Hello, I’m Adrian Smith and I’m going to tell you about the PREPARE guidelines for planning animal research and testing.

This presentation and the PREPARE guidelines themselves are available at the web address norecopa.no/PREPARE

I work for the Norwegian 3R centre Norecopa. The PREPARE guidelines were written in collaboration with Professor Eddie Clutton at the University of Edinburgh in Scotland, Senior Scientific Officer Elliot Lilley at the RSPCA in the UK, Associate Professor Kristine Hansen at the Norwegian University of Life Sciences in Oslo, and Research Advisor Trond Brattelid at the Western Norway University of Applied Life Sciences in Bergen. The PREPARE guidelines are based upon our experiences over the last 30 years in planning and supervising animal research, and they were developed in connection with courses in Laboratory Animal Science for researchers.

My email address is on this slide, and you are welcome to contact me if you would like more information.

I’d just like to start with giving you a brief overview of some of the things that we do.

Norecopa arranges international consensus meetings, where we focus on those species which are not discussed so often at mainstream lab animal meetings: in particular fish, wildlife and farm animals. We have a policy of ensuring that all the presentations from our meetings are available afterwards on our website.

We also have a comprehensive website, norecopa.no, most of which is in English. It looks like this: the main menu is in the blue field, and then there are submenus for each topic. At present there are about 7,500 web pages.

There is also an intelligent search engine built into the site, to help you find what you’re looking for.

Part of the website consists of a database containing information on about 3,000 commercial products which can be used as alternatives or supplements to animals in education and training. A large number of homemade educational aids are now also being produced. We arranged a workshop about these in Oslo in April 2018, and we have a section of the website describing these.

We also have a lot of videos illustrating procedures for handling, injecting and bleeding laboratory animals. This is one example: a short video showing a refinement of the technique for scruffing rodents. The video is also available in Spanish.

We also have a lot of information on how to construct good searches in the scientific literature, together with an overview of global databases of relevance to laboratory animal science.

There is also a comprehensive international Meetings Calendar, updated several times each week, and we also produce a newsletter, in English, which is issued 7-8 times a year. You can subscribe to the newsletter using the white field at the bottom right hand corner of every webpage. We are also on Facebook and Twitter.

I’m now going to explain why we felt there was a need for the PREPARE guidelines. Over the last few years, there has been increasing concern about what has become known as the reproducibility crisis: the inability to be able to reproduce the results of animal experiments, even in the scientist’s own lab. For the pharmaceutical industry, this is a major barrier to the translation of animal research into treatments for humans.

Surveys have also shown evidence of poor experimental design, incorrect use of statistical analyses and under-reporting of the use of pain-killing drugs in surgical research.

This concern about reproducibility is actually not new. Over 60 years ago, Berti and Cima published a paper showing that the toxicity of chlorpromazine in mice varied over 300 times, depending upon the temperature of the room in which they were kept. And a few years later, Hurni published a long list of variables which influence the performance of laboratory animals.

In an attempt to solve this problem, many guidelines have been written on how to report animal experiments, based upon the hope that scientists will understand the need for a detailed description of the conditions under which the animals were kept. Today, the best known are the ARRIVE guidelines, which have been endorsed by over 1,000 journals. Unfortunately, there is evidence that many researchers publishing the results of animal experiments in these journals, have not heard about them or are not complying with them.

The ARRIVE guidelines consist of a checklist of 20 main items and a large number of additional topics under these items.

We believe that reporting guidelines, like ARRIVE and others, are an important part of the process of ensuring the quality of scientific research and improving communication between researchers. However, in our experience over the last 30 years, there are a large number of additional items to be considered, which are rarely described in scientific papers. Some of these are the responsibility of the animal facility, not the scientists, but it is important that the scientists are aware of them, since they may have a large impact on study quality, animal welfare and health and safety. Animal welfare is very important, not just because we have a moral duty towards animals, but also because happy animals give better science. Animals that are in harmony with their surroundings will give more correct scientific data if stress is prevented.

So we look upon planning and reporting guidelines as two complementary resources: one to be used from day one of planning, and the other to be used when the experiments are written up and published. Importantly, experiments (rather like bread) cannot be improved by describing them: the only solution is to change the ingredients and conditions under which they are performed.

So PREPARE helps scientists ensure that important items (which they may not need to describe in their papers) are considered. Here is a list of some of those which, in our experience, are not always given sufficient attention:

* poor literature searches
* lack of humane endpoints
* poor experimental design
* vague distribution of work and costs between the scientists and the animal facility
* insufficient evaluation of the facility’s competence and infrastructure
* too little attention to transport and acclimation
* ignoring health risks for all involved
* lack of standard procedures for necropsy
* poor planning of waste disposal
* little discussion about the fate of the animals

The PREPARE guidelines were pre-published in the journal *Laboratory Animals* in August 2017, and appeared in the paper version in April 2018. They consist of two things:

First of all, there is a 2-page checklist, rather like the ARRIVE checklist, consisting of 15 topics. This checklist has been translated so far into over 15 languages.

PREPARE stands for: **P**lanning **R**esearch and **E**xperimental **P**rocedures on **A**nimals: **R**ecommendations for **E**xcellence.

PREPARE covers 15 topics:

**Formulation of the study**

1. Literature searches
2. Legal issues
3. Ethical issues, harm-benefit assessment and humane endpoints
4. Experimental design and statistical analysis

**Dialogue between scientists and the animal facility**

1. Objectives and timescale, funding and division of labour
2. Facility evaluation
3. Education and training
4. Health risks, waste disposal and decontamination

**Methods**

1. Test substances and procedures
2. Experimental animals
3. Quarantine and health monitoring
4. Housing and husbandry
5. Experimental procedures
6. Humane killing, release, reuse or rehoming
7. Necropsy

The topics in pink on this slide are examples of ones which are not highlighted in the ARRIVE guidelines, but which are important to consider when *planning* experiments.

But importantly, there is much more to PREPARE than the checklist. On the Norecopa website there are webpages for all the topics on the checklist. Here you will find explanations of the topics, and links to quality-controlled guidelines on these topics, produced by international experts. These include advice on topics like housing and husbandry, injection volumes, blood sampling, anaesthesia and analgesia, humane endpoints and experimental design.

You may be wondering if it is necessary to go through such a long checklist every time an animal experiment is planned. Not all the items will be equally important each time. Experienced scientists will know about many of the topics already. But a checklist is always a good idea, for two reasons: first of all, it encourages close contact with the animal facility from day one of planning: this makes sure that the staff are involved at a very early stage. They will be able to give good advice about the details of the experiment, long before it is performed and they know the strengths and weaknesses of the facility.

Secondly, things may get forgotten if a checklist is not used. For example, experienced pilots use many checklists, even on routine flights where everything goes well. I can recommend a lecture, available on the internet, by Colin Dunlop and Nathan Koch. Both are veterinarians, and they talk about the need to improve the quality of veterinary anaesthesia. What is particularly interesting, is that Nathan Koch is also an airline pilot. He demonstrates the similarities between planning a procedure on animals, and planning a flight in an aircraft.

So in connection, for example, with an experiment involving the intravenous injection of a radioactive isotope in mice, the scientists might want to focus particularly on items like

* literature searches (to find refinements of the technique);
* legal issues (because there will be national regulations for the use of radioactivity);
* division of labour (who will give the injections? this is particuarly important if they are to be given at weekends as well);
* an evaluation of the facility (does it have the infrastructure to handle radioactive agents?)
* and an evaluation of the staff skills (do they need extra training?);
* consideration of the potential health risks, all the way through to safe waste disposal and decontamination of the rooms;
* and a discussion of how to house the animals, where to perform the procedures and how to conduct safe necropsies on radioactive animals.

The PREPARE website also includes a number of other resources. One of them is a suggestion for a simple contract between the scientists and animal facility, to share responsibility and costs for the various parts of the project. This consists of a list of items which should be considered, and three columns, so that responsibility for the items can be allocated either to the animal facility, or to the research group, or be crossed off as not relevant. A copy of the completed contract is kept by both parties, and serves as a checklist and reminder of who is responsible for what. This avoids unpleasant discussions after the experiment, for example when a paper has been submitted to a journal and they ask for more details. If the research group cannot provide the information the journal requests, for example room temperature during the experiment, it may be difficult to publish the study, wasting human resources and animal lives.

Another suggestion on the PREPARE website is for the use of a Master Plan. In its simplest form this is a weekly planner, where tasks which need to be performed during the study are listed on the left hand side, and open rings placed in the columns for the weeks in which they are to be performed. As the study progresses, the person who performs the tasks writes his or her initials inside the circle. This gives a good visual record of the study, making it easy to identify who has done what, and it reduces the risk that tasks which are not performed often get forgotten.

*May I ask you for a favour?*

If you have found this presentation interesting, please spread information about Norecopa and our resources to your colleagues, at home and abroad.

If you would like to translate this presentation into your native language, you will find the commentary as a Word file, and the slides as a Powerpoint file, on the PREPARE website:

[norecopa.no/PREPARE](https://norecopa.no/PREPARE)

*Thank you for listening!*