Research Article

Russell and Burch’s 3Rs Then and Now: The Case of Switzerland

Christian Rodriguez Perez1, Kirsten Persson1,2, Rosa M. Cajiga Morales1, Bernice S. Elger1,3 and David M. Shaw1,4

1Institute for Biomedical Ethics, University of Basel, Basel, Switzerland; 2Institut für Tierhygiene, Tierschutz und Nutztierethologie, Stiftung Tierärztliche Hochschule Hannover, Hannover, Germany; 3Center of Legal Medicine, Faculty of Medicine, University of Geneva, Geneva, Switzerland; 4Care and Public Health Research Institute Maastricht University, Maastricht, The Netherlands

Abstract

Since Russell and Burch introduced and defined the 3Rs, i.e., the replacement, reduction, and refinement of animal use in research, in 1959, different definitions have emerged and been implemented in guidelines and policies. Switzerland is known for having some of the most restrictive legislation regarding the use of animals, in which the 3Rs are also defined and implemented. To our knowledge, the purpose and definitions of the 3Rs used in the Swiss Animal Welfare Act, Animal Protection Ordinance, and Animal Experimentation Ordinance have never been compared with Russell and Burch’s original purpose and definitions. In this paper we make this comparison with two aims: to reveal ethically relevant departures from the original purpose and definitions, and to provide an ethical evaluation of the current Swiss law regarding the 3Rs. In doing so, we first expose the similarity of purposes. We then identify one risky departure from the original definition of replacement in Swiss law, which shows a problematic focus on species. Finally, we address Swiss law’s failure to apply the 3Rs in the most effective way. With respect to this last point, we discuss the need for 3R conflict resolution, the timing of application of the 3Rs, problematic prioritizations and choices of convenience as well as a solution to apply the 3Rs more effectively using Russell and Burch’s concept of total sum of distress.

1 Introduction

W. M. S. Russell and R. L. Burch first introduced the 3Rs principle (3Rs) in their 1959 publication The Principles of Humane Experimental Technique (Russell and Burch, 1959). They did this by defining the terms replacement, reduction, and refinement as the three ways in which distress in animal experimentation can be diminished or removed.

Since then, their ideas have attracted interest in the scientific community and are now considered as a standard for animal experimentation and implemented in guidelines and policies around the globe. However, current definitions of the terms “replacement”, “reduction”, and “refinement” differ among these and from Russell and Burch’s original definitions. These differences may have ethical implications and pose risks that the original goals of the 3Rs are not reached.

These implications and risks were analyzed by Tannenbaum and Bennett in their 2015 article Russell and Burch’s 3Rs Then and Now: The Need for Clarity in Definition and Purpose where they compared 3Rs definitions of several institutions in the US with the original definitions of Russell and Burch (Tannenbaum and Bennett, 2015). In that work, eight possible ethically relevant departures from the original definitions were presented, and the risks they posed to the goal of diminishing or removing distress were analyzed.

Switzerland is known for having some of the most restrictive legislation regarding the use of animals in research, in which the 3Rs are also defined and implemented. To our knowledge, the purpose and definitions used in Swiss law have never been compared with Russell and Burch’s original purpose and definitions.

In this paper we make this comparison with two aims: to reveal ethically relevant departures from the original purpose and definitions, and second, to provide an ethical evaluation of the current Swiss law regarding the 3Rs. From now on, when we mention Swiss law, we refer to the body of legislation comprising the Swiss Animal Welfare Act (AniWA), Animal Protection Ordinance, and Animal Experimentation Ordinance.
completely freed of operations irrelevant to the object in view” (Russell and Burch, 1959, p.54), e.g., painful necessary procedures. In contrast, contingent distress is defined as “the infliction of distress as an incidental and inadvertent by-product of the use of the procedure, which is not necessary for its success” (Russell and Burch, 1959, p.54) / (ibid.), e.g., poor husbandry and transport. The diminution, and when possible removal, of distress is not only meant by Russell and Burch at an individual level for each animal, but also as a total sum of distress (TSD) for all animals used in a given experiment, a research program, and in animal research generally.

When we talk about TSD of an individual animal, in their view distress can be represented as a rank on a scale going from acute distress at one end to complete wellbeing at the other, with mere absence of distress somewhere in the middle. This idea is illustrated in Figure 1. In their article, Tannenbaum and Bennett have shown that some interpretations of Russell and Burch conclude from the fact that the authors wrote “we can aim at wellbeing rather than at mere absence of distress” (Russell and Burch, 1959, p.23) that the purpose of the 3Rs is to attain wellbeing for research animals. In this article, we follow Tannenbaum and Bennett’s interpretation that aiming at wellbeing is simply meant by Russell and Burch as a means to diminish, and when possible, remove, distress, i.e., to attain the mere absence of distress. In this sense, the 3Rs are modes or ways in which the purpose of diminishing, and when possible removing, distress can be achieved.

2 Russell and Burch: Original purpose and definitions of the 3Rs

2.1 Original purpose of the 3Rs

In their analysis, Tannenbaum and Bennett (2015) demonstrate that the way Russell and Burch introduce and define the 3Rs (i.e., replacement, reduction and refinement) makes it clear that the purpose of each of the Rs is the diminution, and when possible removal, of animal distress without compromising scientific and medical progress.

In The Principles of Humane Experimental Technique, distress is characterized by a number of negative mental states that animals experience such as pain, fear, conflict, or frustration of need. The authors distinguish two kinds of distress, direct and contingent distress. They define direct distress as “the infliction of distress as an unavoidable consequence of the procedure employed, as such, even if it is conducted with perfect efficiency and
3. Refinement means any decrease in the incidence or severity of inhumane procedures applied to those animals which still have to be used.

3 Swiss law: Purpose and definition of the 3Rs

3.1 The 3Rs and animal experimentation in Swiss law

Switzerland is known for having some of the most restrictive legislation regarding the use of animals in research, as metrics like the Animal Protection Index[2] attested in early 2023[3]. The AniWA was approved by Swiss voters in 1978 and implemented in Switzerland in 1981 along with the AniPO. A major revised version of these texts was implemented in 2008, and up to now we count 8 revisions of the AniWA and more than 25 of the AniPO. While the principles of replacement and reduction were already defined before the 2008 edition, an important addition to the definition of the principle of refinement appeared in this new one. In any case, these definitions have evolved, and we will use the 01.01.2022 version of the AniWA (Swiss Confederation, 2022) and the 01.06.2022 version of the AniPO (Swiss Federal Council, 2022) in this article.

Other texts in Swiss law are of interest for animal ethics in general, and animal experimentation in particular, for example the AEO, which classifies the severity of animal experiments into four degrees (FSVO, 2010). Switzerland has agreements of mutual recognition with Europe[4]. In this sense, the European Directive 2010/63/EU (EU, 2010) on the protection of animals used for scientific procedures, in which the 3Rs are present, also has an influence on Swiss law. However, for the purpose of our comparison of the purpose and definitions of the 3Rs, we can limit ourselves to the use of the AniWA and both the AniPO and AEO, which are two ordinances that are not themselves primary legislation but supplement the AniWA.

3.2 Purpose of the 3Rs in Swiss law

Regarding the purpose of the 3Rs, we can refer to the purpose of the AniWA and its supplementary ordinances in which the 3Rs are included. The purpose of the AniWA is “to protect the dignity and welfare of animals”. Swiss law recognizes that animals (and plants) have dignity, meaning that they have an “inherent worth” that must be respected. The AniWA states in its Art. 3a that “if any strain imposed on the animal cannot be justified by overriding interests, this constitutes a disregard for the animal’s dignity”. We will not elaborate further on questions of weighing of interests and justification here, because while these key mandatory steps in Swiss law relate to the 3Rs, they fall outside their scope. Regarding the term “welfare”, we consider it a synonym of “well-being”, since in German, French and Italian the AniWA uses the same word in both cases[5]. Wellbeing is defined in Art. 3b of the AniWA as what is present for the animals when:

1. husbandry and feeding are such that their bodily functions and their behavior are not disturbed, and excessive demands are not made on their capacity to adapt,
2. species-specific behavior within the limits of their biological capacity to adapt is guaranteed,
3. they are clinically healthy,
4. pain, suffering, harm, and anxiety are avoided.

Three additional types of strain are mentioned along with the definition of dignity in Art. 3a of the AniWA:

1. humiliation,
2. major interference with the animal’s appearance or its abilities,
3. excessive instrumentalization.

Finally, according to Art. 112 of the AniPO, we can add that provisions on animal experimentation apply to vertebrates; decapods and cephalopods; mammals, birds and reptiles in the last third of the gestation period prior to birth or hatching; and larval stages of fish and amphibians that take in food freely.

3.3 Definition of the 3Rs in Swiss law

Unlike Russell and Burch, Swiss law does not offer a clear definition for each R. Thus, in order to extract the definition of each R as precisely as we can from the law, we will need to uncover the principles in these texts by analyzing their relevant parts. The criteria we used to select these parts is their relevance in connection with the original definitions as well as to the typology of departures we will present later.

Most relevant parts come from Art. 137 “Criteria for assessing the dispensability of constraining animal experiments” in Section 4 “Performance of animal experiments” of the AniPO. The other relevant parts come from the chapters “General provisions” and “Handling of animals” in the AniWA. The AEO will be useful once we start our comparison.

We will not try to reformulate these parts into new definitions to avoid introducing any imprecision.

3.3.1 Definition of replacement in Swiss law

The relevant parts of the AniWA and the AniPO we must consider to define replacement according to Swiss law are the following: AniWA, Art. 20: “Conduct of experiments:

2. Experiments on animals higher on the evolutionary scale may only be carried out if the purpose of the experiment cannot be achieved in animal species that are lower on the

---

[1] As Tannenbaum and Bennett show in their article, for Russel and Burch the words “inhumanity” and “distress”, as well as “inhumane” and “distressful”, are equivalent.


[3] Out of seven possible grades ranging from “A” (highest score) to “G” (weakest score), Switzerland is rated “A” on the criteria “Protecting animals used in scientific research” (accessed 21.02.2023). The relevant articles of the AniWA, AniPO and AEO are presented as justifications for the grade.


[5] In German, French and Italian, the same word is used to define the purpose of the act as the protection of “welfare” in Art. 1 and to define the “well-being” of animals in Art. 3, respectively “Wohlergehen”, “bien-être” and “benessere”. 
evolutionary scale and no suitable alternative methods are available.”
AniPO, Art. 137: “Criteria for assessing the indispensability of constraining animal experiments:
2. The applicant must also show that the objective of the experiment cannot be achieved using procedures without animal experiments that are suitable according to the state of the art.”

Following these statements, we conclude that replacement according to Swiss law is the use of “procedures without animal experiments” or “alternative methods” instead of animal experimentation as well as the use of “animal species that are lower on the evolutionary scale” instead of “animals higher on the evolutionary scale” if a scientifically valid method is available. Here, we could interpret that “alternative methods” and “procedures without animal experiments” are used as synonyms or that “alternative methods” is similar to relative replacement.

3.3.2 Definition of reduction in Swiss law
Regarding reduction, there is only one relevant part, and it is in the AniPO:
AniPO, Art. 137: “Criteria for assessing the indispensability of constraining animal experiments:
4a. An animal experiment and its individual parts must be planned in such a manner that the smallest number of animals necessary is used and efforts are made to ensure the least possible constraint of the animals.”

Following this statement, we conclude that reduction according to Swiss law is to plan an animal experiment “in such a manner that the smallest number of animals necessary is used”.

3.3.3 Definition of refinement in Swiss law
Finally, the relevant parts of the AniWA and the AniPO we must consider to define refinement according to Swiss law are the following:
AniWA, Art. 4: “Principles:
1b. Any person who handles animals must ensure their well-being as far as the intended purpose permits.”
AniPO, Art. 6: “General provisions:
1. Any person who keeps or looks after animals must feed and care for them properly and provide them with the activities and freedom of movement needed for their well-being as well as shelter where necessary.”
AniWA, Art. 17: “Limitation to the indispensable minimum:
Animal experiments which inflict pain, suffering or harm on animals, induce anxiety in them, substantially impair their general well-being or which may disregard their dignity in any other way must be limited to the indispensable minimum.”
AniWA, Art. 20: “Conduct of experiments:
1. Pain, suffering or harm may be inflicted on, or anxiety induced in, animals only if this is unavoidable for the purpose of the experiment.”
AniPO, Art. 137: “Criteria for assessing the indispensability of constraining animal experiments:
4a. An animal experiment and its individual parts must be planned in such a manner that the smallest number of animals necessary is used and efforts are made to ensure the least possible constraint of the animals.”

Following these statements, we conclude that refinement according to Swiss law is to plan an animal experiment “in such a manner that efforts are made to ensure the least possible constraint of the animals” while bearing in mind that “pain, suffering or harm may be inflicted on, or anxiety induced in, animals only if this is unavoidable for the purpose of the experiment”, that such experiments “must be limited to the indispensable minimum” and that “well-being” must be ensured “as far as the intended purpose permits” in handling as well as in husbandry.6

4 Comparison of Russell and Burch and the Swiss law

4.1 Comparison of purpose
In our view, the way wellbeing and dignity are defined in Swiss law makes the purpose of the 3Rs in Swiss law similar to the original one, i.e., the diminution, and when possible, removal of animal distress. Indeed, if wellbeing is protected, it means that each of the four conditions stated earlier are satisfied, and that would correspond at least to rank 0 on the distress-wellbeing scale presented above, i.e., mere absence of distress. The term “anxiety” seems important, since it can cover a wide range of negative states in a similar way as distress does for Russell and Burch.

The protection of an animal’s dignity, i.e., of their “inherent worth”, is not to be viewed as an addition to the original purpose of the 3Rs. While the concept of dignity in Swiss law has the advantage of taking into consideration specific types of strain, i.e., humiliation, major interference with appearance and abilities, and excessive instrumentalization, the protection of dignity is simply defined as the protection from unjustified strain. The 3Rs contribute to the protection of unjustified strain only insofar as they remove unnecessary (and therefore unjustified) strain, which is a purpose consistent with the original one. But we said that the evaluation of a strain as justified or unjustified falls outside the scope of the 3Rs. Indeed, we have seen that, according to Russell and Burch, any strain could be justified by the higher goal of scientific and medical progress. In Swiss law, a similar justification could result from the weighing of interests, which plays a role distinct from the 3Rs to ensure that animal experiments causing distress are kept to the indispensable minimum. We therefore conclude here that there is no ethically relevant departure from the original purpose of the 3Rs in Swiss law.

4.2 Typology of departures
By comparing Russell and Burch’s original definitions to those of several institutions in the US, Tannenbaum and Bennett suggested a series of 8 possible departures from the original defini-

---

6 AniPO, Art. 135 “Conduct of experiment” provides additional guidance on how to pursue refinement.
As we have seen, in relative replacement animals are still required, though in the actual experiment they are exposed, probably or certainly, to no distress at all. In absolute replacement, animals are not required at all at any stage.

In any case, the Swiss definition of replacement does not correspond to this kind of departure from the original definition. As we have seen, in relative replacement animals are still required, while being exposed, probably or certainly, to no distress at all. These include cases where animals are euthanized before their tissues are used.

We will now present these departures in detail and assess whether some are the case in Swiss law by distinguishing consistent definitions, safe departures, and risky departures. By “consistent definitions” we mean definitions that are not cases of departures, i.e., that are consistent with the original definitions. By “safe departures”, we mean definitions that, in the context of Swiss law, do not pose an actual risk to the purpose of the 3Rs. Finally, by “risky departures”, we mean definitions that pose an actual risk to the purpose of the 3Rs.

4.3 Consistent definitions
Replacement as not using animals at all
This kind of definition implies that only Russell and Burch’s absolute replacement is replacement. In this sense, it would not consider relative replacement as replacement. As we have seen, in relative replacement animals are still required, while being exposed, probably or certainly, to no distress at all. These include cases where animals are euthanized before their tissues are used.

If we consider replacement alone, this departure poses the risk of resulting in more distress because of the failure to consider relative replacement. But if we think about the 3Rs as a whole, we can conclude that these unconsidered cases would still fall in the category of reduction or refinement (or both). Indeed, even if we consider that a case of relative replacement is not a case of replacement, we should nonetheless consider it as potentially reducing the number of animals used or the amount of distress imposed. This leads us to the consideration that some measures do fall into multiple categories of the 3Rs, a topic we will address in more detail later.

In any case, the Swiss definition of replacement does not correspond to this kind of departure from the original definition. As we have seen, Swiss law considers as replacement cases where “animal species that are lower on the evolutionary scale” are used instead of “animals higher on the evolutionary scale” and may also consider cases of relative replacement in what they call “alternative methods”. In this sense, there is not an actual risk of not considering cases of relative replacement.

<table>
<thead>
<tr>
<th>Russel &amp; Burch’s original definitions</th>
<th>Departures from the original definitions</th>
<th>Risk for the purpose of the 3Rs</th>
<th>In Swiss law</th>
</tr>
</thead>
<tbody>
<tr>
<td>Replacement means the substitution for conscious living higher animals of insentient material. In relative replacement, animals are still required, though in the actual experiment they are exposed, probably or certainly, to no distress at all. In absolute replacement, animals are not required at all at any stage.</td>
<td>Replacement as using less sentient animals</td>
<td>Larger TSD using less sentient animals</td>
<td>Risky departure</td>
</tr>
<tr>
<td>Reduction means reduction in the numbers of animals used to obtain information of a given amount and precision.</td>
<td>Reduction as minimization of the numbers of animals</td>
<td>Waste and repetition of studies</td>
<td>Safe departure</td>
</tr>
<tr>
<td>Refinement means any decrease in the incidence or severity of inhumane procedures applied to those animals which still have to be used.</td>
<td>Refinement as reduction of distress to an absolute minimum</td>
<td>Inability to refine</td>
<td>Safe departure</td>
</tr>
<tr>
<td></td>
<td>Refinement as enhancement of wellbeing</td>
<td>Inability to refine</td>
<td>Safe departure</td>
</tr>
<tr>
<td></td>
<td>Refinement as diminution or removing of something other than distress</td>
<td>Neglected distress</td>
<td>Safe departure</td>
</tr>
</tbody>
</table>
As we have seen, the original definition of reduction does not directly pose the risk of choosing the study design with the smallest number of animals even if it results in a larger amount of distress.

A case of absolute replacement, even pursued as a goal in itself, cannot result in any distress (here we do not consider the involvement of animals to initially test and certify the alternative). This is less clear in the case of relative replacement, since we can imagine a case where we must choose between a distressing relative replacement in which we cannot euthanize nor anaesthetize the animals still required and an animal experiment using a method causing almost no distress at all. In this example, there is a conflict between replacement and refinement. As we will discuss later, such cases of conflict between two of the Rs are significant risks to the purpose of the 3Rs. This departure from the original definitions would lead to cases where priority is given to relative replacements resulting in larger amounts of distress than other available alternatives. But the Swiss law definition of replacement does not correspond to this kind of departure. As we have seen, the purpose of the 3Rs according to Swiss law is “to protect the dignity and welfare of animals”. In this sense, replacement is not a goal in itself but a means for this purpose.

**Reduction as a goal in itself**

As in the case of replacement, defining one of the Rs as a goal in itself rather than a means for the purpose of the 3Rs can pose a risk to this purpose. In the case of reduction, it also poses the risk of creating a conflict with refinement. The aim of reduction is not equal to the aim of diminution or removal of distress. In fact, one could successfully reduce the number of animals used in an experiment while imposing more distress both at an individual level on each animal and as a TSD in the experiment.

But the definition of reduction in the Swiss legislation does not correspond to this kind of departure from the original definition. As we have seen, the Swiss definition of reduction is directly tied to that of refinement in the same sentence, i.e., “planned in such a manner that the smallest number of animals necessary is used and efforts are made to ensure the least possible constraint of the animals”. For this reason, reduction does not appear as a goal irrespective of refinement. Additionally, just as we discussed in the case of replacement, these definitions are means to achieve the purpose of the 3Rs, which is “to protect the dignity and welfare of animals”. Therefore, the Swiss law definition of reduction does not directly pose the risk of choosing the study design with the smallest number of animals even if it results in a larger amount of distress.

### 4.4 Safe departures

**Reduction as minimization of the number of animals**

As we have seen, the original definition of reduction does not indicate that the absolute minimal number of animals must be determined and used if we want to apply the principle of reduction. All things being equal, reducing the number of animals to the minimum, without changing the procedure or compromising the scientific soundness of the experiment, will always be aligned with the purpose of the 3Rs, i.e., it will always diminish the TSD. But in practice, aiming at the minimal number could put at risk the soundness of the experiment, since we aim at a number which is at the frontier between enough and not enough animals, and science is not infallible (Button et al., 2013; Fenwick et al., 2011). In case of error, all the distress experienced by the animals may have been in vain and the study may have to be repeated. As Tannenbaum and Bennett suggest, even if Russell and Burch emphasize the usefulness of statistical analysis to indicate the minimal number of animals needed in an experiment, they still stress the fact that we must ensure enough animals have been used.

For these reasons, this case of departure poses a practical risk to the purpose of the 3Rs. Aiming at the minimal number could, in practice, lead to waste or repetition of studies. In the case of waste, the total sum of distress would not have led to the desired scientific or medical progress. In the case of repetition, the same is true but in addition more distress may have to be experienced by other animals to reach this progress in the future.

Swiss law defines reduction as planning an animal experiment “in such a manner that the smallest number of animals necessary is used”. The term “smallest number” indicates that it is an absolute minimum. In this sense, the Swiss definition of reduction corresponds to this case of departure. However, we do not consider it an actual risk because it seems to us that, in practice, the way “necessary” is defined avoids this risk. Indeed, we know that statistics apply margins of error in calculations and that the “smallest number of animals necessary” tends to be understood as “necessary to avoid any risk of scientific invalidity” and not as “necessary to have the information”.

One could argue that the definition of “necessary” and the use of a margin of error is not enough to avoid this risk in practice. One way to find out would be to look at the number of experiments being considered unsound because of a lack of statistical power as well as those that needed to be repeated. The discussion about margins of error also opens the door to the problem of surplus animals, e.g., animals which were supposed to be used but ultimately were not or animals who do not fit the criteria of the study due to genetic or other non-anticipated reasons. While such cases of conflict need further investigation, we will stay focused on Tannenbaum and Bennett’s typology for now.

**Refinement as reduction of distress to an absolute minimum**

While Tannenbaum and Bennett do not explicitly cite this departure in their list of possibilities, the way they introduce the original definition of refinement suggests it is a possibility worth considering. Indeed, they make this introduction in two parts. First, the definition is presented alongside the other Rs by Russell and Burch in chapter 4 of their book, which defines refinement as “any decrease in the incidence or severity of inhumane procedures applied to those animals which still have to be used”...
(Russell and Burch, 1959, p.64). Then, in a subsequent comment in chapter 7, Russell and Burch write that the “object [of refine-
ment] is simply to reduce to an absolute minimum the amount of
distress imposed on those animals that are still used” (Russell
and Burch, 1959, p.134). Tannenbaum and Bennett finally con-
clude that the first part, considered in our article as the original
definition, is better suited to express the ultimate aim of refine-
ment as well as the reality of practice (i.e., diminishing the total
amount of distress even when we are not sure we will achieve the
absolute minimum).

It is not the aim of this paper to question this conclusion, and
we agree that a definition of refinement which would only in-
clude cases where distress has been reduced to an absolute min-
imum would prove impractical. Such a departure from the origi-
nal definition poses the risk of inability to refine, since in most
cases we do not have the means to define nor guarantee to attain
the absolute minimal amount of distress. Nevertheless, since
Russell and Burch used the terms “absolute minimum” in a sub-
sequent chapter as well as “minimize” in other papers, we will
consider that aiming at the absolute minimum is a good means to
diminish distress, but that the definition of refinement should not
exclude other degrees of diminution.

The Swiss definition of refinement demands the planning of
an animal experiment “in such a manner that efforts are made to
ensure the least possible constraint of the animals”. These con-
straints are defined by four degrees of severity in the AEO. The
four degrees are severity grade 0, “no strain”, severity grade 1,
“mild strain”, severity grade 2, “moderate strain”, and severity
grade 3, “severe strain”. We argue that the way “constraint” is de-

defined makes it practically feasible to determine, aim, and achieve
a specific degree of constraint.

In this sense, we consider the Swiss law’s definition of refine-
ment as a safe departure from the original definition, because
there is no risk of inability to refine. Once a degree of strain has
been determined in the design of the experiment, we can suppose
that additional efforts will be made in the conduct of the exper-
iment to diminish distress even further following the other parts
of the definition, i.e., “pain, suffering or harm may be inflicted
on, or anxiety induced in, animals only if this is unavoidable for
the purpose of the experiment”, that such experiments “must be
limited to the indispensable minimum” and that “well-being
must be ensured “as far as the intended purpose permits”. But
none of these seem to indicate a risk of inability to refine.

Refinement as enhancement of wellbeing

As we saw when discussing the distress-wellbeing scale, Rus-
sell and Burch do think of complete wellbeing as the positive
end of available experiences for animals. They also consider
that aiming at wellbeing is a good means to diminish or re-
move distress, and that we should do it. At first glance, a depar-
ture from the original definition that considers refinement as
the enhancement of wellbeing seems aligned with the purpose of
the 3Rs. If we follow the logic of the distress-wellbeing scale, any move from distress in the direction of wellbeing will
necessarily diminish, and eventually possibly remove, distress.

But such definitions still pose a risk to the purpose of the 3Rs.
As Tannenbaum and Bennett suggest, it is complex enough to
define and assess distress but to define and assess wellbeing
would be an additional task. In this sense, they show that insti-
tutions in the US which engaged in this kind of departure from
the original definition failed to be clear about what they meant
by wellbeing. If the ultimate purpose of the 3Rs is to remove
distress, it could be useful to keep these two kinds of issues
separated, the authors suggest. We could question this conclu-
sion, since Russell and Burch state that aiming at wellbeing
could prove much more effective at removing distress than fo-
cusing on decreasing distress, but that is not the aim of this
paper. We will agree here that this departure from the original
definition of refinement poses a risk of inability to diminish or
remove distress because of a confusion between the definitions
of distress and wellbeing.

Here again, the Swiss law definition of refinement corresponds
to this kind of departure but is not actually exposed to the risk
we just described. While Swiss law states that “well-being” must
be ensured “as far as the intended purpose permits”, we showed
above that the definition of wellbeing in the AniWA is similar
to the absence of distress rather than the pursuit of any positive
states of the animal, e.g., pleasure. For this reason, a risk of in-
ability to diminish or remove distress because of a confusion be-
tween the definitions of distress and wellbeing is not present in
Swiss law.

Refinement as diminution or removing of something other
than distress

This case of departure from the original definition of refinement
concerns definitions in which we consider as refinement the
diminution, and when possible removal, of something other than
distress, e.g., pain, fear, discomfort and so on.

As stated above, Russell and Burch characterize distress in
terms of a number of negative mental states that animals expe-
rince such as pain, fear, conflict, or frustration of need. We can
only imagine that this list is not exhaustive, or at least that there
are still nuances to be drawn in each of these categories. The
point is that a departure from the original definition that sub-
stitutes distress with one of these words alone, or with another
word such as discomfort, poses the risk of neglecting distress.
Indeed, a definition stating that refinement is the diminution or
removal of fear will fail to consider other kinds of distress.

But such a departure could also prove to be better at achiev-
ing the purpose of the 3Rs. If a definition of refinement used
another word than distress while having a more exhaustive list
of these negative mental states which, as Russell and Burch
state, could lead, if protracted, to physiologic stress syndrome,
then the departure would not pose a risk but rather represent an
advantage.

Once again here, the Swiss definition of refinement corre-
sponds to this departure, but we do not see an actual risk of
unconsidered distress. While many different terms are used in
Swiss law to describe the kind of negative states animals could
experience in experimentation as well as in other contexts, the
ways the AniWA defines wellbeing and uses the term when stating the purpose of the act appears consistent with the original definition of refinement.

As we have seen in Section 3.2, the four conditions in Art. 3b of the AniWA under which an animal would experience wellbeing, which is similar here to the absence of distress as we argued, include terms like disturbance, health, pain, suffering, harm, and most importantly, anxiety. This latter word seems to suggest psychosomatic and long term effects, which are important in the original concept of distress. For this reason, even if the terminology used is not the same, we consider that there is no actual risk of not considering some kinds of distress because of the use of multiple complementary terms.

Nonetheless, it should be noted that Switzerland faces challenges in translations since its legal texts are written in German, French and Italian. Some of them are even translated to English and Romansh, but these translations have no legal force. When mentioning the four degrees of severity we presented earlier, the English translations of the AniWA and AniPO talk about severity of “constraint”, while the AEO presents these as degrees of severity of “strain”. Strain and constraint do not mean the same thing. We would argue that “strain” is more appropriate in this context, which is the direction chosen in the Italian version, which uses the word “sofferenza”7 in the AEO. However, the German version uses “Belastung”8 and the French one “contrainte”9, two terms more in line with “constraint”. We do not think that these cases pose a risk of neglected distress, since all these terms are clearly imbedded in the context of wellbeing and the types of procedures and consequences are presented in detail. However, there is a need here for clarification and for a more accurate translation.

4.5 Risky departures
Replacement as using less sentient animals
In our view, the only case of departure from the original definitions which actually poses a risk to the purpose of the 3Rs in Swiss law is the following one: Replacement as using less sentient animals. As Tannenbaum and Bennett indicate, some institutions in the US talk about relative replacement when using this definition. However, as we said before, Russell and Burch define relative replacement as a replacement in which animals (regardless of their level of sentience) are still required, though in the actual experiment they are exposed, probably or certainly, to no distress at all.

Russell and Burch do talk about cases of substitution of one animal with another using the terms “comparative substitution”. In chapter 5 of their book, titled “Replacement” they write: “A more difficult question arises when we consider the free-living metazoan invertebrates. We have arbitrarily excluded them from consideration as objects of humanitarian concern. It remains to consider them in the light of possible substitutes for vertebrate subjects. Such a procedure may be called comparative substitution.” (Russell and Burch, 1959, p.69)

However, they do not consider such cases as cases of replacement, which indicates that such invertebrates are not considered as sentient material. Indeed, in the same chapter they give examples of invertebrates having “highly-evolved responses to damaging and startling stimuli” (Russell and Burch, 1959, p.70), which makes their decision to arbitrarily exclude them from consideration seem inconsistent. They also state that “we may regard comparative substitution as a limited gain, while admitting that the argument should be used with caution” (Russell and Burch, 1959, p.70). In any case, Russell and Burch drew a line between vertebrates and invertebrates, which is not the case when replacement is defined in terms of using less sentient animals. Therefore, we consider that defining replacement as using less sentient animals is a departure from the original definition.

At first glance, replacing a research animal with a less sentient animal seems like a good means to diminish the TSD. Since the animal is less sentient, a similar procedure on that animal should result, all things being equal, in a smaller TSD. But in reality, this definition poses a risk to the purpose of the 3Rs for two reasons, both related to conflicts between the Rs. First, because nothing indicates that we would carry out such a replacement only if the procedure on the less sentient animal will result in a smaller TSD. If the choice of using a less sentient animal precedes the choice of procedure to be used, there could then be cases where a procedure conducted on a less sentient animal is so severe that it results in a larger TSD than another procedure would have on the more sentient animal. Second, the number of less sentient animals needed to conduct a scientifically sound experiment could be substantially higher than the number of more sentient animals needed with another experimental design. Here again, we could end up with a larger TSD due to the number of animals used, even if each less sentient animal would experience less distress than each more sentient animal, individually.

As we have seen, according to Swiss law, replacement is the use of “procedures without animal experiments” or “alternative methods” instead of animal experimentation as well as the use of “animal species that are lower on the evolutionary scale” instead of “animals higher on the evolutionary scale” if a scientifically valid method is available. Here we understand “animal species that are lower on the evolutionary scale” and “less sentient animals” as interchangeable. While “procedures without animal experiments” are what Russell and Burch define as absolute replacement and “alternative methods” are either absolute or relative replacements, the use of “animal species that are lower on the evolutionary scale” instead of “animals higher on the evolutionary scale” is not a case of replacement according to the original definition.

The Swiss law’s definition of replacement actually poses the risks we stated above, since nothing in the law seems to exclude
cases where the procedure done on a less sentient animal is so severe that it results in a larger amount of distress than the initial procedure would have on the more sentient animal, or cases where the number of less sentient animals needed to conduct a scientifically sound experiment is so much larger than the number of more sentient animals needed with another experimental design that it also results in a larger amount of distress.

An interesting statement can be found in the document “Weighing of interests for proposed animal experiments” from the Ethics Committee for Animal Experimentation (ECAE) of the Swiss Academies of Arts and Science (2017). There, it is written:

“The requirement that experiments on animals higher on the evolutionary scale may only be carried out if the purpose of the experiment cannot be achieved with animal species lower on the evolutionary scale stands in need of interpretation since, from a biological perspective, no such evolutionary hierarchy exists. The ECAE recommends that ‘lower on the evolutionary scale’ be taken to mean ‘less sentient’ or ‘less subject to strain as a result of the proposed experiment’.” (Swiss Academies of Arts and Sciences, 2017)

The interpretation of “lower on the evolutionary scale” as “less subject to strain as a result of the proposed experiment” suggested by the ECAE would avoid the first risk we presented, i.e., larger TSD due to a more severe procedure imposed on the less sentient animal, because it would only allow such replacements in cases where the experiment is already “proposed” and therefore would have a similar severity in a less sentient or more sentient animal. Nonetheless, the second risk, i.e., larger TSD due to the larger number of less sentient animals needed, is not addressed by the ECAE.

5 Ethical evaluation of the current Swiss law

5.1 A similar purpose and significative progress

As we have seen, the purpose of the AniWA is “to protect the dignity and welfare of animals”. “Welfare” is here a synonym of “wellbeing”, which we defined earlier. While Swiss law uses other terms than Russell and Burch, the purpose of the 3Rs is similar in both cases. As we have said, if wellbeing is successfully protected for an animal, it would mean it is at least rank 0 on the distress-wellbeing scale, i.e., mere absence of distress. We have also seen that the protection of animal dignity is not a change in the purpose of the 3Rs, since the 3Rs contribute to the protection of animal dignity only insofar as it removes unnecessary strain, which is consistent with the original purpose. While purposes remain similar, Swiss law made significative progress in comparison to Russell and Burch regarding the types of distress and animals considered. As we pointed out, the definition of dignity requires to consider that strain is present in cases of humiliation, major interference with appearance and abilities, as well as excessive instrumentalization. Moreover, while Russell and Burch only considered conscious living vertebrates, we said that provisions in the AniPO apply not only to vertebrates, but also to decapods and cephalopods; mammals, birds and reptiles in the last third of the gestation period prior to birth or hatching; and larval stages of fish and amphibians that take in food freely.

5.2 Confusion about the purpose

Tannenbaum and Bennett have shown that some departures from the original definitions of the 3Rs reflect an underlying view that it is preferable not to use animals in research, regardless of the goal of diminishing or removing distress. This also seems to be the case in the European Directive 2010/63/EU, which states in Section 10 of its preamble:

“However, this Directive represents an important step towards achieving the final goal of full replacement of procedures on live animals for scientific and educational purposes as soon as it is scientifically possible to do so.” (EU, 2010)

Such departures suggest a change in the purpose of the 3Rs, which could be considered to be to “reduce and if possible end animal use in research”. While ending animal use in research would be aligned with the original purpose of the 3Rs (even if it fails to consider cases where animals are used without experiencing any distress), we have seen that reducing the numbers, as a goal in itself, would not be aligned with the original use.

The 2022 vote on the Swiss popular initiative “Yes to the ban on animal and human experiments – Yes to research that brings safety and progress” indicates that part of the public in Switzerland holds such views on animal experimentation. This gap between the purpose of the 3Rs defined in Swiss law and the one perceived by part of the public and other stakeholders causes confusion. For example, when the Federal Statistical Office revealed that the number of animals used in research increased by 3.3% in 2021, this resulted in some criticism from the public. But the number of animals used is not an indicator of the success of the 3Rs. Indeed, if in 2021 the 3Rs helped reduce the amount of animal distress per unit of information gathered, but a lot more information was gathered (resulting in more animals being used and maybe a larger TSD), it would still be a success for the purpose of the 3Rs. From this confusion follows that the measure of the 3R effect is an important goal for the Federal Food Safety and Veterinary Office.10 It seems that finding a way to assess the “avoided distress per study” and the “total sum of avoided distress” would be a place to start, but there is no doubt that this topic should and will receive more attention in the future.

5.3 Problematic focus on species

The risky departure from the original definitions of the 3Rs we emphasized in Swiss law is the definition of replacement as, in part, the use of “animal species that are lower on the evolutionary scale” instead of “animals higher on the evolutionary

---

experiments on species outside this scope, but such species could very well experience distress. In addition to the difficulty of ranking species, there is the problem of conflict between the Rs. Interaction between the principles is a crucial part of the application of the 3Rs, and it is useful to have a framework to illustrate it. In their article The interplay between replacement, reduction and refinement: Considerations where the Three Rs interact, De Boo et al. (2005) showed that all 3R measures, from training to new procedures, can be classified in ten categories of a Venn diagram as either one of the Rs, a combination of two Rs or of the three Rs, or a conflict between two Rs. They call this an interplay diagram (see Fig. 2).

The cases of conflict between the Rs we presented in this article, as well as those of positive co-operation, can therefore be categorized in this diagram.

As we have seen, the departure of Swiss law from the original definition of replacement poses the risk of a replacement resulting in a larger amount of distress, because the use of animals that are lower on the evolutionary scale is mandatory independent of the number of animals (conflict between replacement and reduction) or the severity of procedures (conflict between replacement and refinement). We have said that the ECAE’s recommendation to interpret “lower on the evolutionary scale”
as “less subject to strain as a result of the proposed experiment” would prevent cases of conflict between replacement and refinement. But firstly, it is only a recommendation, which means that there is no legal requirement to follow it. Secondly, cases of conflict between replacement and refinement would still occur. Therefore, the focus on species in Swiss law is problematic. But this is not the only example in which Swiss law fails to acknowledge and effectively confront cases of conflict between the Rs, as we will now see.

5.4 Need for conflict resolution among the 3Rs
Unresolved conflicts are potentially harmful in many aspects of life, and this includes the 3Rs. There is now a substantial body of literature on the conflicts between the Rs as well as on solutions to resolve them. Studies have also revealed that such conflicts, in particular between reduction and refinement, cause members of animal ethics committees to disagree with each other (Fenwick and Griffin, 2013).

While some of these conflicts are acknowledged in other states’ guidelines and policies, this is not the case in Swiss law. For example, in Section 25 of its preamble, the European Directive 2010/63/EU states: "The number of animals used in procedures could be reduced by performing procedures on animals more than once, where this does not detract from the scientific objective or result in poor animal welfare. However, the benefit of reusing animals should be balanced against any adverse effects on their welfare, taking into account the lifetime experience of the individual animal. As a result of this potential conflict, the reuse of animals should be considered on a case-by-case basis." (EU, 2010)

In comparison, Swiss law presents the application of the 3Rs as a linear and straightforward process. The statement in Article 137 of the AniPO, in which we found parts of the definitions of reduction and refinement, is a good example of this: "An animal experiment and its individual parts must be planned in such a manner that the smallest number of animals necessary is used and efforts are made to ensure the least possible constraint of the animals." (Swiss Federal Council, 2022)

The potential conflicts between measures of reduction and refinement are not acknowledged; it seems here that one could give priority to either reduction or refinement. If such prioritization is what Swiss law really implies, it should be made explicit, along with the ethical foundation of any such prioritization. As we will argue in the final section of this paper, Swiss law does indeed open the door to unethical prioritization instead of focusing on the one relevant aspect for the purpose of the 3Rs: TSD.

5.5 Choosing designs with the smallest TSD
Timing plays an important role in the 3Rs. The application of the 3Rs during the design of the experiment and during the conduct of the experiment are distinct, and the application for a license to perform an animal experiment serves as a frontier between the two. The design stage of an animal experiment can take months or even years. Since innovation happens all the time, we must suppose that 3R measures available to researchers are always changing. When applying for a license, researchers favor one design among all scientifically valid alternatives. But the application of the 3Rs does not end with that decision. During the conduct of the experiment, new opportunities to replace, reduce or refine may become available at any point according to innovations and circumstances. In this stage however, many aspects of the experiment will already be defined, and as a consequence some 3R measures will be ruled out (e.g., a species-specific refinement innovation will be ruled out if a different species is used in the experiment).

During the design stage, researchers must choose the design which, to the best of their knowledge, will result in the smallest TSD. To do that, they must assess, to the best of their ability, the TSD of all alternatives. Figure 3 below illustrates how three alternative designs (A, B and C), each using multiple 3R measures, should be compared for TSD. It is clear that prioritizing any aspect other than TSD, be it species, procedure, constraint on the individual animal, number of animals or any other, could result in a failure to choose the alternative resulting in the smallest TSD. In this final section, we argue that this is precisely what current Swiss law allows to happen.

Swiss law does not distinguish between the application of the 3Rs during the design and the conduct of the experiment. Neither does Swiss law require a TSD assessment of alternative designs. Therefore, aspects of the design such as species, procedure, reduction or refinement, could be prioritized without justification. In other words, one could deliberately rule out alternatives in the design stage. Going back to Figure 3, prioritizing reduction would lead to choosing design A, and that choice would be acceptable (in terms of the Swiss law) as long as the number of animals and the distress of them has been minimized for that specific design. The same would be true if design B is chosen by prioritizing refinement. But choosing design A or B instead of design C, which in this case will result in the smallest TSD, is not consistent with the purpose of the 3Rs.

We will give two additional examples of problematic prioritization in Swiss law. The first one is a case where priority is given to refinement without any consideration of the number of animals used. The document “Dignity of the animal: guide to the ‘weighing of interests’” by the Federal Food Safety and Veterinary Office states that if an “alternative entailing less strain for the animal is available” and “can be conducted reasonably”, then it “should be given preference” (FSVO, 2017a). We cannot help but notice here that the term animal is used in its singular form.

The second example comes from another document from the Federal Food Safety and Veterinary Office and is even more problematic. It states that the difficulty or the costs of a design’s implementation could be sufficient reason to dismiss it. The document is titled “Dignity of the animal Explanatory notes on the ‘weighing of interests’” and states: "[...] when considering a particular intervention, there will often be alternatives which can indeed be used to achieve the
be a necessary step in the application for a license to perform an animal experiment. While applicants and animal ethics committees may conduct such assessments in practice, the law should not rely solely on good practices. Otherwise, the threat of problematic prioritizations and choices of convenience would be greater.

One could argue here that assessing and therefore comparing TSDs is too difficult, or even impossible. But if this was the case, it would also be true for the assessment of distress in individual animals. Additionally, applicants and animal ethics committees already perform a similar assessment for the harm benefit analysis in the process of applying for a license to perform an animal experiment. It is accepted that an assessment of distress is possible, and we know it is a difficult task. It becomes even more difficult when we must assess a TSD and compare it to others, but we argue that it is necessary to pursue the purpose of the 3Rs in the most effective way. In this matter, we can hope that the advancement of science will allow to assess distress with more precision in the future.

6 Conclusion

In this paper we compared the original purpose and definitions of the 3Rs with the ones in the Swiss legislation with two aims: first to reveal ethically relevant departures from the original intended aim and entail less strain for the animal but are more difficult or more costly to implement (e.g. more labor intensive or more expensive) than the intervention being considered. The question arises of when use of the alternative can be imposed instead of the intervention originally considered. This question should be assessed from the perspective of reasonableness. The greater the strain imposed by the original procedure in terms of dignity, the greater the effort or expense the stakeholders can reasonably be expected to accept in relation to the alternative.” (FSVO, 2017b)

To compare the interest in an accessible and affordable implementation against the interests of animals is not an easy task. If the implementation is impossible, it could stop scientific and medical progress, which would result in more distress for humans and for animals and is contrary to the purpose of the 3Rs. But here again, circumstances which are not directly relevant to the purpose of the 3Rs are used to rule out design alternatives. This opens the door to the risk of choosing aspects of an experiment, such as procedure and species, based on convenience – which is contrary to the spirit of the 3Rs.

We can then conclude by saying that if Swiss legislation is to pursue the purpose of the 3Rs in the most effective way, it should prevent problematic prioritizations and choices of convenience. To achieve that, requiring a TSD assessment of all scientifically valid alternative designs, or at least of the most promising ones, would be a necessary step in the application for a license to perform an animal experiment. While applicants and animal ethics committees may conduct such assessments in practice, the law should not rely solely on good practices. Otherwise, the threat of problematic prioritizations and choices of convenience would be greater.

One could argue here that assessing and therefore comparing TSDs is too difficult, or even impossible. But if this was the case, it would also be true for the assessment of distress in individual animals. Additionally, applicants and animal ethics committees already perform a similar assessment for the harm benefit analysis in the process of applying for a license to perform an animal experiment. It is accepted that an assessment of distress is possible, and we know it is a difficult task. It becomes even more difficult when we must assess a TSD and compare it to others, but we argue that it is necessary to pursue the purpose of the 3Rs in the most effective way. In this matter, we can hope that the advancement of science will allow to assess distress with more precision in the future.

Fig. 3: Assessing alternatives for TSD

![Diagram of Assessing alternatives for TSD]
pose and definitions, and second to provide an ethical evaluation of current Swiss law.

Regarding the purpose of the 3Rs, we revealed that the original purpose and the one stated in Swiss law are similar. Although the terminology is different, the aim of the 3Rs is, in both cases, to diminish, and when possible remove, animal distress without compromising necessary scientific and medical progress. It has been shown, however, that there is confusion among part of the public and stakeholders about how to measure the effects of the 3Rs. We argued that the 3Rs should use a measure of “avoided distress” and that this topic needs further investigation.

By comparing definitions using Tannenbaum and Bennett’s typology of departures, we found that there is one ethically relevant departure in Swiss law from the original definition of replacement that poses the risk of replacements resulting in more distress. Swiss law uses species ranking on the evolutionary scale to prioritize which species to use in case scientifically valid methods are available. But as the ECAE states, “from a biological perspective, no such evolutionary hierarchy exists”. In any case, the relation between species membership and the capacity to experience distress is not clearly defined in Swiss law. While the ECAE gives recommendations on how to interpret this prioritization, a clarification is needed to avoid inflicting more distress erroneously. In addition to the difficulty of ranking species, there is the problem of conflict between the Rs. Swiss law’s prioritization of species does not acknowledge the cases of conflict between the Rs, in this particular case between replacement and refinement or reduction (or both). We argued that the interaction between the Rs and membership of the species poses a new ethical challenge.

This led us to the observation that Swiss law fails to acknowledge such cases of conflict among the Rs, unlike, for example, the European Directive 2010/63/EU, which does it explicitly. In cases of conflict, Swiss law allows for the prioritization of aspects which, considered alone, are irrelevant, i.e., species, reduction of the number of animals, reduction of the constraint on individual animals, difficulty of implementation, costs of implementation. While such prioritization may be aligned with the purpose of the 3Rs during the conduct of the study, during the design of the study it opens the door to the deliberate exclusion of alternatives.

Therefore, timing has also been presented as a crucial aspect in the application of the 3Rs. We argued for a distinction between the application of the 3Rs at the design stage and at the conduct stage, the application for a license to perform an animal experiment serving as a frontier between the two. Such distinction might not be considered accurate by researchers who might consider that they apply the 3Rs on a daily basis or that the 3Rs is a state of mind. Nevertheless, every animal experiment in Switzerland is approved at a specific time based on a harm benefit analysis involving the design chosen by the applicant. This decision, favoring one design among all scientifically valid alternatives, defines the number of animals from a specific species and the degree of severity imposed upon each of them. If approved, the distress resulting from the design would be considered justified for up to three years, even if no additional 3R measure was implemented due to lack of opportunity or other constraints. Thus, the design stage and the application for a license to perform an animal experiment are, in fact, the key times to prevent problematic prioritizations and choices of convenience. Empirical research is needed to investigate whether current practices and processes allow for the design to be continuously optimized to reduce TSD, involving key roles such as the Animal Welfare Officer. A step in this direction would be to reduce the duration of authorizations or to add an intermediate review of the design.

Whether it is in the design or the conduct stage, researchers are dependent on available 3Rs measures. For that reason, investing resources in the development of measures that minimize TSD is necessary. Swiss law fails to address this issue, and it is not clear whether the proper attention is given to it in Switzerland. To pursue the purpose of the 3Rs in the most effective way, legal dispositions should ensure that priority is given to the development of such 3Rs measures, e.g., animal-free research methods, more suitable animal models.

We concluded our assessment by stating that to pursue the purpose of the 3Rs in the most effective way, Swiss law should prevent problematic prioritizations and choices of convenience by returning to Russell and Burch’s original concept of TSD. We argued that to achieve that, requiring a TSD assessment of all scientifically valid alternative designs, or at least of the most promising ones, would be a necessary step in the application for a license to perform an animal experiment. As a matter of fact, it is the only way to ensure one chooses the design with the smallest TSD.

While applicants and animal ethics committees may perform such assessments in practice, empirical research on stakeholders’ perspectives and practices is needed to investigate if they do. In any case, the law should not rely solely on good practices. Otherwise, the threat of problematic prioritizations and choices of convenience would be greater. Regarding this, it would be interesting to empirically investigate what constraints, if any, applicants feel when designing an animal experiment in Switzerland. It would also be an opportunity to investigate which differences, if any, result from the translation of the law into three national languages (i.e., German, French, Italian) and sometimes more (i.e., Romansh, English), which is a challenge for Switzerland as we have shown with examples.

We argued that the assessment and comparison of TSDs should not be considered too difficult or impossible, since applicants and animal ethics committees already do a harm assessment for the harm benefit analysis in the process of application for a license to perform an animal experiment. Nonetheless, it remains a complex task, and its successful implementation would require guidance from experts as well as support for applicants, who might see it as an additional burden. However, the fact that the current process already has the metrics (i.e., degree of severity, number of animals, species) and the tools (i.e., application for a license, proof of necessity, weighing of interests)
needed for such a TSD assessment and comparison is an important advantage for Switzerland. Finally, our decision to adhere to the original purpose and definitions of the 3Rs to suggest such TSD assessment at a time when alternative frameworks are proposed, can be called into question. If we take the example of Beauchamp and DeGrazia’s (2020) six principles of animal research ethics, we can see that aspects that go beyond the 3Rs (e.g., sufficient value to justify harm, expected net benefit or upper limits to harm) are given a key role in modern propositions. In this sense, our goal is not to argue that adding a TSD assessment to the current Swiss framework is the only or the best way to make ethical progress in animal research. Rather, we intend to point out a flaw in the current Swiss framework – a flaw which could be corrected by our suggestion.

References

Conflict of interest
On behalf of all authors, the corresponding author states that there is no conflict of interest.

Data availability
No datasets were generated or analyzed during this research.

Acknowledgement
The SNSF – Swiss National Science Foundation – funded this research (Grant ID: 206472).