

The ethics of the Three Rs principle: a reconsideration

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Abstract

In the past decades the Three Rs concept, famously launched by Russell and Burch in their 1959 book The Principles of Humane Experimental Technique, has gained a prominent place in the landscape of societal and ethical concern about animal use. Important scientific and institutional initiatives have been taken in order to promote replacement, reduction and refinement. It appears, however, that conceptual and ethical thinking about the presuppositions and changing contexts of the Three Rs concept has lagged behind the scientific and practical efforts. In this paper, first, I argue that there is a threefold argument to make for the need to reconsider the moral basis of the Three Rs concept. Second, I outline a number of standard assumptions of the traditional approach to the Three Rs and question the tenability of these assumptions. Third, I propose some elements of a new framework for the Three Rs principle and connect this to a number of developments in science and society. I conclude with four remarks on the future of the ethics of the Three Rs principle.

Keywords: animal welfare, ethical committees, ethics, humaneness, Three Rs principle, values

Introduction

For the purposes of this article, I define morality as a specific pattern of duties and motivating principles, values and dispositions. This pattern directs the conduct of individuals and groups, and their judgments regarding whether conduct is right or wrong, acceptable or unacceptable, justifiable or unjustifiable — and not just expedient or efficient. Ethics is a systematic reflection about this, often implicit, pattern, with the aim of analysing, describing and/or criticising it. Human societies and communities cannot exist without morality because this pattern lends structure and meaning to their activity and defines their identity; we therefore find moralities relating to all kinds of human practice and with all kinds of content. Not every element of a morality will automatically determine conduct; for example, certain elements within a morality might be inconsistent. Because different moralities are often not compatible, there is a natural human tendency toward ethical reflection; however, ethical reflection is also unavoidable for other reasons. For example, with time, circumstances and realities change to such an extent that a morality that has organised conduct and judgment satisfactorily for a given period becomes obsolete, insufficient and in need of re-thinking. In this paper I intend to reconstruct the morality that has supported the Three Rs principle in the past and to argue that there is a need for a reconsideration.

In accordance with this general conception of ethics, I will use, in this paper, the notion of the Three Rs principle in a way that differs somewhat from Russell and Burch's (1959, reprinted 1992) use of 'principles'. In my view, Russell and

Burch use the notion mainly to cover and integrate the different assumptions, possibilities and strategies that may be used to lend substance and feasibility to the objectives of replacement, reduction and refinement of animal experiments. In referring to the Three Rs principle, I will take it as a general, morally motivated directive concerning experimental and scientific practice involving animals and, correspondingly, I will emphasise the various moral assumptions that may be invoked to underpin and specify the Three Rs.

Reasons for rethinking the Three Rs principle

There are three types of argument which support the statement that there is a need for reconsideration of the Three Rs principle. Each of these types of argument originates in a different dimension of societal change, although the dimensions are interlocking and mutually reinforcing. The first type of argument concerns ideological or moral changes regarding the use of animals in science. Two relevant changes are an increasing appreciation from the general public of the value of animals, and a more ambivalent attitude toward the claims of science and technology that these practices, unproblematically, contribute to welfare and progress.

Since the 1960s the public has been confronted with setbacks from technological applications that have been implemented too quickly and without reliable investigation into potential side-effects (Carson 1962). The public has become acquainted with controversies between scientists on important issues (Engelhardt & Kaplan 1987; Latour 1987; Machamer *et al* 2000) and has developed a more sober, and sometimes sceptical, attitude toward the

promises of substantial improvements from technology and industry (Tenner 1996). To a certain extent, these changes in attitude result from a second set of changes from within various political and public institutions. The influential and multiple ways in which information and opinion are mediated by television and the internet have led to more openness, more transparency, and greater pressure on scientists and politicians to legitimate their decisions and practices in a trustworthy manner (Habermas 1991; Beck 1992). The Three Rs principle, as introduced by Russell and Burch in 1959, was largely an affair of scientists. Nowadays, it is part of a practice — animal experimentation — that is highly contested in society, and often on fundamental moral grounds. One of the consequences of the ill-informed and radicalising public discussions of animal experiments is that the Three Rs are often identified with ‘alternatives’ (Smythe 1978), and alternatives, in turn, are equated with the complete replacement of animals in scientific procedures. The sometimes subtle relations between the Three Rs, and the variety of opportunities to improve the situation of laboratory animals, need to be emphasised against this tendency to perceive complete replacement as the *only* objective.

A second important institutional change concerns the progress toward transnational economic and political unity in Europe and the institutional consequences of globalisation. While Russell and Burch, understandably, concentrate on scientific experimentation as a more or less self-contained process, there is nowadays, because of these institutional processes, much more reason to promote the Three Rs in addition — and, perhaps, primarily — in the interstices between the practices of scientific research, risk assessment, legal regulation and political negotiation. In these interstices, harmonisation, efficiency, differential risk perceptions (Cranor 1990), and the dynamics of public and institutional powers complicate matters.

The third type of change concerns technological change. Technological change is without doubt the main driving force in animal experimentation, as it is in other areas (Feenberg 1995), and it has a two-sided effect on the Three Rs issue. On the one hand, advances in areas such as image technology, chip technology and biotechnology contribute to replacement, reduction and refinement, sometimes unintentionally, for example, in cases where more precise technology makes for better science and reduces the need for the use of living animals (Joles & Vorstenbosch 1999). On the other hand, technologies such as telemetry and biotechnology cause dilemmas that enforce a difficult balancing of the moral weight of numbers of animals used versus the length and intensity of suffering of individual animals (Morton *et al* 2003). Furthermore, the possibility of using genetic techniques to create animals that do not feel pain confronts us with the recognition that it is not only the pains and pangs that occur in the animal as part of the experiment that worry us, but also that there is a living subject, with a life and standing of its own, that experiences these pains and pangs (Regan 1984).

Consequences for the Three Rs principle

How do these changes have an impact on the Three Rs principle? The answer is in many ways, sometimes quite different ways, which are too numerous to expand on in this paper. For example, the differences between reduction and refinement alternatives, which start out from the assumption that the use of animals in the procedure is necessary and acceptable, and replacement strategies, which aim at making the use of animals unnecessary, should be taken in account. But, if I may rely on the research and discussions within the project group Anim.A1. See (<http://www.inemmcnr.it/animalsee/disseminations.html>; see Acknowledgements), we can draw three general conclusions.

First, the search for replacement, reduction and refinement strategies and applications should not be limited to a single experiment and the condition of the animal *in* the procedure, but should be approached in a more *inclusive* way, by taking into account the complete life of the laboratory animals — breeding, birth, weaning, housing, feeding, using and killing.

Second, animal experiments and testing are embedded in practices of science and regulation. These practices are dynamic and complex, internally as well as in respect of external conditions and motivations. This *embeddedness* requires a broader analysis and discussion of the reasons for, and the value and importance of, animal use. But it also offers a broader range of possibilities to apply the Three Rs on other levels and in other phases than the single experiment. Distinguishing between a *narrow*, science-based conception of replacement alternatives, which accepts the motives of scientific and regulatory purposes, and a *broad* conception of replacement strategies, which takes the underlying motives, approaches and contexts of scientific procedures into critical account, is desirable from the point of view of public debate and policy. Translating this distinction into viable procedures, in institutional settings or Ethics Committees, might contribute to an approach toward animal experimentation that is both more focussed and more critical. It will also help to counter the arguments that the Three Rs are only a strategy of scientists and politicians to sidestep the more fundamental question of whether animals should be used at all in scientific procedures (for a discussion of this fundamental question see, eg, Regan 1984).

Third, animal experiments fit into a wider pattern of human society, which thrives on scientific, technological and economic dynamics that constantly enforce legal, moral and political changes. As a result of these factors, we witness an intricate and complex pattern of reasons, values and considerations that influence public and political decision making. Recognition of the fact that *multiple* standard frameworks — scientific, economic, legal, political, cultural and ethical — have to be taken into consideration and balanced is unavoidable if we are to find a way of taking on the many challenges and opportunities that the principle of the Three Rs harbours. Special attention should be given to the possibilities of giving scientific, economic, as well as ethical, arguments in favour of an ‘alternative’ and against the existing experimental practices, so as to make the strongest possible case for innovation and replacement.

The prospects and promises created by this threefold reorientation of the Three Rs principle, as well as the obstacles and objections that it will meet, cannot be detailed in this article; they are too many and diverse. Instead, in the rest of this paper, I will focus on the basic standards and moral assumptions that are involved in this reorientation. I will explicate four standard presuppositions that, in my view, determine much of the actual practices of exploring and implementing Three Rs strategies. I will discuss them and work out some arguments to put these presuppositions into perspective and then go on with sketching an alternative grounding of the Three Rs principle.

The existing background of the Three Rs principle

Based on a critical reading of Russell and Burch's text (1959, reprinted 1992), and especially on a general impression of Three Rs practices, I hypothesise the following four features of the standard background of the Three Rs. I will not go into the difficulties of differentiating between *moral* and *standard* features. It suffices, in this context, that these features have important and even compelling action-guiding consequences.

The first feature is a generalised belief in the *supreme value* of science and scientific method, not only as a method for obtaining reliable knowledge of the physical and biological reality, but also as founding the overriding duty of scientists. This belief invites further grounding, as it can be easily made relative by showing that much of what goes on in science, especially in applied sciences, is motivated by purposes other than the advancement of knowledge as such.

The second standard feature is *anthropocentrism*. Science is needed to sustain and further human health and welfare. Eventually this feature can also serve to ground the search for knowledge as intrinsically valuable, because this knowledge can only be had and appreciated by human beings and contributes to their pleasure and/or worth. Of course, sometimes animals themselves are the primary beneficiaries of research, as in veterinary medicine, but besides this, the majority of animal experimentation is motivated by human interests in the use of animals and is required because of the often harmful effects of the way these interests are pursued, for example, as in intensive husbandry.

The third standard feature consists in a specific type of moral self-esteem and self-appreciation of scientists in the context of carrying out experiments using animals, and it can be considered as a natural consequence of anthropocentrism; taking human beings as agents and subjects of moral self-knowledge. This self-appreciation has efficiency, quality, prudence and at its foremost, humaneness as elements. In a way this is the *central* element in the traditional ethics of the Three Rs principle, as expressed in the reference to 'humane' experimental techniques in the title of Russell and Burch's 1959 book. This feature is rather complex and I can single out only two aspects — efficiency and quality — leaving humaneness for later elaboration. The standard reasoning that underpins the Three Rs effort on the basis of standards of efficiency and quality is that much of what is done in scientific animal experiments can

be improved. This claim is based not only on reasons of human decency and morality, the principle that sentient beings ought not to be hurt or harmed, but also on reasons of efficiency and quality of science. The Three Rs not only serves a more humane science, because human beings ought to care for animals, but also promotes more efficient scientific practice and more valuable scientific results. In many cases, caring for the animals and promoting the value of the science are positively related and compatible at the least, or so it is argued (Russell & Burch 1959, reprinted 1992).

The fourth feature concerns the morally relevant factors in the situation of animals used in experiments. Not so much in the original work by Russell and Burch (1959, reprinted 1992), but in many practical and legal regulations, this is limited to the avoidance, as far as compatible with scientific purposes, of experiences of pain *in* the experiment. There is a strong emphasis on negative experiences, amounting to what Peter Singer (Singer 1985) has called *pathocentrism* — which considers the suffering of animals and not their positive experiences or welfare — in addition to other potentially morally relevant aspects in the centre of moral concern to do with killing animals and interfering with their natural life conditions. This might be an effect of the fact that what concerns most people morally in animal experiments is the deliberate induction, not necessarily intended but at least foreseen, of pain and distress in animals as an inevitable consequence of many experiments. This conflicts with a deep-seated moral principle not to harm sentient beings, a principle that humans hold on to in their dealings with other humans and animals. As a consequence of this pathocentrism, there are, in the context of science and experimentation, other circumstances and occasions which invite scrutiny from a broader moral point of view, taking animals and their welfare as a comprehensive standard, and that are less noticed by scientists and the public. This bias will be one of the reasons to propose an alternative grounding for the Three Rs principle. But first I will take a critical look at these four features.

Some critical notes concerning the background of the Three Rs principle

The standard features of the Three Rs principle that have been discussed can be criticised as being either too indiscriminate or too limited and biased, or both. Take the idea of scientific methods as a superior way of acquiring knowledge, or of evaluating or justifying knowledge claims, or take the having of scientific knowledge as a supreme value. Although it can be acclaimed that for professional scientists it is more or less inevitable that scientific standards and attitudes take pride of place, it is evident that this value is from a societal point of view not supreme, neither in an epistemological sense nor in a moral sense. As to the epistemological value, scientific results have to be interpreted, evaluated, translated and disseminated before they come to be endorsed by society and politics as a reliable basis for action and policy. Their epistemological value is not to be underestimated, but it gets into a process in which many other sources and claims of knowledge play their own role. As to the place of science in our moral

pattern of values, many scientifically interesting projects, including those of overriding interest to human health, are founded on the moral principle that we ought not to treat human beings purely as a means to our own ends, and on the moral rule of informed consent. So, moral standards can override scientific values. But by far the most important argument, when it comes to the use of animals in scientific procedures, is that an indiscriminate and general support for what goes on in science, let alone a free hand for scientists, would fall short of the moral concern for animals that has been developing in society in modern times. Scientists are, after all, human beings, and capable of every human shortcoming and failing, not only overestimating the value of their research, relative to what the moral costs are, but also to a lack of sense, feeling, carelessness, laziness etc. These aspects of scientific practice, as with every human practice, can only be counteracted by relying on the intentions and attitudes of scientists. The moral concern of animals is better served by working out a well-founded and intelligent system in which the performance of scientific researchers concerning the treatment of laboratory animals is assessed and monitored. The system should also find a way of balancing the relative value of scientific efforts and projects against the moral costs of animal suffering in a transparent, critical and socially acclaimed way.

This brings us to the appreciation of the second feature, that anthropocentrism is widely present in society. Does this fact not confront us on a deeper and perhaps more sound basis of justification than that of the consensus in scientific circles, to judge that of general *public* agreement and consent, with the same general undervaluation of the moral position of animals? To a certain extent, yes. Science is a practice that depends in many respects on societal support and it could not exist without being accepted as, in general, a respectable social practice. This also holds for animal experimentation. But here the details of societal support are important. There is a general conviction in society that not everything which is valuable or interesting to some, or even many, human beings is sufficient reason for inflicting harm on animals. The fact that this conviction has, until now, not resulted in substantial changes in the practice of animal experimentation can be explained in various ways; for example, by the claim that the results of animal experiments are rewarding in terms of overriding interests in the health and welfare of human beings. But instead of raising such general and indiscriminate claims, it is far more realistic to accept that until now it has proven to be very difficult to develop institutions, standards and instruments of evaluation that are capable of answering the questions surrounding animal experiments. It seems more a matter of practice than of principle that anthropocentrism, taken as implying that *every* human interest is sufficient ground to use and harm animals, survives in many contexts.

I can only touch upon a few elements of the discussion about the evaluation of the concepts of efficiency, humaneness and quality that make up the third feature of the existing ethics of the Three Rs principle. Here we have to differentiate between ideas of efficiency and quality, which lend themselves to

more objective standards, and the attitudinal ideas of prudence and humaneness. I observe that efficiency and quality are multidimensional ideas that presuppose purposes to be reached and a diversity of criteria. It depends on the exact nature of the purpose and the methodological constraints set as to whether an experiment is efficient or not, and the scientific quality of an experiment involves a variety of criteria, such as the statistical, methodological and innovative quality of the research. Limiting ourselves to this argument, it is clear that refinement and reduction do not always contribute to the efficiency and quality of scientific findings, unless one makes the matter tautological by introducing in the blanket-concept and non-informative phrases such as (refinement) 'as far as possible' or 'as far as compatible with science'. Much depends here on the purpose, the questions and the objectives of research, as might be seen from the fact that Russell and Burch already made a distinction between *contingent* inhumanity, which is not essential to the scientific objective, and *direct* inhumanity, which is essential to the scientific objective (Russell & Burch 1959, reprinted 1992 p 54).

Humaneness deserves, in the context of this article, more comment. I have the impression that the use of this idea is intriguingly committed to two different moral frameworks. On the one hand, to act humanely refers the moral judgment to a specific *attitude* of the scientist, and so is grounded in a moral theory of virtue, comparable to notions such as 'decent' that we also find in this context. To act humanely means that we are supposed to develop an attitude that does justice to our own value as human beings. It does not depend on a relationship with the object of treatment, the animal, or on some intrinsic properties that ground a moral duty toward animals, but on a specific relation with *ourselves*. On the other hand, the *content* of the attitude and the obligations to which this idea gives rise are derived from the fact that animals are sentient beings that can feel pain, and more broadly from a utilitarian theory of *duty* of which the central principle reads 'always act so as to maximise the balance of good, or pleasure, over bad, or pain'. It would take us too far to discuss these two sides of the concept of humaneness, but I refer the reader to the next section where I will propose a different grounding of the Three Rs principle.

The fourth feature, pathocentrism, connects with a value-theory called hedonism that underpins a version of utilitarianism, but takes the reverse of hedonism (which literally means 'pleasurism'), suffering, as a central negative value. Pathocentrism can be criticised on two counts. First, the welfare of animals also consists of positive states and feelings, and certainly cannot be reduced to units of pain (Stafleu *et al* 1996). A more realistic picture of animals interprets pain feelings as meaningful feedback that enables the animal to function well. The welfare of animals, according to this observation, should be seen as a complex and enduring process in which the animal, as a living, sentient and responsive agent, is the subject. Second, even when we take this process into account, it is not obvious that we can, in the ethics of the Three Rs principle, leave out all

elements that are not directly related to the experiment itself, such as the physical integrity, the natural state of the animal and the life of the animal.

Toward a different standard framework: moral and procedural proposals

The two main, and related arguments against the ethics of the Three Rs principle that I have described previously come down to the following. First, it does not grant animals a moral standing of their own, but only in so far as the practice of science and the underlying motives and purposes for it allow for the better treatment of animals. Only when there is a suitable alternative that conforms to the expectations already made up by humans (or, for that matter, limited groups of humans, such as scientists) will animals be spared. One can object that the Three Rs principle *as such* does not block any further and deeper criticism of the reasons for which animals are used in science. It is only limited — and positively committed — to an improvement in the situation of animals within the existing scientific order. This is true. But against this, two things can be said. First, emphasis on the Three Rs principle, in its narrow interpretation, does not encourage critical scrutiny of the motives for animal use. Second, and more important, I hold that, on closer inspection, many issues that relate to the evaluation of ‘alternatives’ for existing procedures involve more fundamental values, standards and choices. In many cases, the purposes and motivations of research are closely interwoven with the scientific procedures chosen; they cannot be prised apart. One cannot change the procedures without consequences for the purposes, standards or motivations of the research. This also implies that often the choice between alternatives is not, or rather is not only, to be located on the level of single experiments but also on more principled levels of scientific approach, setting of standards and research strategies (LaFollette & Shanks 1996). Ideally, a balanced system should be established in which scientific merit, public accountability and the possibilities of alternatives are reviewed by suitable and socially accepted members *both* at the principle levels of scientific approach *and* regulatory policy and at the executive level of single experiment.

The second argument against the existing moral framework is that the emphasis on humaneness does not recognise that the ultimate answer to the question, of whether the Three Rs principle is to be implemented and at what cost, is not to be found in the conscience and intention of the individual scientist, but in an institutional and public process of justification. Dispositions and virtues of the individual scientist are an important and even indispensable element in the ethics of the Three Rs principle, especially because the expertise, openness and feelings of responsibility of scientists are inevitable in establishing a structured process of assessment and justification. But the standards, decisions and limits concerning the Three Rs principle are to be found in an institutionalised, scientific and societal dialogue, in which scientists are supposed not only to do their scientific job but also to participate as citizens.

Elaborating on these two arguments, an alternative ethical framework for founding the Three Rs principle begins to unfold. This framework incorporates the valuable elements of the traditional view into a larger standard whole. The first element of this framework is the recognition of the intrinsic value of animals. To foreclose principled objections against this much contested idea, I emphasise that I attach no meta-physical meaning to it and also do not imply that animals are morally on a par with human beings. As a matter of fact, I think that intrinsic value has only a meaningful content on the assumption that there are human beings who can attribute intrinsic value, as opposed to purely extrinsic or instrumental value, to animals. The meaning of the attribution of intrinsic value to animals is procedural; it recognises that animals are not at the mercy of individual human beings or groups who can do with them what they want. As soon as there is a reasonable presumption that the interests of animals are harmed by human conduct, there is a duty to justify this conduct on moral grounds. This grants animals a moral standing in the community of human beings. This principle lays a foundation for the Three Rs principle, as well as for further moral debate about the use of animals in scientific procedures. It is directed against the first two assumptions of the traditional framework: the assumption that decisions about animal use in science is primarily a matter of science and scientists.

This procedural starting point naturally invites further explanation of the moral position and meaning of animals. For it still leaves many options open even to the extent that *nothing* changes in our conduct toward animals, although our conduct is now mediated and vindicated by a justificatory procedure. The procedure has to be elaborated with some value-theory about what property, or properties, of animals or broader, what factor, ground this moral standing of animals. Which morally relevant properties of animals could or should be used to balance the interests of animals and human beings? From a variety of theories in animal ethics, I mention the following potentially relevant properties: sentience (Singer 1985), which is without doubt the most prominent candidate and an element of almost all other theories; having a telos (Rollin 1989), ie an internal formative principle that explains the functioning of an animal; having a good of its own (Taylor 1986); being the subject of a life (Regan 1984); naturalness (Musschenga 2002); and integrity (Vorstenbosch 1993; Rutgers & Heeger 1999. (For a more sceptical position concerning the moral value of animals see Frey 1980; Carruthers 1992; Leahy 1994.) Not all of these properties are equally plausible and applicable in all cases in which animals are used, especially not in the context of animal experimentation. But the range of factors broadens the debate well beyond that offered by pathocentrism. It is likely that that the framework of values that will result from this debate is not monistic, based on painful experience as the only relevant state for granting moral status and the only relevant standard factor, but pluralistic (Warren 1997).

The moral and practical implications of the efforts of the philosophers that have launched the concepts and principles, mentioned in the previous paragraph, can only be determined by taking two further steps. First, the concepts have to be linked to the growing body of insights in animal welfare studies, as has been convincingly argued by Professor David Fraser (Fraser 1999). Only when ethical and conceptual efforts in animal ethics go side by side with developments in scientific and empirical research in animal welfare studies can progress in moral arguments and in practical and legal guidelines be achieved. What is called for in this respect is a much needed unity of action between scientists, who are conversant with the scientific state of affairs and the technical aspects and limits of animal experiments, and ethicists, who are familiar with the critical evaluation of moral concepts and assumptions, and with the way these concepts need to be interpreted to gain a meaningful and ethically acceptable role in political and social debates. Second, the practical consequences of the progress achieved, regarding the ethical foundations and implications of the Three Rs principle, have to be determined in a process of well-informed and transparent discussions between scientists, public officers, politicians and society. The conditions for these discussions are to be such that all relevant viewpoints and stakeholders get a fair hearing and say.

This brings us to the second element of the new moral framework, which I have already mentioned: the essential role of democratic, public and institutional discussion and justification in taking decisions and establishing standards and objectives of the Three Rs principle. The disciplinary efforts in the scientific areas that deal with developing and validating Three Rs alternatives, as well as the further development of moral theories and principles in animal ethics are indispensable for achieving progress with the Three Rs principle. But neither science nor ethics can determine on its own which reasons are good enough to use animals, or at what cost, or what kind of costs (eg moral, financial, human safety) are warranted to decide on a Three Rs alternative. The details, principles and procedures of this justification process cannot be set out here. But, taking into account that in many countries a system of Animal Welfare and/or Animal Ethics Committees has been established, an important role should be assigned to these institutions to mind, mediate and monitor Three Rs performance (Vorstenbosch 2000).

Conclusion and animal welfare implications

I conclude with four remarks. They make up an agenda for the future development of the ethics of the Three Rs, which is, for all the rightly acclaimed moral achievements with regard to the Three Rs principle, to my mind a neglected subject.

First, scientists and ethicists should join forces to rethink the moral assumptions, challenges and opportunities of the Three Rs on a scientifically sound, critically sophisticated and practically effective basis.

Second, the plurality of values that define the concepts of animal welfare, as well as other morally relevant concepts in animal ethics, should be clarified and brought to bear on

the Three Rs practice. The possibility of creating and adapting animals for scientific procedures, by means of genetic modification, has added a new and morally ambiguous dimension to this plurality. This possibility might prompt us to bring out the subjective, sentience-based and the objective, functional dimensions of the valuation of animal life and to rethink the relation between the two dimensions. Concepts that articulate the value of animals should also be incorporated with human-centered values in models that enable stakeholders to assess, appreciate and balance the diversity of standard factors that determine the use of animals in science (for examples see Smith & Boyd 1991; Porter 1992; Jensen 1996; Stafleu *et al* 1999).

Third, because it is difficult, time consuming and often impossible to review the broader merits and relevance of every single experiment, it is more efficient, more transparent, and morally and practically rewarding to direct more of the efforts and methods, with regard to the Three R principle, to the level of projects and programmes, general conditions for animal use, categories of scientific procedures and generally practiced regulations and tests. This approach should not divert attention from the opportunities of realising the Three Rs on the experimental level and within established projects and practices. But, by highlighting efforts to realise piecemeal the Three Rs, it aims at counteracting a tendency to evade more fundamental discussions on the relevance and acceptability of animal experiments.

Fourth, stakeholders, public officers and politicians should join together in establishing a transparent, feasible, consensual system of allocating responsibilities for moral assessment, high level Three Rs performance and technically competent execution of animal use.

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