minimized and appropriate for the expected benefits, IRB members noted that sponsors, particularly industry sponsors, are very specific about their study designs. Demonstrating some of the power dynamics at play, an IRB member commented, "Study design tended to be more of a challenge to ask for [changes]. … Because the sponsor's already really well invested into their study design. You know what I'm saying?" (IR08). Another declared, "Pharmaceutical companies will be resistant to change. For a Phase I study, an IRB or I would be resistant to asking to change the design of a protocol" (IR02). Reflecting on the commercial nature not only of clinical trials but also IRB review itself, a Phase I investigator who was also a longstanding member of a central IRB criticized IRBs for being a "rubber stamp" rather than serving "a legitimate, supervisory, and critical review function" (PI02). He elaborated, saying:

> Statements like, you know, "At some level, we just have to trust the sponsor and trust the investigators." And every one of those statements, to me, is an argument against the very need for an IRB. *We're not supposed to trust*. We're supposed to review and challenge. … I'd like to see a really specific articulation that IRB responsibilities are a policing function. They're expected to be critical, and they're expected to exercise control actively and not wait until some bad thing hits them over the head. (PI02, emphasis added)

For this informant, IRBs' trust in sponsors and their inability to demand protocol changes was colored by a financial conflict of interest and has resulted in a major problem in how many IRBs function.

Even the prior scientific review that IRB members used as justification for IRBs to avoid such evaluation of protocols raised some concerns about its rigor. For example, an IRB member confided:

> I think that there are sometimes problems with investigators reviewing other colleagues' and investigators' work. I think that there is sometimes a hesitancy to sort of really dig deep and be critical about people's work, and we've kind of seen that in the quality of

> scientific review from sometimes particular research units, and that gets to be a little bit of a problem. (IR02)

Similarly, the Phase I investigator who served on an IRB criticized the extent to which IRBs took prior FDA review as sufficient from a human subject protection standpoint. He proclaimed:

> The FDA's approach is, "We don't tell you how you have to do things, but if we don't like the data when you bring it to us, then we'll tell you that you have a problem."… You can give general guidelines, including ethical ones, and you can blow a whistle if you think they're clearly over the line, but otherwise, it's a good old, free country and you gotta wait 'til a problem shows up. (PI02)

In other words, his perspective is that FDA does not actually provide scientific review, but instead gives industry guidance on how to produce data that the FDA can use for new drug approvals. For this informant, IRB members are misconstruing FDA review and potentially leaving protocols without any scientific review at all.

Concerns about the process of scientific review for animal research similarly centered on IACUCs' lack of meaningful review of both the quality and value of protocols. The reminder that protocols have undergone prior scientific review, especially for externally funded contracts or grants, even created tension for IACUC members when evaluating the necessity of protocol refinements, which are used to address animal welfare. An IACUC member explained:

> I think there's always a gray line between whether or not the IACUC… can really push that [funded] science to change if it's something that is a technique or something that maybe should be refined. That's one of the biggest challenges because technically the IACUC is not supposed to look at the science, but sometimes the science may be something that needs to be looked at. (IA12)

Therefore, while prior scientific review can help IACUC members trust that the protocols have already been vetted, concerns about animal welfare may make the IACUC question whether changes to the science are nevertheless necessary for the research to proceed.

Unlike with the IRB informants, IACUC members also had more forceful articulations that the lack of clear guidance for IACUCs to do scientific review was particularly troubling. For instance, an IACUC member argued:

> I think probably the biggest weakness is we have not been able to sort out the proper role of the Institutional Animal Care and Use Committee in their work with regard to the scientific review. There's still that question of whether it's appropriate or not. And there's not been a lot of guidance. There's been almost no guidance on how or what is a good practice in that area. (IA13)

Likewise, another IACUC member elucidated the difficulty of ensuring animal welfare while ignoring aspects of a protocol's science related to design and value in order to avoid overstepping IACUC purview:

> Without looking at that experimental design or without looking at some of the reasons behind why are they using animals for this, you… may not be able to go through and ask the right questions for the welfare side of things. So, I think that's where I've heard or personally experienced some of the dueling messages about what the IACUC's role is and the science behind what is being proposed. (IA14)

Another IACUC member specified why scientific quality and value are important with respect to animal welfare:

> We want to have a general reassurance as a committee that the research that's being proposed is an appropriate use of animals and that the research is described in a way that we can feel convinced that the proposed study will provide useful scientific information. So, in other words, we want to feel confident that it's a well-designed study, that using these animals is an appropriate use of animals, [and] that you're not doing bad science, for example, or you're just wasting the lives of these animals. (IA10)

"Wasting" animals was a major concern among some IACUC members when it came to understanding the need for scientific review, and one that is quite different from how the problem is articulated about human research where human lives will not be sacrificed for the science. For these IACUC members, the concern is to avoid approving research proposals that do not justify the taking of animal lives.

Another difference between IACUC and IRB members' criticisms of their respective oversight systems was that the IACUC members did not explicitly challenge another organization's purported role in conducting scientific review. However, like their IRB counterparts, IACUC members worried about the system as a whole actually enacting rigorous scientific review of protocols. One IACUC veterinarian summarized the problems that come with different aspects of scientific review being done by different parties:

> So, there's kind of three questions… One is evaluating the harms to animals and what can be done about them. One is evaluating the value of doing the work. And one is evaluating the quality of the proposed work. And that those are sort of done by

> three separate entities… So we make these societal determinations of resource allocations [about] what's worth asking. And then the scientific merit is done by experts in the actual field. And then the welfare assessment is done by the IACUC. And so, not only is it done by three separate bodies, they're three bodies that aren't really in communication with each other. The IACUC may know that, "Oh, this got peer review." And the peer reviewers will know that, "Oh, this won't get final approval without the IACUC deciding that it's worth it." (AR18)

As a result of this dynamic, he said that "for the most part, the IACUC just sort of has this armchair, 'Yeah. I guess this is important. Oh, and look, they were reviewed by NIH, so I guess we'll approve it'" (AR18).

Discussion

Our findings suggest that *overall* ethical assessments of the value of human and animal research is not being done by IRBs or IACUCs. Instead, these oversight committees commonly focus on whether prior scientific review has been done, and assume that such review, particularly when associated with funding, affirms both the rigor and value of the research protocols. We hypothesize that this position is primarily due to IRB and IACUC members' lack of clarity about the extent to which scientific review is within their mandate and how any such review should be conducted, and it is seemingly further rationalized by their trust in the research enterprise as a whole.

Human and animal research oversight is part of a much larger system of research funding and governance, and coupled with the ambiguity in US federal regulations about IRBs' and IACUCs' charge related to scientific review (Budda and Pritt 2020; Stark 2012), it may appear that these oversight committees are fulfilling their regulatory roles. However, the scientific review taking place outside of research oversight is frequently not sufficient to fulfill the ethical mandate for human and animal subject use. For example, the FDA was perceived by some IRB informants to offer relevant scientific review, but it, in fact, has a more narrow role in adjudicating the science that will promote drug approval (see, e.g., FDA 2013). Similarly, vertebrate animal research funded by the NIH is vetted for whether the proposed study is "Acceptable or Unacceptable" with respect to its science, but this determination does not address overall social and scientific value in comparison with animal harms (NIH 2010). The result of such dispersed specific goals regarding scientific review may thus be that both the human and animal research oversight systems are characterized by a *mission lapse* wherein no organizational body is clearly responsible for ensuring that the research being conducted is both scientifically rigorous and has the potential to advance science and/or benefit society.

Previously, both IACUCs and IRBs have been accused of "mission creep" when they become too focused on research design (Bledsoe et al. 2007; Pritt et al. 2016). As the literature has shown, IRBs' inappropriate scientific review of protocols has problematically limited researchers' academic freedom and even censored research (Prentice, Crouse, and Mann 1992; Schneider 2015; Tierney and Blumberg Corwin 2007). Likewise, IACUCs face a similar challenge of reviewing the science of animal research protocols by becoming overzealous in their scrutiny of research design issues (Haywood and Greene 2008; Everitt and Berridge 2017). Indeed, many of our own informants illustrate the delicate balance they are trying to achieve in assessing the scientific value of research without engaging in off-mission levels of review and intervention into study design that do not directly speak to the protocols' potential to contribute positively to science and knowledge production or to improve subject welfare.

However, criticism of mission creep, while often justified, may also steer IRBs and IACUCs to avoid scientific review *even when it is appropriate*. Such steering is evidenced by our informants' descriptions of being hesitant or unable to ask investigators to make changes to their research protocols, even if the request was warranted. This hesitancy was especially apparent when reviewing funded research and protocols from industry sponsors, illustrating the pressure IRB and IACUC members face because of financial conflicts of interest within the larger system of research. On the whole, some oversight members raised concerns about the lack of rigorous review that can occur on the part of funding agencies and the FDA, as well as the impact of commercial interests on human subjects research and the potential "waste" of animal life in science. These internal critiques of the oversight system reveal how IRB and IACUC members can experience this broader mission lapse, and these findings signal that questions about whether and how scientific review should be conducted by oversight bodies continue to be fraught both in the literature and on the ground.

Although the question of what role IRBs and IACUCs should have in scientific review is a contentious one, it is clear that scientific review is critically important to ensure that research is ethically

justified by its rigor and potential for scientific and/or broader societal benefits. Rather than asking whether IRBs and IACUCs should be engaging in scientific review, our study affirms the better question is *how* they should ensure that research is scientifically and ethically justified. Some scholars have previously argued that IRBs and IACUCs should have a more proactive role in enhancing the quality of research (e.g., Borgerson 2014; Mohan, Barbee, and Silk 2018). For example, in the domain of human clinical trials, scholars have labeled some studies as "bad deal" or "bad gamble" trials because of the high risk for and unlikely individual benefit to participants (Eyal 2017; Jansen 2005). Nycum and Reid (2007) make the case that IRBs are unduly generous in their appraisal of research benefit, which leads to trials that have limited social benefit and exploit participants' altruistic motivations or hope for therapeutic benefit. They conclude that there needs to be a higher standard for social and/or scientific benefit in clinical trials, suggesting that IRBs can facilitate this improvement to human research. On the IACUC side, Everitt and Berridge (2017) argue that reproducibility and clinical translatability are overlooked elements of the scientific value of animal research, and in addition to welfare review, they advocate for IACUCs to attend to the relevance, robustness, and reproducibility of animal studies. Prentice, Crouse, and Mann (1992) even suggest that IACUCs have more responsibility than do IRBs for assessing scientific merit because animals, unlike humans, are not given the choice to participate in research, so IACUCs must "ensure the ethical costs of the research are justified" (18). Thus, an overarching theme in this literature is that both human and animal research oversight bodies should take more responsibility for confirming as part of their review that research protocols justify the involvement of subjects.

Our study reveals that current practice both on IRBs and IACUCs tends to overly rely on trust. As our findings indicate, these oversight bodies may place too much trust in other organizational actors to do scientific review, as well as too much trust in specific investigators to conduct rigorous and valuable science. This latter finding is also reflected in the published literature, which has shown that IRBs are not simply reviewing isolated protocols but are largely evaluating how much they can trust the researchers to protect their institutions' and participants' interests (Hedgecoe 2020; Stark 2013). The reliance on trust in lieu of scientific review may stem not only from ambiguity in IRB and IACUC mandates, but it may also be a result of insufficient scientific expertise represented on IRBs and IACUCs, a problem that was noted by our informants. Previous research has also raised concerns about how the scientific expertise of IRBs and IACUCs is limited by each board's membership (Fitzgerald and Phillips 2006; Silverman 2016; Steneck 1997), another issue raised by some of our informants. With the increasing complexity of drug development, the problem may worsen when IRBs and IACUCs have an inadequate understanding of the scientific basis for novel research protocols (Gunsalus et al. 2007; Landi, Everitt, and Berridge 2021). The regulations explicitly permit IRBs and IACUCs to engage outside consultants when their expertise is needed for protocol review (Fitzgerald and Phillips 2006; Mohan, Barbee, and Silk 2018), but when boards rely on their trust in investigators, it may be less clear to members that they need to seek out expertise beyond their membership.

Our findings should be considered in light of the study's limitations. Because there is not, to our knowledge, a database to compare our sample to existing IRB and IACUC member demographic information, we cannot be sure whether our purposive sample is representative of the research oversight population. Our sample is not diverse in terms of race and ethnicity, and skews older in terms of age. In addition, IRB members tended to have served on central IRBs, while IACUC members served at academic institutions. Finally, there are more IACUC than IRB members represented. Regarding the lack of a national database for oversight committee members, IACUC membership is often hidden from the public because of privacy concerns, making it impossible to discover who serves on these committees. Similarly, we cannot be sure that our sample is representative of the different types of research oversight committees (i.e., central or academic). However, clinical human subjects research is largely conducted by commercial pharmaceutical companies and overseen by central IRBs (Fisher 2009), and it stands to reason that IACUCs are mostly in academic settings given the requirement for inspections which necessitates local review. Therefore, we have reason to believe that our sample may be representative of the different types of research oversight committees. We posit that the reason more animal researchers in our sample had oversight experience is because this dual role is more common among academic animal researchers than it is among human subject researchers. Because our themes were well established with both groups, we do not believe the difference in numbers between IACUC and IRB members impacted our qualitative analysis.

A risk with research oversight is that those involved in the enterprise simply assume—and place trust in—the quality and value of research, believing that all scientific inquiry has the potential for societal benefit. Our findings reveal many similarities in how IRB and IACUC members understand the roles and limitations of their respective oversight committees, but these findings also indicate how US federal regulations—and their lack of a clear mandate for the conduct of scientific review—may undermine ethical engagement with the question of whether human and animal research is scientifically justified. As Babb (2020), Stark (2012), and others have noted, ambiguous regulations do not merely allow IRBs and IACUCs to exercise local discretion in deciding how to oversee their research programs; they also encourage "compliance bureaucracy" and "audit culture." Checking boxes may be needed to manage vast oversight programs, but the system as a whole suffers from a mission lapse. More attention needs to be given to how the research oversight system can ensure that human and animal research is ethically justified by its overall quality and potential for scientific advancement or societal benefit.

Notes

1. For empirical studies, this different level of attention to IRBs compared to IACUCs likely results from social science and humanities researchers' consternation about how their research protocols have been managed by IRBs (e.g., Bledsoe et al. 2007; Bosk and De Vries 2004; White 2007). In bioethics, the greater focus on IRBs is likely due to the largely human-centric nature of the field as whole, despite important work on animal ethics also being done (e.g., Beauchamp and DeGrazia 2020; Garrett 2012; Walker 2019).
2. For US PHS-funded research, researchers must also "base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals*" (National Research Council 2011). Many IACUCs use "The Guide" as the basis of their work, interpreting all "should" statements as requirements (Haywood and Greene 2008).
3. The AWA has been enforced for covered species through the US Department of Agriculture, Animal and Plant Health Inspection Service since the service was founded in 1972 (Cardon, Bailey, and Bennett 2012).
4. Despite the emphasis on minimizing risk and conducting risk-benefit assessments, the regulations do not instruct IRBs on how to do these tasks. This is particularly problematic when IRBs often manage uncertainty by mobilizing the precautionary principle to manage risk (i.e., assuming that the worst might happen) and "a sanguinity principle" in their view of benefit (i.e., assuming that science is de facto beneficial) (Barke 2009). Rid and Wendler (2011) developed a framework to inform IRB deliberations as an alternative to "intuition"-based assessments. Most relevant to this discussion, Rid and Wendler start with the premise that IRBs must "ensure and enhance" the social value of research, wherein scientific "necessity" is an essential but insufficient criterion upon which it is based.
5. Unlike in the US, there is a regulatory requirement in the European Union for animal research boards to do a harm-benefit assessment (HBA) (Maisack 2015). Nevertheless, some commentators argue that US IACUCs should utilize HBA as part of their review (e.g., Everitt and Berridge 2017).

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Data availability statement

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data is not available.

Disclosure of interest

The authors report no conflicts of interest.

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References

Abbott, L., and C. Grady. 2011. A systematic review of the empirical literature evaluating IRBs: What we know and what we still need to learn. *Journal of Empirical Research on Human Research Ethics: JERHRE* 6 (1):3–19. doi: 10.1525/jer.2011.6.1.3.

Babb, S. 2020. *Regulating human research: IRBs from peer review to compliance bureaucracy*. Stanford, CA: Stanford University Press.

Barke, R. 2009. Balancing uncertain risks and benefits in human subjects research. *Science, Technology, & Human Values* 34 (3):337–64. doi: 10.1177/0162243908328760.

Beauchamp, T. L., and D. DeGrazia. 2020. *Principles of animal research ethics*. New York: Oxford University Press.

Bledsoe, C. H., B. Sherin, A. G. Galinsky, N. M. Headley, C. A. Heimer, E. Kjeldgaard, J. Lindgren, J. D. Miller, M. E. Roloff, and D. H. Uttal. 2007. Regulating creativity: Research and survival in the IRB iron cage. *Northwestern University Law Review* 101 (2):593–641.

Borgerson, K. 2014. Redundant, secretive, and isolated: When are clinical trials scientifically valid? *Kennedy Institute of Ethics Journal* 24 (4):385–411. doi: 10.1353/ken.2014.0029.

Bosk, C. L., and R. G. De Vries. 2004. Bureaucracies of mass deception: Institutional review boards and the ethics of ethnographic research. *The ANNALS of the American Academy of Political and Social Science* 595 (1):249–63. doi: 10.1177/0002716204266913.

Budda, M. L., and S. L. Pritt. 2020. Evaluating IACUCs: Previous research and future directions. *Journal of the American Association for Laboratory Animal Science: JAALAS* 59 (6):656–64. doi: 10.30802/AALAS-JAALAS-20-000077.

Burris, S., and J. Welsh. 2007. Regulatory paradox: A review of enforcement letters issued by the Office for Human Research Protection. *Northwestern University Law Review* 101 (2):643–85.

Cardon, A. D., M. R. Bailey, and B. T. Bennett. 2012. The Animal Welfare Act: From enactment to enforcement. *Journal of the American Association for Laboratory Animal Science* 51 (3):301–5.

Cooper, J. A., and L. McNair. 2014. What is the role of a statistician on the IRB? *Journal of Empirical Research on Human Research Ethics: JERHRE* 9 (5):89–90. doi: 10.1177/1556264614554899.

DeGrazia, D., and T. L. Beauchamp. 2019. Beyond the 3 Rs to a more comprehensive framework of principles for animal research ethics. *ILAR Journal* 60 (3):308–17. doi: 10.1093/ilar/ilz011.

Dresser, R. 1990. Review standards for animal research: A closer look. *ILAR Journal* 32 (4):2–7. doi: 10.1093/ilar.32.4.2.

Emanuel, E. J., D. Wendler, and C. Grady. 2008. An ethical framework for biomedical research. In *The Oxford textbook of clinical research ethics*, ed. E. J. Emanuel, C. Grady, R. A. Crouch, R. K. Lie, F. G. Miller, and D. D. Wendler, 123–35. New York: Oxford University Press.

Everitt, J. I., and B. R. Berridge. 2017. The role of the IACUC in the design and conduct of animal experiments that contribute to translational success. *ILAR Journal* 58 (1):129–34. doi: 10.1093/ilar/ilx003.

Eyal, N. 2017. The benefit/risk ratio challenge in clinical research, and the case of HIV cure: An introduction. *Journal of Medical Ethics* 43 (2):65–6. doi: 10.1136/medethics-2016-103427.

FDA – Food and Drug Administration. 2013. Guidance for clinical investigators, sponsors, and IRBs: Investigational new drug applications (INDs) — determining whether human research studies can be conducted without an IND. U.S. Department of Health and Human Services, Rockville, MD.

Ferdowsian, H., L. S. M. Johnson, J. Johnson, A. Fenton, A. Shriver, and J. Gluck. 2020. A Belmont report for animals? *Cambridge Quarterly of Healthcare Ethics: CQ: The International Journal of Healthcare Ethics Committees* 29 (1):19–37. doi: 10.1017/S0963180119000732.

Fisher, J. A. 2009. *Medical research for hire: The political economy of pharmaceutical clinical trials*. New Brunswick, NJ: Rutgers University Press.

Fisher, J. A., and R. L. Walker. 2019. Advancing ethics and policy for healthy-volunteer research through a model-organism framework. *Ethics & Human Research* 41 (1):4–14. doi: 10.1002/eahr.500001.

Fitzgerald, M. H., and P. A. Phillips. 2006. Centralized and non-centralized ethics review: A five nation study. *Accountability in Research* 13 (1):47–74. doi: 10.1080/08989620600588944.

Garrett, Jeremy R., ed. 2012. *The ethics of animal research: Exploring the controversy*. Cambridge, MA: MIT Press.

Goldman, J., and M. D. Katz. 1982. Inconsistency and institutional review boards. *Jama* 248 (2):197–202. doi: 10.1001/jama.1982.03330020041027.

Graham, K. 2002. A study of three IACUCs and their views of scientific merit and alternatives. *Journal of Applied Animal Welfare Science: JAAWS* 5 (1):75–81. doi: 10.1207/S15327604JAWS0501_7.

Gunsalus, C. K., E. M. Bruner, N. C. Burbules, L. Dash, M. Finkin, J. P. Goldberg, W. T. Greenough, G. A. Miller, M. G. Pratt, M. Iriye, et al. 2007. The Illinois white paper: Improving the system for protecting human subjects: Counteracting IRB "mission creep." *Qualitative Inquiry* 13 (5):617–49. doi: 10.1177/1077800407300785.

Haywood, J. R., and M. Greene. 2008. Avoiding an overzealous approach: A perspective on regulatory burden. *ILAR Journal* 49 (4):426–34. doi: 10.1093/ilar.49.4.426.

Hedgecoe, A. 2020. *Trust in the system: Research ethics committees and the regulation of biomedical research*. Manchester, UK: Manchester University Press.

Jansen, L. A. 2005. A closer look at the bad deal trial: Beyond clinical equipoise. *Hastings Center Report* 35 (5):29–36.

Landi, M., J. Everitt, and B. Berridge. 2021. Bioethical, reproducibility, and translational challenges of animal models. *ILAR Journal* 62 (1–2):60–5. doi: 10.1093/ilar/ilaa027.

Landi, M. S., A. J. Shriver, and A. Mueller. 2017. The role of the IACUC in the design and conduct of animal experiments that contribute to translational success. *ILAR Journal* 58 (1):129–34.

Maisack, C. 2015. Harm-benefit analysis according to directive 2010/63/eu, article 38: What does it mean and how to realize it? *ALTEX Proceedings* 4 (1):24–7.

Mann, M. D., and E. D. Prentice. 2004. Should IACUCs review scientific merit of animal research projects? *Lab Animal* 33 (1):26–31. doi: 10.1038/laban0104-26.

Maschke, K. J. 2008. Human research protections: Time for regulatory reform? *The Hastings Center Report* 38 (2):19–22. doi: 10.1353/hcr.2008.0029.

Mohan, S., R. W. Barbee, and S. B. Silk. 2018. Contribution of the breadth and depth of IACUC membership to experimental design as a factor in research reproducibility. *Journal of the American Association for Laboratory Animal Science: JAALAS* 57 (2):104–9.

National Commission. 1979. The Belmont report: Ethical principles and guidelines for the protection of human subjects of research. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Washington, DC.

National Institutes of Health (NIH). 2010. Clarification on the roles of NIH scientific review groups (SRG) and institutional animal care and use committees (IACUC) in review of vertebrate animal research. Last Modified

September 1, 2010. Accessed May 13, 2022. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-128.html.

National Research Council. 2011. *Guide for the care and use of laboratory animals*. 8th ed. Washington, DC: National Academies Press.

Nycum, G., and L. Reid. 2007. The harm-benefit tradeoff in "bad deal" trials. *Kennedy Institute of Ethics Journal* 17 (4):321–50. doi: 10.1353/ken.2008.0004.

Plous, S., and H. Herzog. 2001. Reliability of protocol reviews for animal research. *Science (New York, N.Y.)* 293 (5530):608–9. doi: 10.1126/science.1061621.

Porter, J. P., and G. Koski. 2008. Regulations for the protection of humans in research in the United States. In *The Oxford textbook of clinical research ethics*, ed. E. J. Emanuel, C. Grady, R. A. Crouch, R. K. Lie, F. G. Miller, and D. D. Wendler, 156–67. New York: Oxford University Press.

Prentice, E. D., D. A. Crouse, and M. D. Mann. 1992. Scientific merit review: The role of the IACUC. *ILAR News* 34 (1–2):15–9. doi: 10.1093/ilar.34.1-2.15.

Pritt, S., J. A. McNulty, M. Greene, S. Light, and M. Brown. 2016. Decreasing institutionally imposed regulatory burden for animal research. *Lab Animal* 45 (8):297–300. doi: 10.1038/laban.1067.

Rid, A., and D. Wendler. 2011. A framework for risk-benefit evaluations in biomedical research. *Kennedy Institute of Ethics Journal* 21 (2):141–79. doi: 10.1353/ken.2011.0007.

Russell, W. M. S., and R. L. Burch. 1959. *The principles of humane experimental technique*. London: Methuen.

Schneider, C. E. 2015. *The censor's hand: The misregulation of human-subject research*. New York: New York University Press.

Schrag, Z. M. 2010. *Ethical imperialism: Institutional review boards and the social sciences, 1965–2009*. Baltimore, MD: Johns Hopkins University Press.

Silverman, J. 2016. Too many IACUCs in the kitchen. *Lab Animal* 45 (4):137. doi: 10.1038/laban.975.

Stark, L. 2012. *Behind closed doors: IRBs and the making of ethical research*. Chicago, IL: University of Chicago Press.

Stark, L. 2013. Reading trust between the lines: "Housekeeping work" and inequality in human-subjects review. *Cambridge Quarterly of Healthcare Ethics: CQ: The International Journal of Healthcare Ethics Committees* 22 (4):391–9. doi: 10.1017/S096318011300025X.

Steneck, N. H. 1997. Role of the institutional animal care and use committee in monitoring research. *Ethics & Behavior* 7 (2):173–84. doi: 10.1207/s15327019eb0702_8.

Thulin, J. D., J. F. Bradfield, V. K. Bergdall, L. A. Conour, A. W. Grady, D. L. Hickman, J. N. Norton, and J. M. Wallace. 2014. The cost of self-imposed regulatory burden in animal research. *FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology* 28 (8):3297–300. doi: 10.1096/fj.14-254094.

Tierney, W. G., and Z. Blumberg Corwin. 2007. The tensions between academic freedom and institutional review boards. *Qualitative Inquiry* 13 (3):388–98. doi: 10.1177/1077800406297655.

Walker, R. L. 2006. Human and animal subjects of research: The moral significance of respect versus welfare. *Theoretical Medicine and Bioethics* 27 (4):305–31. doi: 10.1007/s11017-006-9008-7.

Walker, R. L. 2016. Beyond primates: Research protections and animal moral value. *The Hastings Center Report* 46 (4):28–30. doi: 10.1002/hast.602.

Walker, R. L. 2019. Virtue ethics and laboratory animal research. *Institute for Laboratory Animal Research (ILAR) Journal* 60 (3):415–23.

White, R. F. 2007. Institutional review board mission creep: The Common Rule, social science, and the nanny state. *The Independent Review* 11 (4):547–64.