



Replacement in animal research – a qualitative study of barriers and opportunities

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November 6 2018

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Replacement – the “challenging R”

The 3Rs (*Replacement, Reduction, Refinement*) of animal experiments is getting increased attention in legislation and guidelines

Among animal researchers:

-Considerable support for the principles of the 3Rs

-However, little effort to develop Replacement techniques and belief that it is possible

- NC3R (2008): **73%** of animal researchers in the UK reported that “Complete replacement...will never be achieved”; **12%** report to have developed replacement techniques
- Fenwick et al (2011): Animal researchers in Canada identified more obstacles with respect to implementing replacement techniques compared with reduction/refinement techniques
- Nøhr et al (2016): **79%** of animal researchers in Denmark reported that “Complete replacement...will never be achieved”; **29%** report to have developed replacement techniques

Calls for more insights into possible social and cultural processes that underpin the Replacement challenge

“It may be useful for animal use policymakers to consider what steps are needed to make replacement a more feasible goal”

(Fenwich, Danielson, Griffin 2011)

Interdisciplinary group recommended to carry out:

...new research in the humanities and social sciences to inform emerging discussions and priorities on the governance and practice of laboratory animal research” (Davies et al 2016)

Study aim: Barriers and opportunities regarding Replacement (in Denmark)

Study funded by the Danish 3R centre

Research group:

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Study aim: Barriers and opportunities regarding Replacement (in Denmark)

Distinguishing between different research cultures

ie. public and private organization

WHY?

Qualitative interview study

Questionnaire-based survey (Nøhr et al 2016) of animal researchers working in Danish research institutions identified...
 Major differences between publicly and privately employed researchers in culture of care

- (i) communication in the organization
- (ii) awareness of and use of the local animal ethics committee
- (iii) understanding of Refinement
- (iiii) reluctance towards implementing animal welfare concerns
- (iiiii) work phase where the 3Rs are considered

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Qualitative interview study

Personal interviews with

- animal researchers
- managers
- internal consultants

Interview persons were embedded in the same organization

In total 12 individuals from three different organizations were interviewed

Duration: 37-60 minutes

Embedded interview persons



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Explorative techniques with small n's are useful and necessary...

When there is little knowledge and theory to draw on

Method to understand and contextualise the differences identified in questionnaire study

- **Helps to identify hitherto unknown salient themes (barriers and possibilities)**
- **Follow-up studies can quantify the explorative findings**

Results

(i) Attitudes to and understanding of the 3Rs and Replacement

Support for 3R as well as the use of lab animals

Clear support for the intentions behind the 3Rs

But also clear support for the use of lab animals

- a necessary research method to study e.g. diseases and drug tests *in vivo*
- good lab animal welfare

Researcher: "*...It is my impression that our laboratory animals are 100 times more well off than the average pet*"

Need more knowledge...

Development of non-animal-methods (NAM) require in-depth knowledge about in vivo mechanisms

Researcher: *"...If we had exact knowledge about the mechanism that produce an effect, perhaps we could design experiments where cell cultures or other experimental systems are used"*

This requires prior in vivo animal studies

- **Many interview persons mentioned that this type of basic mechanism research takes place predominantly at universities**
- **Privately employed researchers called for more mechanism research at universities**

Optimism in private companies

Technological optimism among privately employed informants

Techniques are being developed and refined that will help the implementation of the 3Rs, including replacement

University managers: replacement projects constitute a carrier risk

Considerable risk for university researchers to work with Replacement, because outcomes are uncertain

Manager: *"...Replacement involves a major risk [of failure]. And the researchers know that"*

(ii) Researcher access to
knowledge and tools

Animal researchers stress the importance of access to knowledge about Replacement

In the form of novel methods, creativity, and cross-disciplinary collaboration

Considerable differences between publicly and privately employed researchers

Privately employed researchers experience plenty of access to relevant Replacement knowledge

Good cross-disciplinary work and knowledge sharing

-Perceived as pivotal in the development of new techniques

Management / organizational support

-In one company, a 3R section exists

- with updated knowledge about 3R techniques
- help researchers to search for possible 3R techniques

-Management "patience" so that NAM techniques can be developed

Researcher: *"...We have been very dependent on management back-up. It took time to reach the goal, and it was difficult. But the company said that they were keen on this and wanted to prioritize that it would get up and running"*

University researchers report lack of access to Replacement knowledge

Even though interviewed managers specified that there are rules and guidelines

The researchers experience a lack of management support

- No active and clear goal formulation regarding 3R implementation
- No formal rules/guidelines as to how to think about the 3Rs
- No support for cross-disciplinary work and knowledge sharing

Call for knowledge concentration, e.g. a centre:

Researcher: *"...It might improve the situation to have a centre that one could visit where there would be people that are knowledgeable about other methods. Engineers and others that know about computer [modelling] and stuff like that"*

(iii) Routines and organizational conditions

Different conditions and management styles in universities and private companies

Explain differences in organizational focus on the 3Rs

In private companies, research projects and allocation of resources are top-down directed

Hence, 3R strategies and prioritisation of Replacement require support from management

This support is largely in place

Manager: *"We have the necessary tools in-house and a wide array of expertise...the disciplines are tightly interwoven and we can define common goals"*

Similarly, animal researchers in private companies experience high level of support for 3R implementation from management

- Cross-disciplinary cooperation
- 3R section
- Resources and incentives

The basic steering mechanism in private companies (profit, capital investment) sometimes is a barrier

Researchers report that time- and market pressure means that too few resources sometimes are allocated to focus in-depth on 3Rs and Replacement

Researcher: *"If there is anything that is not allowed in this firm it is time delay of projects. Because it affects the bottom-line. Someone calculated that if we are behind the timeline by just a month, there may be many millions at stake. It is also about being the first to reach the market with a new product"*

In universities, research projects and resources are governed by researchers/research groups

University culture sometimes referred to as “organized anarchy” (Musselin 2006)

Animal researchers experience lack of management focus

- **Animal welfare and the 3Rs not a priority for university management**
- **Little investment (financially or value-based)**
 - Lack of resource allocation and knowledge sharing centers
 - Lack of clearly communicated strategy, rules, and guidelines about the 3Rs
 - There ARE rules / guidelines (as specified by the managers) – but they ARE NOT well-known by researchers

So, getting and using resources to work with the 3Rs and Replacement requires very engaged researchers

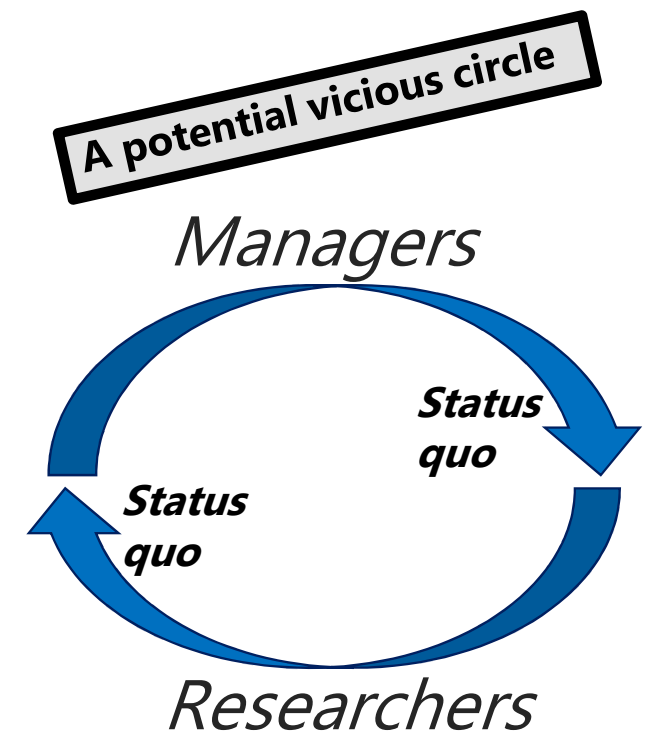
University managers respect researcher autonomy and researchers expect autonomy

(Extract from interview with university managers):

Interviewer: *How do you get the researchers to implement new routines in their research?*

Manager 1: *This is a really difficult question. You know, a university consists of many small groups. There is no common ground.*

Manager 2: *It's a change in culture, right. This is something that happens slowly.*



(iiii) External demands

External demands play very limited role with respect to pushing Replacement forward

Many external demands that result in animal welfare considerations in research design

- Requirements stem from in-house veterinarians, governmental authorities, project funders

However, in a Replacement perspective external demands are typically non-existent or even limits potential Replacement initiatives

Publicly employed researchers

Do not mention explicit demands from external funders to describe how Replacement is considered in and factored into the research

Privately employed researchers/managers

Mention that explicit demands from public authorities to test new products in vivo are potential barriers

Outdated guidelines

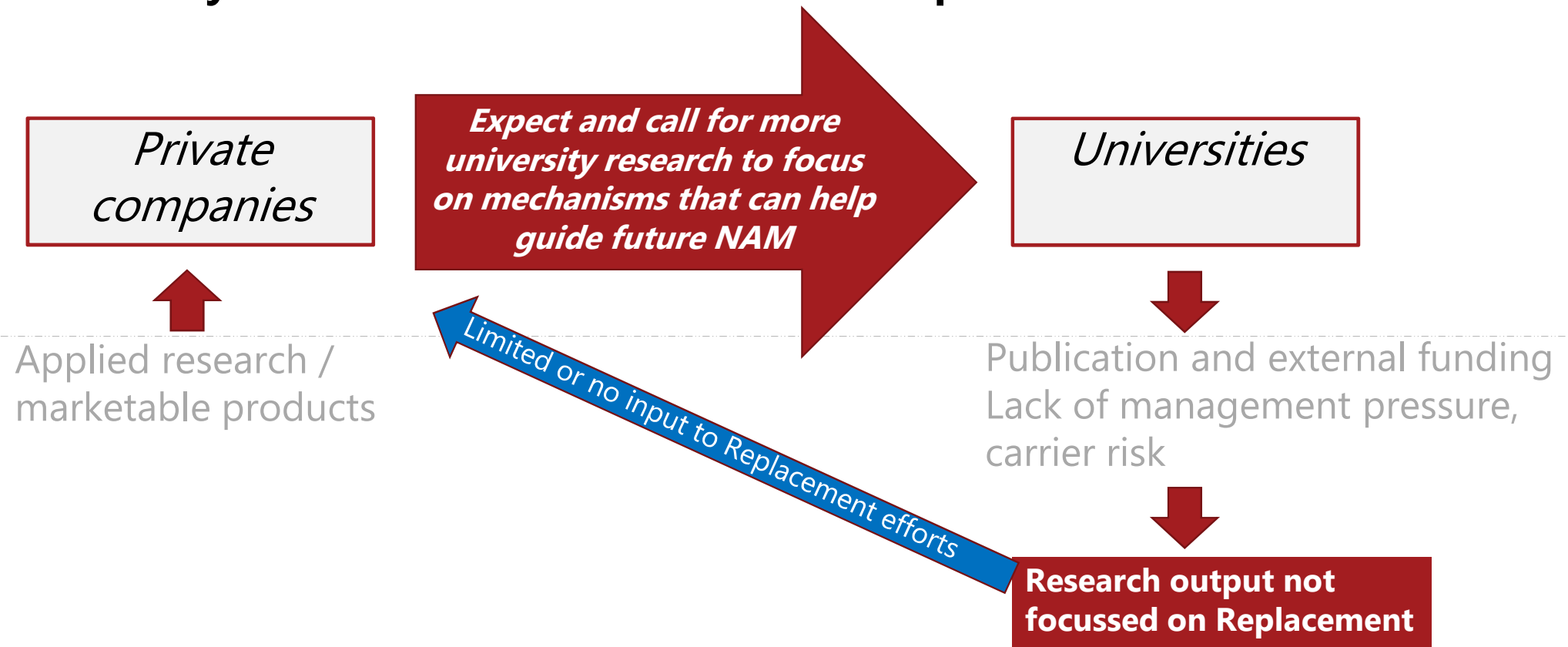
***Manager:** "In government regulated studies our animal models are determined by guidelines. If these guidelines were altered, it would be easy for us to stop the use of animals. If the guidelines cannot be altered, it is completely impossible to replace the animal experiments"*

Summing up

	Barriers	Opportunities
University research culture	<ul style="list-style-type: none"> -Decentralised management -Lack of resources (finance and help) -No experience of local, formal guidelines -Carrier risk 	<ul style="list-style-type: none"> -Cross-disciplinary cooperation -Investment (time, resources) -Engaged researchers -Local knowledge sharing -External networks -Formal routines and rules -Clear and management policies that can be implemented
Private company research culture	<ul style="list-style-type: none"> -Demands from governmental authorities -Time pressure -Market pressure 	<ul style="list-style-type: none"> -External demand

Possible barrier owing to the division of labor between universities and private companies

Disconnect between privately employed researchers' expectation to university research and actual research output



What to do? (1)

Public authorities must be frontrunners in developing guidelines / rules that...

make use of Non-animal-methods possible

- this is an international issue
- necessary to map whether / how national, regional, international rules constitute barriers to replacement
- national 3R centres or similar assemblies can initiate this at a cross-national level

require research projects and project funders to think in terms of Replacement, i.e.:

- To justify the use of lab animals
- To scan the literature for possible Non-animal-methods

What to do? (2)

3R centres should stress earmarking grants to researchers that want to work with Non-animal-methods techniques

- **This could be in the form of funding from national 3R centres**
- **Other public provisions of research funding**

What to do? (3)

Management, primarily at universities, must improve institutional focus on Replacement

Not enough to develop rules and guidelines

Allocation of resources

- to procure and share knowledge about Replacement
- to develop new Replacement techniques or report about possible Replacement / NAM techniques
- attempt to increase external research funding regarding the 3Rs through coordination/communication with funders (e.g. basic research councils)

Make research about the 3Rs a trustworthy and secure carrier route

- so it does not constitute a major risk for interested researchers

3R centres have central role as consultants and initiators in this process

Formulation of binding rules and routines/guidelines

- so possible non-animal alternatives are taken into consideration
- e.g. through an internal review process at the section or department level

THANKS

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