frontiers | Frontiers in Animal Science

POLICY AND PRACTICE REVIEWS
published: 25 April 2022
doi: 10.3389/fanim.2022.800186

# Relevance, Impartiality, Welfare and Consent: Principles of an Animal-Centered Research Ethics

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The principles of Replacement, Reduction and Refinement (3Rs) were developed to address the ethical dilemma that arises from the use of animals, without their consent, in procedures that may harm them but that are deemed necessary to achieve a greater good. While aiming to protect animals, the 3Rs are underpinned by a process-centered ethical perspective which regards them as instruments in a scientific apparatus. This paper explores the applicability of an animal-centered ethics to animal research, whereby animals would be regarded as autonomous subjects, legitimate stakeholders in and contributors to a research process, with their own interests and capable of consenting and dissenting to their involvement. This perspective derives from the ethical stance taken within the field of Animal-Computer Interaction (ACI), where researchers acknowledge that an animal-centered approach is essential to ensuring the best research outcomes. We propose the ethical principles of *relevance*, *impartiality*, *welfare* and *consent*, and a scoring system to help researchers and delegated authorities assess the extent to which a research procedure aligns with them. This could help researchers determine when being involved in research is indeed in an animal's best interests, when a procedure could be adjusted to increase its ethical standard or when the use of non-animal methods is more urgently advisable. We argue that the proposed principles should complement the 3Rs within an integrated ethical framework that recognizes animals' autonomy, interests and role, for a more nuanced ethical approach and for supporting the best possible research for the benefit animal partakers and wider society.

**Keywords: animal research, animal-centered research ethics, beyond the 3Rs, ethical scoring system, research ethics principles**

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***Specialty section:***
*This article was submitted to Animal Welfare and Policy, a section of the journal Frontiers in Animal Science*

***Received:*** *22 October 2021*
***Accepted:*** *21 March 2022*
***Published:*** *25 April 2022*

***Citation:***
*Mancini C and Nannoni E (2022) Relevance, Impartiality, Welfare and Consent: Principles of an Animal-Centered Research Ethics. Front. Anim. Sci. 3:800186. doi: 10.3389/fanim.2022.800186*

## INTRODUCTION

The use of animals in research is a topic that raises many ethical issues and fuels endless debates. When humans are subjected to research, it is deemed crucial that they express their consent both to the procedures they will undergo and to the use of the data resulting from said procedures. Indeed, obtaining partakers' informed consent is compulsory for both clinical trials and any other studies involving humans (e.g., British General Medical Council—Consent to Research, 2000). Additionally, it is considered imperative that the interests of human research subjects take priority over the interests of science and society (e.g., British Medical Research Council—Ethics Guide, 2004). Conversely, when the research involves the use of animals, it is widely assumed that they are

unable to provide consent to the studies they are involved in, which therefore makes them "objects," rather than subjects, of experimental procedures. Additionally, it is deemed acceptable that the interests of animal subjects are subordinated to the interests of science and society, including the interests of humans or those of animal populations. Worldwide legislation generally accepts these views, and delegates assessment and decision-making authority on issues of consent and interest prioritization to the local committees for the care and use of animals in research (whose responsibility is to peruse and approve or reject experimental protocols) and to veterinarians and caretakers (who are responsible for the detection of possible discomfort and pain arising from experimental procedures).

The present work addresses the ethical and procedural implications of considering animals as active participants in research, capable of consenting or dissenting to experimental procedures, and as stakeholders in the research process, based on the relevance of the research to their own interests. This possibility has been particularly considered within the field of Animal-Computer Interaction (ACI) (Mancini, 2017) but, to the best of our knowledge, such a perspective is yet to be applied to fields of biological research that involve the use of laboratory and farm animals. To this end, this paper explores the possibility of taking an animal-centered perspective on the use of animals in research. We examine the widely applied ethical framework for the use of animals in research—represented by the principles of Replacement, Reduction and Refinement (3Rs) (Russell and Burch, 1959)—and we discuss its limitations. We introduce the animal-centered perspective that underpins research in the field of ACI and propose four ethical principles—*relevance, impartiality, welfare and consent*—to define animal-centered research. We articulate the relation of our proposed principles to the 3Rs and explore their applicability, including opportunities and challenges, to animal research in other fields. We put forward a scoring system that could help researchers assess the extent to which a research procedure complies with the four principles and apply it to three examples of published studies. We conclude by arguing that our proposed principles should complement the 3Rs within an integrated ethical framework, to help researchers and delegated authorities assess the extent to which the involvement of animals in research procedures is more or less desirable, and what adjustments might need to be made in order to increase the extent to which procedures that do involve animals are animal-centered.

## LEGISLATION, ETHICAL FRAMEWORK AND PRINCIPLES FOR THE USE OF ANIMALS IN RESEARCH

The ethical dilemma about using animals in research is based on a recognition that they are capable of suffering while being incapable of consenting to procedures that can harm them. To address this dilemma, Russell and Burch (1959) proposed three principles for humane animal research. The principles of Replacement, Reduction and Refinement (3Rs) can be summarized as follows:

- Replace the use of animals with alternative techniques, or avoid the use of animals altogether;
- Reduce the number of animals used to a minimum, to obtain information from fewer animals or more information from the same number of animals;
- Refine the way experiments are designed and carried out, to make sure animals suffer as little as possible; this includes better housing and improvements to procedures to minimize pain and suffering and/or improve animal welfare.

The 3Rs have been reflected in EU legislation for decades, ever since the first legislation passed on the protection of animals used for experimental and other scientific purposes, dating back to 1986 [EC (European Council), 1986]. However, the 3Rs were spelled out in EU legislation for the first time within the Directive 2010/63/EU on the protection of animals used for scientific purposes (EC, 2010). This Directive makes the 3Rs a firm legal requirement, to be considered systematically when animals are used for scientific purposes, including basic, translational or applied research, regulatory testing and production, education and training. Over the years, the 3Rs approach has offered significant benefits for animal welfare and has substantially contributed to the improvement of animal use by stimulating the adoption of new strategies, including study design, method development and project coordination (Törnqvist et al., 2014). Some specific examples of successful application of the 3Rs, as a result of the efforts carried out by the UK's National Center for the Replacement, Refinement, and Reduction of Animals in Research (NC3Rs, https://www.nc3rs.org.uk/) can be found in the study by Burden et al. (2015). They include: (1) development of *in-vitro* models of human diseases such as asthma, in order to test novel mechanisms and targets of disease and therapeutics; (2) development of a "Rodent Big Brother" software to automatically track individual rat behavior in collective cages, in order to avoid individual housing and potentially stressful conditions which affect animal welfare and impair research outcomes; (3) use of non-animal methodologies (the non-sentient amoeba *Dictyostelium*) to predict potentially emetic compounds (drugs); and (4) design of scientifically robust alternative preclinical development pathways for monoclonal antibodies to replace or reduce the use of non-human primates.

On the other hand, there are also broad fields in which the 3Rs seem to have partially failed (or are yet to succeed) in ensuring the humaneness of research (Richmond, 2000). Firstly, the balance between the 3Rs may involve difficult trade-offs. For example, if we focus on reducing animals at all costs, using fewer animals but subjecting them to more aggressive interventions (or applying less humane endpoints) could increase the total animal suffering as a result. This is also the case when choosing between the use of a lower number of individuals of "higher species" and a higher number of individuals of "lower species" (Richmond, 2000). Secondly, most experimental protocols informed by the 3Rs seem to rely on broad indicators of animal welfare status, rather than focusing on what is meaningful for the animals (for example by using positive indicators of animal welfare), which would open completely new perspectives on refinement strategies. Thirdly, in spite of its widespread application around the globe, today

there is no globally standardized way of reporting on the species-specific application of any of the 3R principles (Törnqvist et al., 2014). As a result, reporting of animal use in relation to the 3Rs varies strongly between different countries, whereas a common reference framework would allow both researchers and ethical bodies to uniformly score research protocols and assess their level of humaneness in the use of animals, therefore helping to discriminate the cases in which the application of alternative methods would be highly recommendable from those in which animals would need to be used.

Although the 3Rs are now generally advocated as the gold standard to achieve the best possible compromise between animal welfare requirements and research interests and have constituted a pillar for the development of an ethics of humane animal research, in 2006 Russell himself confessed: "I hope I won't have to write any more long repetitive papers on the Three Rs," "[I] *would like to hand over to people* [. . . ] *who are still advancing the subject and can say something new*" (Balls, 2015). In this regard, different reviews of the 3Rs have been conducted over the years. For example, Ferdowsian and Beck (2011) argued that human research ethics is aimed at protecting the interests of individuals and populations, sometimes to the detriment of the scientific question under investigation, whereas in animal research often the importance of the scientific question being researched takes precedence over the interests of individual animals, implying the presumption that animal research should proceed based on perceived benefits to humans.

Similarly, more recently, Mancini (2017) noted how the ethical framework of the 3Rs is grounded on the consideration that the use of animals in research can be legitimized to achieve a greater good for society. Thus, within this framework, the consequences are that: (i) any costs to the animals involved can be considered acceptable based on the results of a cost-benefit analysis (i.e., whenever the expected benefits to society are deemed to warrant the envisaged costs to the animals); (ii) the procedures and protocols to be adopted in order to minimize suffering and animal use are effectively subordinated to the aims of the research (i.e., they are adopted only if they do not conflict with the purpose of the research or with the data to be collected); and (iii) there is no explicit provision for enabling animals to consent (or dissent) to their involvement or to withdraw from a procedure (i.e., animals have no control over the procedures they undergo, and are recognized for their role as research objects and representative models, rather than for their individual characteristics and needs).

In other words, within the 3Rs ethical framework animals tend to be considered instruments of research rather than participants in research (Mancini, 2017), with the most important issue being the fact that the animals involved in procedures are not deemed capable of consenting and thus are not afforded the opportunity to consent. Consent has been defined in human medicine as a voluntary, uncoerced decision, made by a sufficiently competent or autonomous person, to accept rather than reject some proposed course of action that will affect him or her (Gillon, 1985). In this sense, consent requires action by an autonomous agent based on adequate information. Consenting implies the ability to understand the contingent and the long-term implications of one's involvement (Faden and Beauchamp, 1986), but obvious cognitive differences and communication barriers make it seemingly impossible to obtain informed consent from animals. For these reasons, in animal research consent is usually not directly given by animals but transferred to and mediated by other subjects (Mancini, 2017): consent for animals is given by mediators, who are capable of understanding the wider implications of animal's involvement in experimental procedures and have the legal authority to consent on their behalf. The most common agents giving consent on behalf of animals are ethical review bodies, though in some cases owners can mediate consent for their animals (e.g., when pets are involved).

When ethical review bodies are involved, their decision to authorize (or forbid) experimental procedures must be based on (i) promoting high standards of animal welfare; (ii) implementing the 3Rs, (iii) enhancing scientific achievements; and (iv) generating a culture of care (RSPCA LASA, 2015), also in response to societal concern. These functions can only be adequately carried out with the complementary contribution of animals' daily carers, animal welfare experts and independent authorities. When an animal-owner relationship is involved, various influences may intervene. For example, historically, especially in agricultural settings, the provision of informed consent had largely an economic foundation (i.e., the need to preserve the value of the animal undergoing diagnosis and treatment by the veterinarian); more recently, economic consideration have largely been replaced by emotional and moral one, and concerns about additional aspects (e.g., quality of life, empathy, anthropomorphism, speciesism) might arise (Fettman and Rollin, 2002), whereby an owner's decisions may not always coincide with what is in the animal's best interests. For these reasons, in veterinary practice, as much emphasis is placed on preventing harm and on treating animals fairly as it is placed on allowing owners to make autonomous choices (Ashall et al., 2018), which means that in certain circumstances animal patients might be better protected outside the consent process.

The same considerations made with regards to the animal-owner relationship apply to laboratory animals or animals used in research, making therefore even more relevant the contribution of ethical review bodies, animal welfare specialists, veterinarians and animals' daily carers for the adoption of good practices in animal research. Merging the 3Rs approach with the principled approach proposed by Beauchamp and Childress (2013) for biomedical research, according to which respect for a subject's autonomy is viewed as one of four guiding ethical principles (alongside beneficence, non-maleficence and justice) (Beauchamp and Childress, 2013), could open new possibilities for reframing animal use in research. In particular, it could enable a shift from a framework in which animals are seen as research instruments unable to consent to their involvement in procedures, to one in which they are seen as research participants able to give a voluntary and autonomous contribution. In this regard, Erren et al. (2017) suggested the addition of a 4th R: recognition. The authors defined Recognition as "*crediting animals for their contribution to research by giving credit where credit is due, that is the Acknowledgments section,*

*unless authorship criteria are fulfilled*." Although it could be argued that recognizing human-animal co-authorship would have mainly symbolic value, animals do indeed contribute to research both as "objects" (e.g., in basic science and as models for preclinical research—Greek and Greek, 2010; Varga et al., 2010) and as "subjects" (e.g., in cognitive research-Vonk, 2016; Boeckle et al., 2020). Therefore, recognizing non-human animals' input in contributorship statements may be ethically required, even if they do not meet the normal standards for authorship (Erren et al., 2017). Recognition might therefore be the first step toward acknowledging animals as active participants and moving toward a different way of viewing animals in research.

## DIFFERENT PERSPECTIVES: TOWARD ANIMAL-CENTERED RESEARCH

Within some fields of applied research, the involvement of subjects in scientific procedures is essential to the development of new knowledge and applications. This is the case for the field of Interaction Design (ID) (Sharp et al., 2019), which focuses on the study and design of interactive systems, informed by disciplines such as psychology, ergonomics, engineering, informatics, social sciences and product design. The fundamental assumption of ID is that, in order to best support those for whom it is intended, interactive technology needs to be informed by their characteristics, as well as the characteristics of their activities, and the environments in which these activities take place. To achieve this, requirements about what a technology should do, and how, are elicited from those who have a stake in its development, primarily those who will interact with it, in order to inform alternative designs, which are then prototyped and evaluated, in an iterative process of incremental improvement. In other words, stakeholders—particularly target users—are regarded as central to the design process (Gould and Lewis, 1985) and their involvement as essential (Schuler and Namioka, 1993), because the effectiveness of interactive systems depends on the extent to which they meet stakeholders' requirements. As with any other research involving human subjects, ethics frameworks regulating research procedures within ID have always required the prioritization of individual human participants' autonomy and welfare above research and societal interests. Recently, within the field of Animal-Computer Interaction (ACI) (Mancini, 2011; Mancini et al., 2017), this ethical perspective has been extended to non-human research subjects involved in the study and design of interactive systems targeted to them.

The extension of said ethical perspective to non-human research subjects is consistent with theories of justice that acknowledge animals' fundamental entitlements, particularly Nussbaum (2006)'s capabilities approach. For the author, animals are agents capable of a dignified existence, with corresponding needs for flourishing and related goals they actively pursue, to which they have a moral entitlement. Influenced by Aristotle's insistence that humans and animals are fundamentally akin and by Marx's conception that one's true functioning depends on one's opportunity to engage in life activities more than on quantifiable resources, Nussbaum's theory extends to animals Rawls (1993) prioritization of individual liberties over societal interests and Sen (2009)'s focus on one's capability to do things one values as a measure of welfare. Thus, the author's capabilities approach differs significantly from utilitarian approaches underpinning the 3Rs, because it regards the balance between pleasure and pain too crude a measure to evaluate animals' functioning. Instead, within her approach, animals' functioning is evaluated based on the opportunity they have to pursue capabilities they value (e.g., an animal may choose to engage in an activity that has value for them even if this causes them pain), and advancing societal interests does not justify violating the capabilities of individuals (i.e., reducing the pain of many does not justify inflicting pain on the few).

Nussbaum identifies basic capabilities, which would allow animals to flourish and to which they are entitled, including: staying alive; maintaining one's bodily health and integrity; experiencing sensory and cognitive stimulation; enjoying nurturing emotions and attachments; setting goals and plans; forming intra- and interspecies affiliations and managing one's social life; having control over one's environment and safeguarding one's territorial integrity. While, for the author, the relevance of capabilities is species-specific (e.g., being killed may cause greater harm to an animal who is capable of making plans that death would frustrate than to an animal who does not have such capacity), animals should be enabled to express their species-relevant capabilities at least to a minimum threshold sufficient to guarantee a dignified existence. In this regard, while admitting that in some cases research which harms animals is still necessary, Nussbaum argues that its injustice should be explicitly recognized in order to shift the perspective from which research practices are assessed, to highlight the urgency of developing alternative practices and to accelerate related innovations.

ACI recognizes the centrality of animals' capabilities for the design of interactive systems and the importance of animals' dignified participation in research to ultimately ensure the effectiveness of said systems. Indeed, we argue that ACI's ethical approach has the potential to contribute relevant innovations in animal research more broadly.

### Animal-Computer Interaction: Research for and With Animals

Animals have interacted with technology for a long time. For decades, wearable biotelemetry has been fitted on wild animals to study their behavior in open fields (Samuel and Fuller, 1994), while laboratory animals have been working with interactive devices employed within behavioral (Skinner, 1959; Dudde et al., 2018) or cognitive (Reiss and McCowan, 1993) studies; farm animals have been exposed to robotic machines deployed to automate agricultural production processes (Rossing and Hogewerf, 1997) or to train them to perform specific behaviors (Dirksen et al., 2021), while dogs have been trained to operate domestic appliances such as light switches and washing machines on behalf of their assisted humans (Mancini et al., 2016). Until recently, the use of animal technology was reported mostly within research fields such as biology or engineering, with a focus on the research for which the devices were employed, but with little or

no detail related to the devices' design and to the role that animals might have played in their development.

In recent years, however, researchers have begun to investigate animals' interaction with technology within ACI (Mancini, 2011), focusing on the design, development and deployment of technology intended for animals, the role that animals play in these processes and how they are affected, not merely as sources of data, but as legitimate stakeholders and contributors. ACI extends the boundaries and core values of ID (Norman, 1986; Norman and Draper, 1986; Sharp et al., 2019) to non-human animals, whether the interaction is active and intentional (Robinson et al., 2014), active and unintentional (Mancini et al., 2015), passive and intentional (Cheok et al., 2011) or passive and unintentional (Mancini et al., 2012), dyadic and direct (Pons et al., 2014; Westerlaken and Gualeni, 2016) or distributed and indirect (Aspling and Juhlin, 2017). Consistent with the tenets of ID, if it is to be used for a specific purpose, as with operant devices, interactive technology is expected to afford good usability for animal users (e.g., being easy to learn how to use, helping users to perform a task efficiently—Zeagler et al., 2014; Robinson et al., 2015); if it is to be worn, as with biotelemetry devices, interactive technology is expected to provide good wearability for animal wearers (e.g., being imperceptible and unobtrusive, or at least acceptable to the wearer—Valentin et al., 2015; Paci et al., 2019). In any case, interactive technology is expected to provide, mediate or lead to good experience for animal stakeholders (e.g., being motivating and stimulating for a user to use, and not interfering negatively with a wearer's daily experience). As a field of research and practice, ACI takes an animal-centered perspective on the study and design of interactive systems, aiming to develop frameworks and methods that enable animals to participate in the design process as legitimate stakeholders and contributors (Mancini, 2011; Robinson et al., 2014; Westerlaken and Gualeni, 2016; Hirskyj-Douglas et al., 2017; Webber et al., 2020).

Recognizing animals as participants in and contributors to the design process is consistent with the 4th R proposed by Erren et al. (2017), but within ACI's animal-centered paradigm to designing interactive systems for and with animals, such a recognition has fundamental implications on multiple levels. Firstly, it requires that the features of an interactive product be informed by the animals' characteristics, and by the characteristics of their activities and of the environments in which they operate. In ACI design, this is exemplified by systems that feature species-specific interfaces (Resner, 2001; Jackson et al., 2013; Pons et al., 2015) or that are seamlessly integrated in learning and working processes already familiar to the animals involved (Robinson et al., 2014; Mancini et al., 2015). Secondly, an animal-centered perspective has methodological implications, whereby approaches to the design process ought to enable the animals involved to express their requirements through appropriate forms of participation consistent with their characteristics. In ACI research, this is exemplified by work in which methodologies typically used in ID or other relevant disciplines have been adapted for use in ACI projects to study interaction in context (e.g., multispecies ethnography—Mancini et al., 2012; ethnomethodology—Aspling et al., 2018), to assess the animal's experience (e.g., ethological observation—Baskin and Zamansky, 2015; Paci et al., 2016; Ruge et al., 2018—preference testing—Lee et al., 2006; Hirskyj-Douglas et al., 2017) or to elicit design requirements (e.g., "quick and dirty" prototyping—Robinson et al., 2014; high fidelity prototyping (Jackson et al., 2013; Westerlaken and Gualeni, 2016). Thirdly, animal-centered design has implications for the ethical perspective adopted by researchers, informing research practices that foster the conditions for animals' autonomous involvement in the design process as legitimate stakeholders and design contributors. Arguably, adopting an animal-centered research ethics that places animals and their interests (as individuals) at the center of the design process is a methodological requirement (Ritvo and Allison, 2014) the fulfillment of which is necessary to foster the conditions for animal-centered design. In this regard, while acknowledging that animals often find themselves involved in human practices they have neither designed nor consented to in the first place, Mancini (2017) proposes that ethics frameworks supporting animal-centered research should be informed by four core principles: relevance to part-takers, impartial treatment of part-takers, part-takers' welfare prioritization and part-takers' consent.

## Fundamental Principles of Animal-Centered Research

Firstly, the principle of relevance (Mancini, 2017) implies that that animals should be involved in any research procedures only if said procedures are directly relevant and beneficial to them. According to current regulations (EC, 2010), in any cost-benefit analysis related to a procedure, envisaged benefits do not have to be to the advantage of the individual animals involved and envisaged costs to the individuals are deemed acceptable if the expected benefits to society are deemed to warrant such costs. Within an animal-centered ethics, such a separation in the benefit-cost equation, where those who pay are not those who gain, is highly problematic. However, the problem is not only ethical, it is also methodological. As mentioned above, in disciplines such as ID and ACI, working directly with stakeholders to develop interactive products that can adequately support their activities is deemed essential. If those who pay the cost of being involved in the research process are also those who are set to gain from the outcomes of the process, any input that researchers receive from their participants is far more likely to be relevant and lead to the development of a product that is ultimately fit for purpose. Conversely, working with those who have no stake in the outcomes of the design process is likely to lead to a product that does not meet user requirements. For example, working with mice to develop the touch-screen interface of a system that macaques are expected to use during tests designed to better understand their cognitive abilities would be counterproductive; in order to enable the macaques to express their abilities, the interface would need to meet the specific usability and user experience requirements of the macaques, as determined by their physical, sensory, cognitive, social and otherwise experiential characteristics.

Secondly, the principle of impartial treatment (Mancini, 2017) implies that ethics frameworks supporting animal-centered research should afford protection to all partakers, not in virtue of their characteristics (e.g., species, sex, age, provenance) and any capacities attributed to those characteristics (including sentience), but in virtue of their role (i.e., the very fact that they part-take in the research process). In current legislation (EC, 2010), only species possessing certain characteristics (e.g., a spinal cord, sentience) are protected and species regarded as companions rather than food (e.g., dogs vs. pigs in Western cultures) enjoy a higher degree of protection regardless of their characteristics, simply based on societal considerations (i.e., from a human perspective). However, within an animal-centered ethics, it is essential that researchers acknowledge and respect the individual characteristics of everyone partaking in research procedures, regardless of taxonomical or other categorizations based on what is necessarily interim knowledge. Researchers should treat all research partakers as individuals equally deserving of consideration and care according to their welfare needs (as defined below). Again, this is important, not only on ethical grounds, but also on scientific grounds. At any given time, knowledge and understanding about the implications of animals' characteristics is inevitably limited, so any form of discrimination on the basis of taxonomic distinctions is likely to bias research findings. It is only by acknowledging and respecting partakers and their characteristics without discrimination that researchers can develop research set-ups and protocols that provide the best possible understanding of those they are working with. Indeed, for a long time, researchers' anthropocentric perspective when studying other species resulted in a significant underestimation of many animals' capacities and in the development of research protocols that reflected human-centric biases, in turn hindering the development of new knowledge about those species (Vonk, 2016).

Thirdly, the principle of welfare prioritization (Mancini, 2017) highlights the importance, for an ethics framework, of prioritizing partakers' welfare at all times in order to support animal-centered research. The author refers to Stamp Dawkins (1998, 2003, 2012) definition of welfare according to which animals enjoy good welfare if they are healthy and have what they want, on the grounds that, in addition to evolving physical adaptations that allow them to thrive in their environment (e.g., a streamlined body to move underground, sharp teeth to open seed shells), animals have also evolved the capacity to want things that are conducive to their health (e.g., wanting to burrow to hide from predators, wanting to gnaw to maintain sharp teeth). Of course, being able to stay safe and acquire resources is essential to maintaining good welfare, to which end animals need to be able to make predictions (to decide what they want) and to exert control so they can act upon those predictions (to obtain what they want). Thus, within an animal-centered ethics framework, researchers should endeavor to respect the animals' biological integrity (i.e., their physical and psychological health) and autonomy (i.e., their ability to express and pursue their wants). They should avoid any procedures that could physically or psychologically harm the animals, and protect individuals from any harm (including death); they should also work in contexts that are habitual for and thus familiar to the animals, and endeavor to avoid obtruding their activities or disrupting their daily life patterns and routines. In brief, researchers should give partaking animals space for expression and control over the research process, and use only forms of interaction that are respectful of and responsive to the animal's needs and wants. Critically, according to the principle of welfare prioritization, when considering the potential impact of a procedure, any cost-benefit analysis of the research should be carried out based on the animal's best interests, and the interests of individual participants should prevail over the interests of science and society.

Although the principles of relevance, impartiality and welfare are all important when considering whether animals are used as objects for a procedure or are enabled to partake as subjects in a research process, consent is the criterion that has mostly been discussed within the related literature (e.g., Beauchamp and Childress, 2013). In this regard, Mancini (2017) argues that, within an animal-centered ethics, researchers have a responsibility to always garner the animals' consent in two complementary forms: mediated and contingent. Mediated consent would be provided by those who are capable of comprehending the wider implications of the research in relation to the animals' welfare needs, who have the legal authority to consent on their behalf, who have in-depth knowledge of partaking animals as a species and as individuals, and who have a vested interest in prioritizing the welfare of the individuals concerned. These competences might be covered by different agents (e.g., the animal's legal guardian and the animal welfare expert might be the same or two different persons; the legal authority may be provided by a legal guardian and by an independent animal welfare and ethical review body as envisaged by the European Directive (EC, 2010) but they should all be represented.

However, garnering consent from mediators would not exempt researchers from garnering consent from the individual animals themselves, since consent implies voluntary engagement and it cannot be assumed that mediators know what individual animals want under specific contextual conditions. The assumption is that, while mediators representing the animals are in a position to assess the wider implications of a procedure, the animals themselves are best placed to respond to the contextual conditions of a research set-up according to the impact that these might have on their own welfare (e.g., an animal might not want to enter an experimental space if they deem it unsafe and the very fear they might experience when in that space may have a severe impact on their welfare). Thus, contingent consent would need to be provided by individual partakers and researchers should ensure that those individuals are afforded sufficient control to make relevant choices, including the choice not to engage. If a partaker could choose the pace and modality of their engagement with a research process at any time, then their response could provide a measure of their consent to engaging with a specific research set-up. To this end, procedural set-ups should enable partakers to assess the situation as much as possible (e.g., allowing the animal to freely explore their surroundings or any research equipment before and during a procedure), to make relevant choices between alternative forms

of engagement (e.g., between different ways of interacting with experimental equipment or between reward mechanisms) and to effectively withdraw or withhold engagement (e.g., plenty of escape routes or comfortable rest areas as appropriate). Since any contextual variations may affect the partaker's assessment of the situation and their willingness to engage, contingent consent should be seen as a dynamic process to be expertly monitored for signs of dissent (as is the case with non-competent human research participants—British Medical Research Council—Ethics Guide., 2007).

## Principles of Animal-Centered Research Ethics and the 3Rs

The principles of the animal-centered research ethics reported above are only partly aligned with the principles of the 3Rs (Russell and Burch, 1959) discussed above. From an animal-centered perspective, the 3Rs present two fundamental limitations. Firstly, these are grounded in the assumption that animals cannot provide consent to their involvement in potentially harmful research procedures and thus provide an approach to manage the ethical conflict between animals' assumed inability to consent and the fact that human society considers their use in such procedures necessary to achieve a greater good. Conversely, the principles of an animal-centered research ethics are grounded in the assumption that animals can provide mediated and contingent consent (or dissent) to their involvement in research procedures, as long as they are allowed to assess a research set-up (and thus make predictions as to the impact on their welfare) and to choose whether and how to engage (and thus exert control to express and attain what they want). In this regard, from an animal-centered perspective, the most ethical research set-ups or procedures would need to make any potential threats to the wellbeing of partaking animals materially explicit and assessable by them, and would give them control as to whether and how to engage. Alternatively, the presentation of such set-ups or procedures would enable those who represent the welfare interests of partaking animals to assess any potential harms, enabling them to prioritize the animals' welfare.

Secondly, albeit animal-welfare-minded, the perspective underpinning the 3Rs cannot be deemed animal-welfare-centered, since procedures that are harmful to the animals involved are still permissible under the 3Rs provided certain conditions. Conversely, within an animal-centered ethics, procedures which are harmful to the participant and to which the participant does not provide consent would simply not be permissible, and the potential risks of any procedures would be primarily assessed with respect to the interests of the individual animals involved. Nevertheless, Mancini (2017) notes how the principles of refinement, reduction and replacement have various degrees of relevance for the animal-centered ethics being discussed here. In particular, the 3Rs principle of refinement is highly relevant as its application can help ensure that any (foreseen or unforeseen) procedural risks to partaking animals are minimized. In this regard, refinement of course pertains both to the design and execution of research procedures, and to their documentation and publication, and its importance for ACI research has been highlighted by Väätäjä and Pesonen (2013). The principle of reduction has relevance also in animal-centered research. But, while the involvement of individual animals should always be justified (and of course their interests should always be prioritized), the criterion of statistical power commonly used for reduction is not the only important factor to be considered, since animals are involved in research not merely as representatives of a category (e.g., species) but also as individuals with their unique characteristics (Robinson et al., 2014).

The principle of replacement, Mancini (2017) argues, is only partially relevant to animal-centered research, wherein partakers are not regarded as the substitutable components of an experimental set-up, and there is an expectation that any procedure they are involved in be relevant and beneficial to them. Therefore, replacing one species with another species (even a less sentient one) would not necessarily be appropriate or beneficial to the animals of either species, unless the individuals of the species involved as a replacement had themselves a stake in the research process. For parts of the research or development process, researchers could apply heuristics, execute technical tests and involve consenting competent humans in preliminary testing before involving the target animals; but these could not be replaced altogether, as they have unique characteristics, interests and requirements that should be allowed to inform the research process at least at key stages, with the proviso that partakers' involvement is justified and their interests prioritized.

In a nutshell, within an animal-centered ethical framework, the welfare and autonomy of individual animals taking part in procedures should always be respected and their individual contribution to the research processes and outcomes should always be sought and valued in its uniqueness. But to what extent could the principles of the animal-centered ethical framework discussed above be extended to other fields of research and practice involving animals? What might be, if any, the benefits of applying such a framework to research fields outside of animal-computer interaction? Arguably animal partakers would benefit significantly, but would research processes and outcomes also benefit and, if so, in what way, to what extent and under what circumstances?

# EXPLORING THE APPLICABILITY OF ANIMAL-CENTERED RESEARCH PRINCIPLES TO ANIMAL RESEARCH

As we have seen, the ethical framework discussed above substantially differs from the general perspective regulating the involvement of animals in research in fields other than ACI, where animal research might take place (e.g., farms, laboratories, slaughterhouses and zoos). As highlighted by Mancini (2017), ethical boundaries are often context-dependent and often need negotiating in specific cases. This means that, in principle, an animal-centered ethics could be applied to a range of research contexts to reduce animal suffering or improve their quality of life. In such cases, when any of the principles of animal-centered research seems incompatible with a research procedure,

it is important for researchers to acknowledge that an ethical concern arises, and that this is not due to the animals' inability to express their consent or dissent to procedures that might harm them, but rather to the prevailing tendency to involve animals as instruments in research processes in which they have no stake. The future of animal-centered ethics in animal research will likely depend on the balance between animals' participatory involvement and animals' instrumental use in research. At the same time, arguably the extent to which animals are involved in research as participants rather than as mere instruments needs to be part of the equation of what counts as "humane research." This section explores the possibility of extending the four core principles of relevance, impartiality, welfare and consent to animal research conducted in different fields. We consider each principle and how different kinds of research might score against it, along a five-point scale ranging from the highest to the lowest compliance, and what different levels of compliance might imply for animal research studies and for animal research policies more generally. Research shows that the reliability of scales drops when scale points are below five or above 10 (Preston and Colman, 2000). Five-, seven- and 10-point scales are comparable for confirmatory factor analysis or structural equation models, although five-point scales tend to be easier for respondents to use (Dawes, 2008). We propose a five-point scale scoring template as a trade-off between reliability and usability for those assessing procedures' compliance with the principles. **Table 1** provides the scoring template we propose to use.

## Principle 1: Relevance to Partakers

A domain in which relevance to partakers can be immediately assessed is animal welfare research. When this kind of research is conducted, for example on farm animals, typically some experimental groups are kept under regular farming conditions (respecting all the requirements set out by animal protection laws), whereas other groups are kept under "high welfare" conditions (e.g., different flooring, bedding material, environmental enrichments, access outdoors, additional space and so on). Example studies of this kind have investigated space allowance for pigs (Nannoni et al., 2019), lighting requirements for pigs (Martelli et al., 2015), flooring systems for beef cattle (Magrin et al., 2019), straw provision and tail docking in pigs (Di Martino et al., 2013), as well as reviewing attitudes toward access to pasture by dairy cows (Charlton and Rutter, 2017). As mentioned, it is clear that the welfare of part of the animals involved in these studies is expected to be improved compared to conspecifics kept under conventional farming conditions. Also, the aim of these trials is usually to propose (or identify) a rearing system that is more respectful of the peculiar needs of the studied species. Overall, although in these trials some invasive measures (e.g., blood samplings) might be deemed necessary to assess welfare levels (e.g., stress hormones), the prospective aim of the trial is to improve the welfare of all animals of the examined species which are raised for commercial purposes. In some cases, these studies are designed to collect data at commercial farms, in order to investigate under which farming systems animals benefit from the best welfare (e.g., Regula et al., 2004—housing systems for dairy cows) or from a reduced risk of lesions (e.g., Taylor et al., 2012—tail biting risk for pigs kept in commercial farms).

In these scenarios, relevance to partakers is maximized: although not all animals participating in the trials might benefit from improved welfare, at least a portion of them does. Moreover, the prospective benefit of these studies might be extended to large populations (e.g., if acknowledged within an animal protection policy, the benefit might be potentially extended to all the animals of the same species farmed under commercial conditions in Europe). Therefore, this kind of research scores very highly against the principle of relevance. Despite this, at present, animal welfare research that directly benefits the animals involved and that might lead to considerable benefits for an entire category still needs to follow exactly the same authorization procedure as any other research protocol. We suggest that, along with fostering the development of alternative methods when research does not benefit animals, policies should facilitate this kind of animal welfare research, thus favoring the improvement of many animals' living conditions (in farms, laboratories, zoos and private houses).

A more controversial example with respect to relevance is the case of pharmacological research: in this case, a drug is tested on a species (which might be either a model or the target species) in order to assess for example its toxicity and mode of action, or to predict its effects on the target species. Whether this kind of research is to be considered beneficial for the partakers will depend on trade-offs between the possible outputs (i.e., benefit for the target species and/or for the model species) vs. the process (i.e., the severity of the procedures to be carried out and their impact on the individuals taking part in the research). Therefore, in this kind of studies, relevance could be considered moderate when animals taking part in the trial belong to the target species (or are expected to receive direct benefits from the use of the drugs in their species, even if they are used as a model). Noteworthy, in this example, is that relevance is assessed in terms of overall benefit for partakers intended as a category, and not as the individuals taking part in the trial. In the absence of direct benefit for the individuals, the highest score for relevance cannot be met. In our framework, the relevance for partakers decreases as the expected benefits decrease. We propose that relevance should be assessed regardless of the number of animals involved, as the 2Rs known as "reduction" and "refinement" are considered a prerequisite to this kind of ethical evaluation.

## Principle 2: Impartial Treatment of Partakers

This principle of animal-centered research is aimed at guaranteeing non-prejudicial treatment to partakers. As the animal-centered ethics we propose values contribution and participation, we believe that, regardless of their species, sex, age, etc., each partaker in the experimental process can contribute to both research and research design. To achieve this, similarly to what has been described above for prototyping in the Interaction Design field, research should be considered as an iterative process of incremental improvement, in which iteration should be preferred over repeatability. To this end,

**TABLE 1 |** Scoring template for assessing research procedures against animal-centered (AC) principles.

| Ethics standard | Compliance with principles of animal-centered research | | | |
|---|---|---|---|---|
| | ***RELEVANCE* to partakers** | ***IMPARTIALITY* toward partakers** | ***WELFARE* of partakers** | ***CONSENT* of partakers** |
| 5. Very high | Procedure is directly relevant and highly beneficial for partakers | Individuals receive highest consideration regardless of their capacities | Procedure enhances partakers' welfare | Partakers are enabled to choose whether and how to engage with procedure |
| 4. High | Procedure is relevant but benefits may not be direct or immediate | Individuals receive high consideration but not as much as others with more capacities would | Procedure does not impact negatively on partakers' welfare | Partakers are mostly able to choose whether and how to engage with procedure |
| 3. Moderate | Procedure has some relevance but benefits are only indirect and only in future | Individuals receive some consideration but notably less than more capable ones would | Procedure has minor impact on partakers' welfare | Partakers have limited ability to choose whether and how to engage with procedure |
| 2. Low | Procedure has little relevance and benefits are only indirect and only in future | Individuals receive significantly less consideration than more capable ones would | Procedure has significant negative impact on partakers' welfare | Partakers are mostly not allowed to dissent or withdraw from procedure |
| 1. Very low | Procedure has no relevance whatsoever and no benefits for partakers even indirectly or in future | Individuals receive very little or no consideration compared to more capable ones | Procedure has severe negative impact on partakers' welfare | Partakers are not allowed to dissent or withdraw from procedure in any way |

the involvement of animals as stakeholders in the research design process is regarded as essential, as it might lead to important design decisions and inform alternative research designs. Impartial treatment is key to enabling this process and should be guaranteed by avoiding prejudicial considerations on animals' sentience or discomfort/pain perception: all animals should be regarded as active contributors, deserving of the best welfare conditions possible, and capable of indicating consent or dissent with their behavior/physiology and to inform changes in experimental design.

Of course, we need to acknowledge that all animal research takes place within a socio-cultural, and legislative, context that does not treat different animals impartially. For example, current European regulation (EC, 2010) grants a higher degree of protection to those that are considered companion species (e.g., cats, dogs) compared to similarly complex species, consistent with the public's greater sensitivity toward companion animals. In a European context, farming cows and pigs for human consumption is regarded as acceptable by most people and is indeed legal, while farming cats and dogs for the same purpose is regarded as unacceptable and is indeed illegal. In a British context, some species, such as house mice or gray squirrels, are considered vermin and the public are encouraged to kill them and are forbidden from rescuing them, while other—similar—species, such as dormice or red squirrels, are protected under the law and harming them is an offense (Countryside and Rights of Way Act 2000 for England and Wales). Admittedly, this kind of socio-cultural and legislative bias might make the impartial treatment of individual animals partaking in research more difficult to achieve, as researchers are themselves part of the socio-cultural, and legislative, context in which they operate and which might bias their perceptions and dispositions. Nevertheless, researchers should endeavor to afford all their research partakers treatment standards equivalent to those that would be warranted to the animal species most protected under the law (the human). Research procedures that take explicit measures to guarantee impartial treatment to all partakers would score very highly against the impartiality principle.

## Principle 3: Partakers' Welfare Prioritization

As described in section Fundamental Principles of Animal-Centered Research, this principle is grounded in the consideration that the interests of individual participants should prevail over the interests of science and society, and any research decision should be based on the animal's best interests. However, sometimes this evaluation is not straightforward, as it may depend upon trade-offs between the importance of preserving the animals' physical integrity (see Stamp Dawkins, 2003) and the potential benefits provided by the research. For example, during an animal welfare study, assessing whether for the animal it would be preferable to live a better life during a trial but undergo a mild procedure that affects his physical integrity (e.g., blood drawing), or not to take part in the trial at all and live a "regular" life might not be straightforward. However, we suggest that this kind of assessment is relevant for the scoring of any study against the *welfare* principle, and therefore it should be attempted to score the envisaged experimental procedures against this principle.

Additionally, it has been argued that under many circumstances killing is an inevitable consequence of animal use once they have fulfilled their scientific utility. This is sometimes

true (when animals are culled because they would otherwise suffer needlessly) but is also associated with a predominantly "welfarist-utilitarian" influence, which regards death as a lesser issue (provided the killing is carried out humanely) and curtailing the life of laboratory animals as of little ethical importance (Franco, 2016). Within our animal-centered framework, we argue that the welfare of partakers should be guaranteed also after their use in research, by adopting a "no-kill" approach whenever possible. This is in line with a new set of "3Rs" (Re-use, Rehabilitation and Rehoming) according to which a high animal welfare level ensured during a trial is also maintained or even improved after the end of the trial (for an extensive review on the topic see Franco, 2016; Franco and Olsson, 2016). The application of these Rs would significantly contribute toward the higher scoring of a study against the *welfare* principle.

It has been observed that providing animals with technology that enables them to better control the functions and environments in which they are already involved affords them the possibility to exert a measure of autonomy, albeit with some conceptual limitation (Mancini, 2017), thus leading to an improvement in their welfare (Weeghel et al., 2016). This is also relevant to the prioritization of animal welfare during trials. Additionally, systems for monitoring animal welfare designed and described for on-farm use (Rushen et al., 2012; Zehner et al., 2012; Matthews et al., 2016; Caria et al., 2017) would also be useful within research environments to enable the quick identification of sick or uncomfortable animals by continuously and closely monitoring specific welfare parameters (e.g., temperature, level of activity, social behavior, use of functional areas). The use of interactive and monitoring technology during trials to enhance animal welfare would contribute toward a higher score against this principle, provided that appropriate measures were taken to guarantee the welfare of partakers (e.g., temporarily or permanently withdrawing individual animals from the trial, or arresting the trial altogether when necessary).

Apart from any ethical considerations, though, evidence shows that good animal welfare is linked to the quality of research data derived from laboratory animals (e.g., validity as models of human disease, number of animals required to achieve statistical significance, reproducibility of *in vivo* studies) (Prescott and Lidster, 2017). This is due to the fact that the endocrine condition and immunology of laboratory animals, which experimenters may assume to be normal, can be compromised by social conditions, developmental history, rough handling, inadequate environment and various stressors in the animal unit or experimental laboratory. These uncontrolled variables may make animals unsuitable subjects for scientific studies, and compel scientists to do everything practicable to ensure the happiness of laboratory animals and therefore the quality of their own research (Poole, 1997).

### Principle 4: Partakers' Consent

The issue of animal consent is what triggered our conceptualization of an ethical framework for animal-centered research beyond the field of ACI. As argued above, animals used in research are usually not given the possibility to assent or dissent to the procedures they undergo. This is likely due to the belief that allowing animals to express their will might limit the execution of several procedures. It should be acknowledged that in many cases animals do clearly express their will, and that it is generally considered acceptable to overlook (to some degree) signs of distress and temporary discomfort for the sake of the ongoing trial—which highlights the need to preventively set adequate humane endpoints (Humane Endpoints, 2016). For example, although farm animals may disagree to being restrained for blood sampling, the procedure in itself is minimally painful and invasive, and results in only a temporary discomfort, so it is generally carried out regardless of the animal's dissent.

Animals' consent or dissent is likely to be evident in the choices they make during experimental procedures. One of the best examples of research in which animals are free to express their choices is the field of preference and motivation testing, whereby animals are asked to indicate with their behavior their preferences for common housing options (such as temperature, illumination, types of bedding and flooring, loading ramps, pens) and to clarify how strongly they avoid various aspects of confinement and methods of restraint (Fraser and Matthews, 1997). However, researchers warn that this kind of preferences may not always be indicative, especially if the choices fall outside the animals' sensory, cognitive and affective capacities, or if animals are required to choose between short- and long-term benefits. These aspects should be carefully considered when assessing a procedure against *consent*.

The 3Rs framework aims to achieve the best possible trade-offs between animal welfare and human benefits. However, once the 3Rs are satisfied, the experimental protocol is deemed to have satisfied all ethical requirements and is allowed to be carried out. In contrast, we propose that animal consent should be regarded as a key principle of animal-centered research. Procedures which enable participants to choose when and how to partake will score highest against this principle, whereas those which do not allow partakers to dissent or withdraw will score the lowest. Although the argument for animal consent might appear purely theoretical, our aim is to table a discussion about animal consent within the real world (where, for example, procedures carried out on animals as a model of human disease might be deemed acceptable because of their expected benefits for human health, regardless of animal consent). With our animal-centered research framework, we wish to recognize and raise awareness of the issue of animal consent as an open ethical question, in the belief that acknowledging its importance, instead of overlooking it, will eventually lead to improvements in animal use in research and related outcomes.

## SCORING RESEARCH PROCEDURES AGAINST ANIMAL-CENTERED ETHICAL PRINCIPLES

As discussed above, different procedures may be more or less consistent with the principles of *relevance*, *impartiality*, *welfare* and *consent*, depending on the aims of the research and on the methods through which those aims are pursued. Scoring against

each of the principles could help researchers assess the extent to which a procedure can be deemed ethical and humane from the perspective of the animals involved, based on scores across all four parameters. Clearly, a procedure that scored high against all the parameters (i.e., that was highly relevant to the individuals involved, that gave equal consideration to the welfare needs of all participants, that was highly compatible with their welfare and that enabled them to give or withhold their consent at will) would be considered ethical and humane from an animal-centered perspective. However, a procedure would not necessarily need to score high against all of the parameters in order to be deemed ethical from an animal-centered perspective.

This section presents three examples of studies conducted with animals to illustrate how our scoring system might be applied to assess a research procedure against the four principles we propose. The scoring process could be undertaken at the point of designing a procedure, to ensure maximum possible adherence to the principles, or retrospectively to evaluate a procedure against the principles and identify opportunities for improvement. The examples are based on published studies.

## Example 1: Investigation of a Dog's Interaction With Dog-Friendly Controls

If a procedure was not particularly relevant to the individuals involved, but was still beneficial to someone related to them or to them in future, and if all participants were treated impartially, the procedure was not detrimental to their welfare, and they were able to choose whether and how to partake, then said procedure might still be deemed relatively highly animal-centered. As a case in point, consider a study conducted to test the readiness with which a dog might learn to use different canine-friendly prototype controls designed to facilitate the work of mobility assistance dogs routinely trained to carry out tasks, such as opening doors or switching lights (Mancini and Lehtonen, 2018). In this study, researchers trained a dog, Zena, who was not a mobility assistance dog and was not on a training program to become one. However, the task they trained her for was similar to one with which she was already familiar and the training took place in an environment that she frequented regularly. During the study, Zena was free to move around and choose whether to engage or walk away, thus setting the pace of the exercise. Bedding, water and toys remained readily accessible to her at all times during the study period. For the duration of the study, she continued to live with her guardian, maintaining her usual routine, receiving her usual exercise and consuming her usual diet; the treats used as a reward during the training sessions and the stimulation provided by the training activities were all extras. The procedure utilized an apparatus, comprising door-opening and light-switching controls, which was specifically designed with canine ergonomic characteristics in mind and which was pre-tested by humans for safety. The training leveraged classical and operant conditioning rules, whereby positive reinforcement was used to teach Zena to interact with the controls, during 4 days distributed over a 2-week period. Each day included several training sessions lasting up to 5 min each, with long breaks in between, depending on Zena's willingness to engage. Sessions were ended either by Zena herself (if she walked away), or by the researchers (if she showed signs of disengagement, including light panting, looking away, sniffing the ground or becoming distracted). Zena's participation in the process directly informed a framework for multispecies participatory design and further requirements for dog-friendly controls.

While the process and outcome of the exercise was not immediately beneficial to Zena, the procedure had relevance in the longer term as the kind of controls she was trained to use could plausibly become commercial products any dog, including her, could use to control aspects of their living environment. Since the procedure did not have immediate relevance for the canine partaker, working with mobility assistance dogs who could immediately benefit from their engagement would have been better. This limitation was partially off-set by the fact that the procedure did not have a negative impact on Zena, as it was consistent with her welfare needs and posed negligible risks, with regards to both the safety of the apparatus and the appropriateness of the training process, during which her body language was continuously monitored for signs of concern. The procedure was highly compliant with the principle of impartiality, since her needs were arguably given the same consideration that would have been given to human participants in the same position and since her input was regarded as a significant research contribution. Finally, Zena was enabled to provide contingent consent, as she could choose whether and how to engage at all times during the study. Overall, she had a significant amount of control over the procedure, and the chance to express her preferences in relation to different prototypes and the interaction modalities that these afforded. The balance of scores for this trial could be summarized as shown in **Table 2**.

In cases like the one described above, although there is clearly room for improvement, the compliance with the four principles of animal-centered research is high or very high. In these cases, animals' ability to exert their agency through their engagement choices, including contingent consent or dissent, is essential to the success of this kind of research. When the research is relevant or highly relevant and beneficial in the short or long term, enabling animals to represent their interest through participation is important, and not including them might be ethically problematic. In this regard, impartiality and welfare are key to ensuring that their participation in a procedure is unincumbered by unmet needs.

## Example 2: Validation of Health Monitoring System for Cows

A procedure might not afford the animals involved the opportunity to provide or withdraw consent, but might be highly relevant to them and beneficial to their welfare, while not impacting negatively on the welfare of the participants who are treated less favorably. For example, consider a study conducted to validate a health monitoring system for cows that captured data about the animals' rumination activity, food and water intake, and locomotion (Zehner et al., 2012). The wireless system included a halter headcollar incorporating a vegetable

**TABLE 2 |** Assessment of the compliance of the dog controls study with the four principles of animal-centered research (Mancini and Lehtonen, 2018), with more relevant descriptors displayed in bold character.

| Ethics standard | Compliance with four principles of animal-centered research | | | |
|---|---|---|---|---|
| | ***RELEVANCE* to partakers** | ***IMPARTIALITY* toward partakers** | ***WELFARE* of partakers** | ***CONSENT* of partakers** |
| 5. Very high | Procedure is directly relevant and highly beneficial for partakers | **Individuals receive highest consideration regardless of their capacities** | Procedure enhances partakers' welfare | **Partakers are enabled to choose whether and how to engage with procedure** |
| 4. High | **Procedure is relevant but benefits may not be direct or immediate** | Individuals receive high consideration but not as much as others with more capacities would | **Procedure does not impact negatively on partakers' welfare** | Partakers are mostly able to choose whether and how to engage with procedure |
| 3. Moderate | Procedure has some relevance but benefits are only indirect and only in future | Individuals receive some consideration but notably less than more capable ones would | Procedure has minor impact on partakers' welfare | Partakers have limited ability to choose whether and how to engage with procedure |
| 2. Low | Procedure has little relevance and benefits are only indirect and only in future | Individuals receive significantly less consideration than more capable ones would | Procedure has significant negative impact on partakers' welfare | Partakers are mostly not allowed to dissent or withdraw from procedure |
| 1. Very low | Procedure has no relevance whatsoever and no benefits for partakers even indirectly or in future | Individuals receive very little or no consideration compared to more capable ones | Procedure has severe negative impact on partakers' welfare | Partakers are not allowed to dissent or withdraw from procedure in any way |

oil-filled silicone tube with a built-in pressure sensor to capture jaw movements, placed over the bridge of the cow's nose, and connected to a data logger unit and a battery unit placed at either end of the silicone tube over the cow's cheeks. Additionally, the system included an accelerometer to capture body motion, placed around the cow's foot. Data related to rumination and food intake was collected from 12 cows for 14 days, water intake data was collected form 5 cows for 22 days and motion data was collected from two cows for three days.

It is unclear whether the same cows were used for collecting data on all the measures or whether different cows were used for different measures, and thus whether some of the cows were fitted with more than one device. It is also not clear whether the cows involved wore the devices for longer than the data collection periods. There is no evidence to suggest that any mechanisms were put in place to allow the cows to consent to being fitted with wearable devices that might have bothered them (particularly those mounted on the headcollar) or to withdraw from the study (e.g., if they showed signs of unease). While the devices in question do not appear to be particularly obtrusive, there is a lack of information about the possible experiential impact of the study on the welfare of individual cows. Said impact might depend on how many devices each might have been fitted with and for how long, or how each might have responded, and on whether the study procedure might have been adjusted as a result. However, the procedure took place in the animals' habitual environments and, aside from the presence of the monitors, did not involve alterations to their daily routines, behaviors and conditions, and no invasive procedures were carried out. The lack of information on the cows' experience during the study suggests that this was not deemed to warrant discussion, which in turn suggests that their perspective was not given the consideration it might have been given to human participants in the same position. On the other hand, the study had direct relevance for the participating cows as it aimed to validate tools that could monitor their welfare, something from which they themselves must have benefitted during the trials and which many other dairy cows were set to benefit from. In brief, while some aspects of the study were not necessarily compliant with our proposed principles for animal-centered research, other aspects were highly consistent with them. The balance of scores for this trial could be summarized as shown in **Table 3**.

In cases such as this, the inability of partakers to choose whether and how to engage may be offset by the fact that a procedure is very relevant and highly beneficial for them directly, presumably in the short as well as in the long therm. However, in these cases, it is important for researchers to ensure that the procedure does not impact on the welfare of the animals, particularly if they are unable to opt out. Similarly, granting them consideration as impartially as possible, compared to human participants in the same position, would help compensate for the fact that the animals are not allowed to provide contingent consent.

## Example 3: Acute Toxicity Test of Pesticides With Mice

A procedure that was not relevant to the individuals involved, that did not give impartial consideration to participants, that was detrimental to their welfare and that did not afford them the opportunity to effectively withhold consent could not be

**TABLE 3 |** Assessment of the compliance of the cow health monitor study with the four principles of animal-centered research (Zehner et al., 2012), with more relevant descriptors displayed in bold character.

| Ethics standard | Compliance with four principles of animal-centered research | | | |
|---|---|---|---|---|
| | ***RELEVANCE* to partakers** | ***IMPARTIALITY* toward partakers** | ***WELFARE* of partakers** | ***CONSENT* of partakers** |
| 5. Very high | **Procedure is directly relevant and highly beneficial for partakers** | Individuals receive highest consideration regardless of their capacities | Procedure enhances partakers' welfare | Partakers are enabled to choose whether and how to engage with procedure |
| 4. High | Procedure is relevant but benefits may not be direct or immediate | Individuals receive high consideration but not as much as others with more capacities would | **Procedure does not impact negatively on partakers' welfare** | Partakers are mostly able to choose whether and how to engage with procedure |
| 3. Moderate | Procedure has some relevance but benefits are only indirect and only in future | **Individuals receive some consideration but notably less than more capable ones would** | Procedure has minor impact on partakers' welfare | Partakers have limited ability to choose whether and how to engage with procedure |
| 2. Low | Procedure has little relevance and benefits are only indirect and only in future | Individuals receive significantly less consideration than more capable ones would | Procedure has significant negative impact on partakers' welfare | Partakers are mostly not allowed to dissent or withdraw from procedure |
| 1. Very low | Procedure has no relevance whatsoever and no benefits for partakers even indirectly or in future | Individuals receive very little or no consideration compared to more capable ones | Procedure has severe negative impact on partakers' welfare | **Partakers are not allowed to dissent or withdraw from procedure in any way** |

deemed ethical and humane from the perspective of the animals involved. Numerous examples, in this regard, are provided by procedures conducted within research aiming to primarily benefit humans, as is typically the case with pharmacological toxicity tests conducted *in vivo* using laboratory animals such as mice, rats, guinea pigs and rabbits. Consider the case of an acute toxicity study conducted to determine what dose of three different commercial toxic agricultural chemicals would result in the animals' death, how long it would take for the toxicity to manifest itself and how the animals' immune response might interact with the substance's toxicity (Belay, 2019). For this experiment, 15 Balb C mice were transported to the laboratory where the procedure was to be carried out. Nine mice underwent the procedure. The mice were divided into three groups, labeled using different colors corresponding to the pesticide that was to be administered to them. They were then placed in separate cages, where they were kept for 2 weeks under standard environmental conditions and daily feeding regime. After this time, blood was drawn from each of them, by puncturing their facial and tail veins, for immuno-assay, after which they were given 3 days to recover, before being dosed with the pesticides. Each group was dosed with a different pesticide and each mouse in the group was given a different dose, using an intragastral tube. Four hours after dosing, blood was again sampled from each mouse for post-treatment comparative immunoassay. The mice where then kept in their cages, fed daily and monitored regularly for 5 days, as opposed to the 24 h typical of acute toxicity tests. Depending on the chemical they had been administered, the mice presented with symptoms ranging from breathing problems, salivation, trembling, lacrimation, miosis, hypo-activity and general weakness. Those who received the highest doses died between 1.5 and 12.5 h after administration, depending on the pesticide; one of the mice who received the second highest dose of one of the pesticides died after 26 h; the other mice appeared to have recovered after a few days but continued to present with significant body weight loss. The conclusion of the study was that the level of toxicity and its resulting symptoms was dependent both on the administered dose and on the effectiveness of the individual's immune response; at lower doses, this seemed able to somewhat neutralize the substance's toxicity, to observe which an observation period longer than the standard 24 h had been required.

This study exemplifies a case in which animals are used as instruments of a scientific apparatus, allowing researchers to observe the pharmacological properties of a substance within a living organism. Clearly, the procedure had no benefit for the individuals involved and it is very doubtful that it had any benefits for the lab-bred species. The chemicals used for the experiment were commercial pesticides, which means their toxicity had already been tested, and the study concluded that a period longer than 24 h might be needed to fully assess the toxicity of a substance at different doses. Far from yielding future benefits for animals, this could in fact result in experimental subjects suffering for a longer period of time (e.g., one of the mice took 26 h to die of their symptoms) before being ultimately euthanized. Since it is doubtful that this kind of procedure could be legally conducted on more complex species such as primates and humans, it seems clear that the procedure did not treat the mice impartially, even though all the mice involved were treated equitably. It seems also clear that the procedure was highly detrimental to the welfare of the mice. All the mice suffered from severe symptoms due to the substance's toxicity and some died as

a result of the symptoms' acuity. It is unclear what happened to the surviving mice at the end of the 5 days of the experiment, but it is likely that they were euthanized. It is also unclear what kind of caging system the mice were kept in and whether any comforts, such as nesting materials or boxes or other forms of enrichment, were provided and how their separation affected them. Finally, no mechanism seems to have been in place to enable the mice to express consent or dissent to their involvement, or to choose whether and how to engage with the procedure. They were transported and kept in cages, which presumably they were not able to leave, and were dosed via intragastric tube, which suggest that they had no choice as to whether to ingest the substance. Had they known what consequences being dosed would have, it is doubtful that they would have consented to the procedure. The balance of scores for this study could be summarized as shown in **Table 4**.

While this kind of studies may be deemed necessary for the advancement of scientific knowledge and for the development of technologies, including pharmaceutical products, that are beneficial to humans, it is important to acknowledge the full extent of the impact that these procedures have on animal subjects. In particular, where a procedure such as the one described above scores low or very low against the principles of relevance, impartiality, welfare and consent, this should to be fully acknowledged and every effort should be made to develop alternative methods to study the same phenomena. In these cases, using our proposed scoring system, could help researchers and delegated authorities to sharpen the focus on such a necessity and further support the case for replacement.

## CONCLUSIONS

The principles of the 3Rs originally proposed by Russell and Burch (1959) are universally regarded as the gold standard for regulating the use of animals in research. They were developed to address the ethical dilemma that derives from the fact that, on the one hand, animals cannot provide informed consent to research procedures that can harm them but, on the other hand, their use in potentially harmful procedures is deemed necessary to achieve a greater societal good. This ethical perspective assumes that animals are unable to assess the implications of a procedure and to consent or dissent to their involvement; because of this inability and of the experiential impact that a research procedure may have on them, it is assumed that their use should be limited, although it is permissible where warranted by a cost-benefit analysis. Although the aim of this ethics framework is to protect animals, such cost-benefit analysis does not prioritize the role and interests of the animals in question. In other words, the 3Rs reflect a process-centered perspective that regards animals as instruments within an experimental apparatus.

However, animals' growing exposure to and interaction with technology is increasingly highlighting the importance of taking an animal-centered perspective on doing research and design, which is informing the fast-developing field of ACI. A growing body of ACI research shows how involving animals in research as legitimate stakeholders and partakers can benefit both the animals and the processes in which they are involved by giving partakers the opportunity to inform design outcomes that are relevant to them and to other stakeholders (including humans).

**TABLE 4 |** Assessment of the compliance of the mouse acute toxicity study with the four principles of animal-centered research (Belay, 2019), with more relevant descriptors displayed in bold character.

| **Ethics standard** | **Compliance with principles of animal-centered research** | | | |
|---|---|---|---|---|
| | ***RELEVANCE* to partakers** | ***IMPARTIALITY* toward partakers** | ***WELFARE* of partakers** | ***CONSENT* of partakers** |
| 5. Very high | Procedure is directly and highly beneficial for partakers | Individuals receive highest consideration regardless of their capacities | Procedure enhances partakers' welfare | Partakers are enabled to choose whether and how to engage with procedure |
| 4. High | Procedure is relevant but benefits may not be direct or immediate | Individuals receive high consideration but not as much as others with more capacities would | Procedure does not impact negatively on partakers' welfare | Partakers are mostly able to choose whether and how to engage with procedure |
| 3. Moderate | Procedure has some relevance but benefits are only indirect and only in future | Individuals receive some consideration but notably less than more capable ones would | Procedure has minor impact on partakers' welfare | Partakers have limited ability to choose whether and how to engage with procedure |
| 2. Low | Procedure has little relevance and benefits are only indirect and only in future | **Individuals receive significantly less consideration than more capable ones would** | Procedure has significant negative impact on partakers' welfare | Partakers are mostly not allowed to dissent or withdraw from procedure |
| 1. Very low | **Procedure has no relevance whatsoever and no benefits for partakers even indirectly or in future** | Individuals receive very little or no consideration compared to more capable ones | **Procedure has severe negative impact on partakers' welfare** | **Partakers are not allowed to dissent or withdraw from procedure in any way** |

It is evident that, when allowed the opportunity, animals are capable of providing *contingent consent* to their involvement and that animal-centered research has the potential to yield the best research outcomes. In other words, existing work in ACI highlights the need to move beyond the 3Rs to integrate these very important principles within an ethics framework that recognizes animals as active partakers and contributors, motivated by their own interests and capable of consenting or, indeed, dissenting.

This paper has explored the possibility of taking an animal-centered perspective on the use of animals in research, beyond the field of ACI. In particular, we have discussed the applicability of what we propose as the four core principles of animal-centered research—*relevance, impartiality, welfare* and *consent*—to diverse research scenarios, highlighting opportunities and challenges. We have proposed a scoring system against which the extent to which a research procedure aligns with these principles could be assessed and, as a way of illustration, we have applied this to three different examples of research studies involving animals. These examples illustrate how our proposed principles could help researchers and delegated authorities consider when the involvement of animals in research might be in their best interests and, conversely, when using alternative methods (Replacement) or the minimizing the number of animals used (Reduction) would be most desirable (as with Example 3). The application of our proposed principles could also help identify where improvements to a procedure (Refinement) should be considered (as with Example 1), or when a less than ideal condition (e.g., the inability to withdraw from a study) might be at least partially off-set by another condition (e.g., the direct benefit of partaking) making a procedure acceptable from an animal-centered perspective (although the overall purpose of the research might not be entirely animal-centered, as with Example 2). While the animal-centeredness of a research procedure would ideally require that all four principles be met, the range of our examples aims to illustrate that a procedure could still be regarded as humane depending on the balance between different principles; for example, if a procedure is not relevant to an animal but presents virtually no risk to their welfare, or if an animal is given the opportunity to withdraw from a procedure that may present welfare risks.

We acknowledge that our proposed framework is general. We believe that its generality is a strength, as it makes it applicable to any procedure and for any species. At the same time, its generality is also a weakness, as it leaves its application open to possibly widely varying interpretation when applied to specific procedures and specific species. To support the standardization of the framework's application, species-specific criteria could be developed to help researchers and delegated authorities consistently score a procedure to determine the extent to which the research aligns with animal-centered principles. Although we believe that a five-point scoring scale might be easier to use and sufficient, particularly when complemented by specific scoring criteria, a more detailed (up to 10-point) scale could also be used.

Notwithstanding these different options, we argue that our proposed principles should complement the 3Rs within an integrated ethical framework that recognizes animals as autonomous agents with their own interests, as primary stakeholders in experimental procedures and as legitimate research contributors. We argue that such recognition, and the application of the envisaged integrated ethics, could support the best possible research for the benefit of animal partakers and wider society.

## AUTHOR CONTRIBUTIONS

CM and EN have contributed to the ideation and discussion of the argument proposed by the article and to the writing of its presentation within it, including the drafting of different sections and revisions of the overall draft. Both authors contributed to the article and approved the submitted version.

## ACKNOWLEDGMENTS

We are grateful to the reviewers who engaged with this work for their constructive feedback and helpful suggestions, which enabled us to improve the quality of the manuscript.

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**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.