Netherlands National Committee
for the protection of animals
used for scientific purposes

Procedures using cats and dogs

Opinion of the Netherlands National Committee for the Protection of Animals Used for Scientific Purposes (NCad) commissioned by the Dutch Minister of Agriculture

The NCad and its methods

The Netherlands National Committee for the protection of animals used for scientific purposes (NCad) was appointed for the protection of animals used for scientific and educational purposes. NCad aims to make a significant contribution to minimising laboratory animal use, both at national and international level. This will involve giving advice, exchanging knowledge and developing both national and international networks. The ethical review of animal procedures is of pivotal importance in this regard, as are the 3Rs (Replacement, Reduction and Refinement).

NCad members

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This advisory report will be published on the NCad website: http://english.ncadierproevenbeleid.nl

Summary

The Netherlands National Committee for the Protection of Animals Used for Scientific Purposes (NCad) has formulated specific recommendations in the opinion submitted, and offers guidance on reducing the use of cats and dogs as laboratory animals without compromising the quality of research and education.

The opinion is set out under three themes:
- research required by law
- education
- fundamental research

The opinion also briefly addresses possible communication strategies.

Re: Research required by law

As research required by law comprises a global component in addition to a European component, the NCad envisages a role for the Medicines Evaluation Board (MEB) because it has access to the relevant circles. Where human medicinal products are concerned, the Minister of Health, Welfare and Sport is the MEB's client, and therefore the Minister of Agriculture will also need to seek assistance from her for this purpose.

1. The European Pharmacopoeia (EP) has abolished the batch/lot safety test for virtually all veterinary vaccines. The test still needs to be carried out occasionally because it is a requirement by third-country supervisory authorities. Ask the MEB to undertake efforts to have the legal requirement for this test waived outside Europe as well. The manufacturers can also initiate discussions with the supervisory authorities in third countries about having the safety test waived.
2. Ask the MEB to undertake efforts at European level for the non-routine retesting of a batch/lot of a vaccine by the supervisory authority in one of the European Member States.
3. Furthermore, ask the MEB to ensure that the study on the approach to be adopted for the release of a batch/lot of a vaccine that is based on using non-animal testing methods (the consistency approach) is endorsed by the supervisory authorities in Europe.
4. The implementing bodies and regulators must be encouraged to exchange data on the use of animal models and alternative methods and, in light of its role as a monitoring body, ask the MEB that it should call applicants to account if they have failed to use alternative methods even though they were available.

Re: Education

1. Assistance should be sought from the AOC Council[1] to abolish the use of cats and dogs as laboratory animals in all paraveterinary training programmes, without compromising the quality of these programmes.
2. Assign Utrecht University a facilitative and coordinative role in practising procedures without having to use live cats and dogs for this purpose.

[1] AOC Council: network of agricultural training and the Vereniging Buitengewoon Groen.

3. The use of a donor card for pets should be optimised by instructing the Netherlands Food and Consumer Product Safety Authority (NVWA) to provide all impounded cats and dogs with a donor card before these animals are offered for relocation, and to encourage that all shelter animals are also provided with donor cards in the future. In addition, an appeal must be made to the animal protection organisations, veterinary practices, breeders and organisations that use dogs, such as the police, to promote the donor card and to donate deceased animals.
4. The wider use of plastinated specimens should be facilitated by, for instance, donating cats and dogs that have been impounded by the NVWA, the Inspectorate of the Dutch Society for the Protection of Animals (LID) and the police, and which cannot be relocated anymore.

Re: Fundamental research

The consequences of the implementation of the revised Experiments on Animals Act *(Wet op de dierproeven)*, which entered into force on 18 December 2014, are not yet visible in the NVWA's annual report.

The NCad expects that the centralised assessment of project applications, on which the Central Authority for Scientific Procedures on Animals (CCD) takes decisions, will ensure that the use of animals in general, and more specifically cats and dogs in the context of this opinion, will be carefully considered.

The NCad believes that the use of new technologies and non-invasive techniques should be encouraged and expects that the implementation of these technologies will reduce the use of animal testing, including the use of cats and dogs.

Furthermore, the NCad believes that the exchange of tissue, organs and blood should be encouraged so that optimum use can be made of an animal by enabling Utrecht University to play a central role given that it already has experience in this area.

Re: Communication

The NCad recommends that the following matters be included in communications:

- The proportion of cats and dogs used in animal testing (0.2% of all animal tests).
- For which research purposes cats and dogs are used.
- The efforts undertaken by researchers and/or education institutes to reduce tests with cats and dogs.
- The efforts undertaken by the MEB in the area of research required by law.
- What the Animal Welfare bodies (IvDs), the Animal Experiments Committees (DECs) and the CCD do in assessing advice concerning research or project proposals involving the use of cats and dogs.

Moreover, the NCad wishes to highlight the importance of communicating the proportion of, and benefits and need for tests on cats and dogs to the public.

Contents

1 Introduction and Context

In 2014, 621,027 animal procedures were registered in the Netherlands, of which 1,098 were conducted on dogs and 244 on cats. Of these, the vast majority were conducted within teaching activities and for the development of medicines and vaccines for cats and dogs. Although in 2014, the percentage of procedures on cats and dogs accounted for approximately 0.2% of the total number of animal procedures, the use of cats and dogs in animal procedures remains a subject of social debate and a target of demonstrations.

In 2011, the Dutch House of Representatives received a citizens' initiative – signed by 57,000 people – to ban the use of cats and dogs in animal procedures. The Dutch House of Representatives took this citizens' initiative into consideration and asked the Minister responsible for this issue whether and how a ban on the use of cats and dogs for scientific and educational purposes could be put into effect.

On 31 March 2015, the Dutch Minister of Agriculture sent a letter to the NCad stating that she was aware of the social objections to procedures on cats and dogs. However, a ban on procedures on cats and dogs would constitute a national limitation that goes further than EU Directive 2010/63/EU. Therefore, such a ban would only be legally feasible if European legislation was changed in this regard. The Minister of Agriculture emphasised that for all animal procedures conducted under the Experiments on Animals Act *(Wet op de dierproeven)*, a project licence must be issued by the CCD (Central Authority for Scientific Procedures on Animals), for which an ethics assessment must be conducted to determine whether the objective of the procedure justifies the use of the animals, including cats and dogs. Nonetheless, the Minister of Agriculture said she wanted to examine whether legal frameworks existed to further address the social objections to animal procedures involving cats and dogs.

In the period after 2003, the number of procedures on cats and dogs seemed to decline, although the number has been rising again since 2011 (see Figure 1). The main objectives for the use of cats and dogs are displayed in Figures 2a and 2b.

Figure 1: Total number of animal procedures involving cats and dogs (2003-2013).

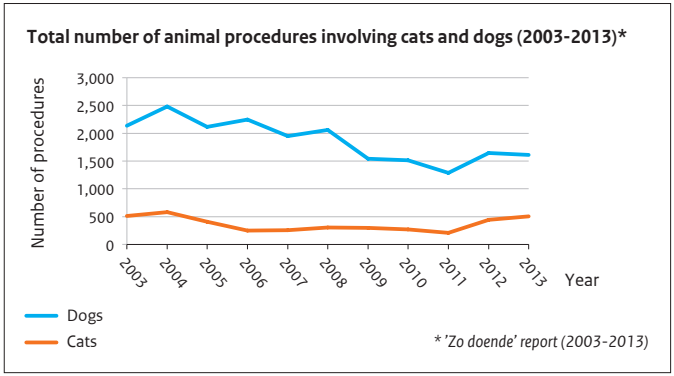


Figure 2a: Total number of procedures on dogs for specific main objectives (2003-2013).

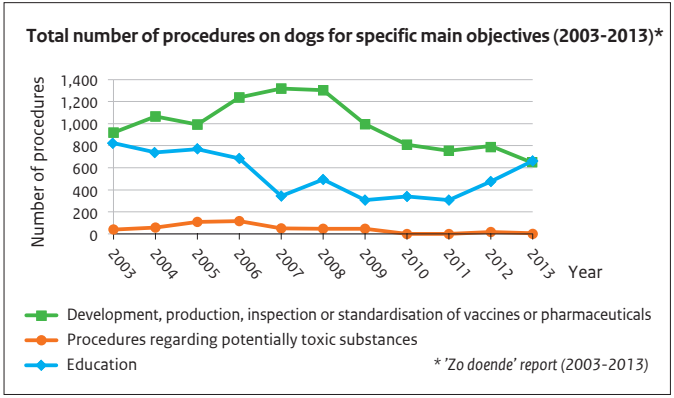
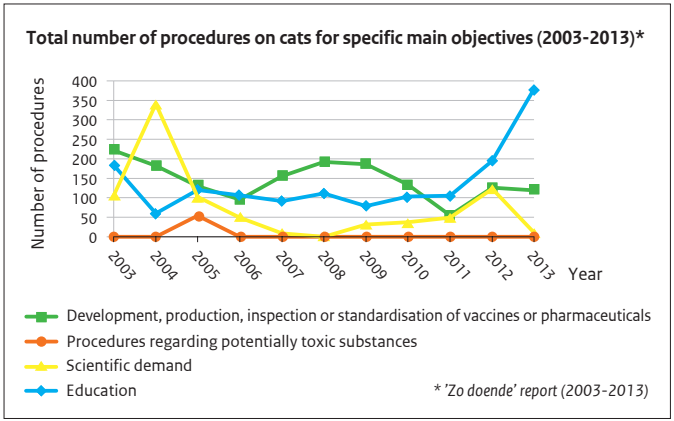


Figure 2b: Total number of procedures on cats for specific main objectives (2003-2013).



The NVWA attributes this increase in the use of cats and dogs for educational purposes to a different interpretation of the definition of animal procedures having resulted in increased registration of such tests.[2]

Due to the adjusted legislation in the field of animal procedures and laboratory animals, a different registration system has applied since 2014, and therefore the number of animal procedures performed from this moment onwards cannot be directly compared to the numbers from the previous years. These figures have therefore not been included in the above figures.

In 2014, 1,098 procedures were conducted on dogs and 244 on cats. For these purposes, 725 dogs and 76 cats were used. For a detailed overview, see Appendix 1.

Analysis of the 2014 *'Zo Doende'* report shows that these cats and dogs were used for various purposes, including for research required by law (51.1% of procedures with dogs and 15.6% of procedures with cats). For an overview, see Figures 4a and 4b.

[2] The definition of an animal procedure includes all activities involving an animal for a particular purpose, when there is a recognised risk of distress. If multiple activities are carried out on an animal, then this is defined as a single animal procedure. The term 'reuse' signifies that the same animal is used for a particular activity performed for the selected objective when a different animal could have been used. The definition of a unit and who will define it is subject to debate (every month, year, lab session). In recent years, the different interpretations have resulted in variation in the numbers of animal procedures. In addition, the new registration system includes a new definition with a lower limit of 'performance of an injection'.

Figure 4a: Percentages of the total number of dogs used for the various objectives in 2014.

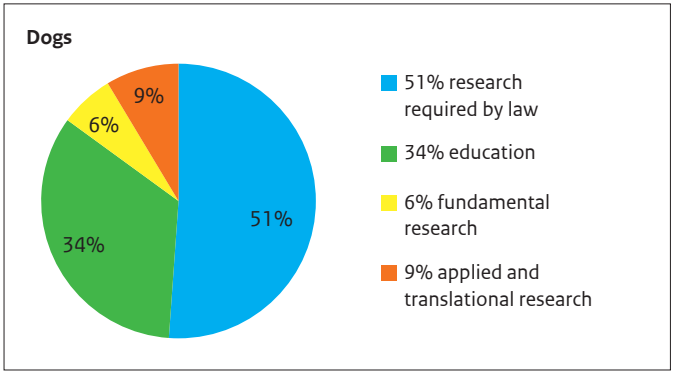
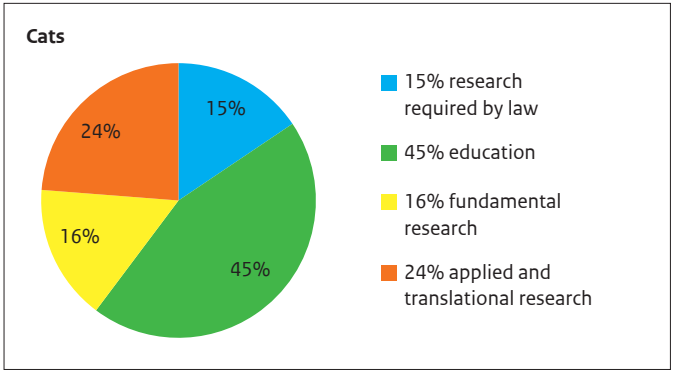


Figure 4b: Percentages of the total number of cats used for the various objectives in 2014.



The legal obligation for these procedures stems from EU legislation and legislation in non-EU Member States.

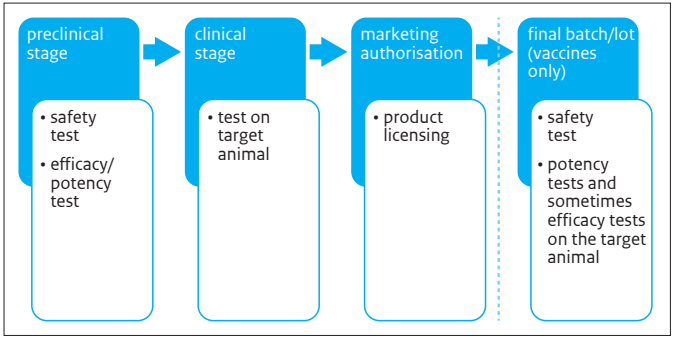
Dogs were predominantly used for the safety assessment of medicines for humans.[3] Cats were not used for this purpose. Both cats and dogs were used at various stages of the development of animal medicines for the target species in question (cats and dogs).[4]

[3] 82.4% of the dogs used in research required by law were used for the development of human medicine. The other dogs were used to research medicines for dogs and residues of these medicines. This related to quality-control research (batch testing) required by law.

[4] 89.5% of the cats used for research required by law were used for the research of medicines for cats and residues of these medicines.

Below is a diagram of the various tests of medicines, including vaccines, for which cats and dogs are used as laboratory animals.

The final batch/lot[5] is tested[6] by the manufacturer. However, the (monitoring) authority is entitled to repeat the tests. Release can be conducted for individual EU Member States or via a central release procedure. In the latter event, the release is conducted by the monitoring authority in one of the Member States. This will subsequently be valid in the other EU Member States.



Institutes in the Netherlands in which procedures on cats and dogs are conducted include academic centres, academic medical centres, institutes for paraveterinary training, pharmaceutical companies, research organisations and contract-research organisations.

Cats and dogs are both used for educational purposes such as surgery practical sessions and for practising invasive procedures such as drawing blood. In 2014, this accounted for 33.9% of the dogs used and 44.6% of the cats.

In 2014, 6.4% of the dogs and 16% of the cats were used for fundamental research.[7] 8.6% of the dogs and 23.8% of the cats were used for applied and translational research.[8] Amongst other matters, this involved research into genetic defects in dogs, taste tests and behavioural research.

[5] The term 'batch' is used if the vaccines are used for veterinary purposes, while 'lot' is used if the vaccines are for human usage. A batch or lot is the collection of ampoules filled during a production run.

[6] A 'potency test' is when the effects of a medicine are tested on a surrogate model and an 'efficacy test' is when the effects of a medicine are tested on the target animal.

[7] The procedures with dogs were categorised as FW/Circulatory and lymphoid organs and FW/Urogenital system. The procedures with cats were categorised as FW/Endocrinology and metabolism and FW/Ethology, animal behaviour and animal biology.

[8] The procedures with dogs were categorised as TO/Animal illnesses and disorders and TO/Human muscular and skeletal disorders. The procedures with cats were categorised as FW/Animal welfare and FW/Animal illnesses and disorders.

2 Request for an opinion

The Minister of Agriculture asked the NCad to develop a national strategy in which intensive cooperation between knowledge institutes – separate from the ethics assessments by the CCD – minimises the number of cats and dogs used in animal procedures. The NCad was also asked to devise an accompanying strategy for public communication. In this regard, it was asked what clients of research on cats and dogs can do to help develop 3R alternatives.

The Minister of Agriculture wants the opinion to be provided in the form of an exploratory study in which both quick wins and possible scenarios are illustrated.

3 Opinion

3.1 Research required by law

1. The European Pharmacopoeia (EP) has abolished the batch/lot safety test for virtually all veterinary vaccines. Sometimes, the test must be conducted if monitoring authorities from non-EU Member States of the EU request it. The NCad advises the Minister of Agriculture to ask the Medicines Evaluation Board (MEB) to make efforts to persuade countries outside the EU to drop the legal requirement to conduct the safety test. As the Minister of Health, Welfare and Sport is the client of the MEB with regard to human medicine, the Minister of Agriculture will also have to consult her. In addition, the Minister of Agriculture can ask the manufacturers to initiate discussions with the supervisory authorities in third countries about waiving the safety test. According to current production figures, this will reduce the number of dogs required for animal procedures by 50 per year.

2. At the European level, the NCad advises the Minister of Agriculture to instruct the MEB to strive for the reduction of routine retesting of batches/lots on cats and dogs (amongst other animals) by the monitoring authorities in individual EU Member States. As standard, the quality of batches/lots of vaccines is tested by the manufacturer. As the vaccines are used for both veterinary and human use, the Minister of Agriculture must also consult the Minister of Health, Welfare and Sport.

3. The NCad recommends that via the MEB, the Minister of Agriculture should ensure that the research into a non-animal testing-based method for the release of batches/lots of vaccines (the consistency approach) is supported by the supervisory authorities in Europe. This is another issue for which the Minister of Agriculture must consult the Minister of Health, Welfare and Sport.

4. The NCad advises the Minister of Agriculture to encourage implementing bodies and regulators to exchange data on the use of animal models and alternative methods and, in the light of its role as a monitoring body, to ask the MEB to call applicants to account if they have failed to use alternative methods even though these were available. For this purpose, see also the NCad's opinion entitled 'Indicators, management and use of data for monitoring use of laboratory animals and 3R alternatives, part 2'. This is another issue for which the Minister of Agriculture must consult the Minister of Health, Welfare and Sport.

3.2 Education

1. The NCad advises the Minister of Agriculture to seek assistance from the AOC Council to abolish the use of cats and dogs as laboratory animals in all paraveterinary training programmes[9], without compromising the quality of these programmes.

[9] Paraveterinary worker: assistant of veterinary physician. Carries out a number of veterinary procedures.

2. The NCad advises the Minister of Agriculture to assign Utrecht University a facilitative and coordinating role in the conduct of procedures that do not require the use of live cats and dogs. In the Netherlands, there is a range of possibilities to pursue a paraveterinary programme at the MBO (secondary vocational education) and HBO (higher professional education) levels, although the content of the programmes differs somewhat between the various institutes. In some institutes, techniques are taught using living animals, although some institutes make use of alternative methods only. Both types of training result in the same qualification being awarded upon completion of the programme.

   Given Utrecht University's experience in applying alternative methods during practical sessions, it can play a facilitative role in getting these institutes to make the transition from live animals to available and equivalent alternatives.

3. The NCad advises the Minister of Agriculture to realise optimal use of donor cards for pets[10] by instructing the NVWA to provide a donor card to all impounded cats and dogs before these animals are offered for relocation, and by ensuring that all shelter animals are also provided with donor cards in the future. In addition, the NCad advises that an appeal should be issued to animal protection organisations, veterinary practices, breeders and organisations that use dogs (such as the police) to promote the donor card and to donate deceased animals. This will mean that no more cats or dogs will need to die for the purposes of anatomy practice. This would spare approximately 30 laboratory animals per year.

4. The NCad advises the Minister of Agriculture to facilitate wider use of plastinated specimens[11]. This can partly be realised by making cats and dogs available that are confiscated by the NVWA, the LID and the police and which cannot be relocated anymore (see also 3.2.2 above).

3.3 Fundamental research/ applied and translational research

As the problem description for this opinion is largely based on the figures from 2014, the consequences of the implementation of the updated Experiments on Animals Act *(Wet op de dierproeven)*, which came into force on 18 December 2014, are not yet visible in these figures.

The NCad expects that the centralised assessment of project applications, on which the Central Authority for Scientific Procedures on Animals (CCD) takes decisions, will ensure that the use of animals in general, and more specifically cats and dogs in the context of this opinion, will be carefully considered. During substantiation by means of a synthesis of evidence, for example, specific attention will be paid to the species of the laboratory animal and the necessity of using it.

[10] Donor cards for animals are comparable to donor cards for humans. After its death, the animal's body is made available for scientific research.

[11] Plastination is a preservation technique for (amongst others) biological material that provides preserved specimens with extremely natural shapes and colours and practically unlimited storage life.

1. *Stimulate the use of new technologies and non-invasive techniques.*

It is expected that the implementation of these technologies will result in a reduction in the use of animal procedures, including procedures on cats and dogs. The NCad is currently working on an opinion entitled 'Phase-out timetable', which will discuss new technologies and their implementation.

2. *Stimulate the exchange of tissue, organs and blood to enable optimal use of individual animals by assigning a central role in this process to Utrecht University.*

At the moment, the exchange of cat and dog tissues is conducted by means of personal contacts. Utrecht University already has experience in the area of tissue exchange. The NCad advises that Utrecht University should be assigned a central role in the exchange of tissue, blood and organs in the event that cat and dog tissues are requested.

3.4 Communication

Permission for any animal procedure is only granted if no alternatives are available and if the use of laboratory animals has been deemed acceptable following an ethics assessment. This is equally the case for procedures on cats and dogs. Upon request by the Minister of Agriculture, the NCad has examined areas in which the use of these species can be limited to an even greater extent than is prescribed by current legislation. A number of recommendations in this regard can be found in the preceding text.

The NCad also advises the Minister of Agriculture to include the following matters in communication regarding cats and dogs:

- the scale of the procedures (0.2% of all animal procedures are conducted on cats and dogs)
- the purposes for which cats and dogs are being used in research
- the efforts being made by research and/or education institutes to reduce tests with cats and dogs
- the efforts being undertaken by the MEB in the area of research required by law
- the efforts being made by IvDs, DECs and the CCD to assess advice concerning research or project proposals that involve the use of cats and dogs

The actors who will put this opinion into practice are:

- scientific research implementing bodies and clients
- the vocational education, higher education and research university sectors
- the MEB

In addition, the NCad wishes to highlight the importance of communicating to the public the proportion of and the benefits and need for tests on cats and dogs, and promoting transparency within the chain regarding the efforts being made to reduce the number of animal procedures.

4 Substantiation

4.1 Research required by law

During the formulation of this opinion, the NCad observed that national and international legislation in the field of research required by law is diverse, complex and enables multiple interpretations. In addition, it is difficult to gain effective insight into the package of requirements set by registration authorities with regard to statutorily required testing of medicines and vaccines.

With regard to the use of cats and dogs in animal procedures, the research required by law relates to safety and efficacy tests, an obligation imposed by both EU legislation and legislation in non-EU Member States. In 2014, 584 animal procedures required by law were carried out (546 on dogs and 38 on cats). It is not possible to ascertain how many extra procedures were required in order to introduce particular medications to the markets of non-EU countries.

Cats are predominantly used for statutorily required research into medicines for cats and the residues of these medicines.

Of the 546 procedures conducted on dogs, 450 were conducted for the purposes of toxicity research and other safety research required by law, such as safety tests relating to human medicines. The other 96 procedures involving dogs were conducted as part of research into medicines for dogs and the residues of these medicines. These were statutorily required quality-control tests.

1. *Instruct the MEB to undertake efforts to have the legal requirement for safety tests waived outside Europe as well*

In the Netherlands, the pharmaceutical industry only uses cats and dogs as laboratory animals in a few locations. These cats and dogs are subjected to tests investigating the safety of vaccines. By testing four vaccines on a dog rather than one, 75% fewer dogs can be used than was the case ten years ago. According to a company that uses this method, the distress caused by these kinds of safety tests is described as minimal. In the event of a systematic reaction, the four vaccines are tested in individual animals. However, this rarely happens.

Batch-safety tests are conducted on every batch in accordance with the above method. In addition, the production capacity is decisive in determining the batch size. Within the EU, batch-safety tests are being increasingly waived as the production process has been optimised to such an extent that routine testing is no longer necessary for tests such as these. For this reason, the European Pharmacopoeia has recently decided to scrap the requirement to conduct safety tests on every batch. However, a number of non-EU countries still require batch-safety testing, such as Australia and Japan. The CCD does not automatically accept the argument that non-EU countries require this test. In order to accept a deviation from European best practices, the CCD must be convinced that the country in question has a substantial market interest or other interest – as well as convincing evidence for said interest – in making the use of cats or dogs a mandatory requirement, even following discussion of alternative and equivalent methods.[12]

[12] The EPAA has taken the initiative to harmonise the waiving of the safety tests and has set up a Biologicals working group for this purpose, which is currently organising international workshops for the purpose of expanding this waiver to the US and Asia.

In addition, in accordance with the TTIP (Transatlantic Trade and Investment Partnership) treaty, harmonisation of approval requirements must be agreed between the various countries involved.[13]

2. *Instruct the MEB to make efforts to reduce routine retesting of vaccines at the European level.*

Amongst other matters, the European Pharmacopoeia prescribes the quality requirements for pharmaceutical end products. This relates to medicines that have already been registered for human and veterinary use but still require testing. The use of cats and dogs is only prescribed for monographs researching vaccines for cats and dogs, primarily for safety research. This means that in principle, these kinds of products are tested on animals multiple times: during the development stage and as a final check of every batch produced[14], with the latter test being conducted by the manufacturer and possibly also retested by a monitoring authority.

3. *Instruct the MEB to promote the implementation of the consistency approach.*

If production is being conducted in line with Good Manufacturing Practice (GMP) guidelines and the consistency of the production process is monitored via non-animal testing methods, then batch testing on animals is unnecessary. The applicability of this approach, known as the consistency approach, is currently being established in an extensive European project. The NCad expects that this approach will result in a significant reduction in the use of animals, including cats and dogs, and the NCad advises the Minister of Agriculture to instruct the MEB to promote the implementation of the consistency approach.

4. *Promote data exchange between implementing bodies and regulators during the development of medicines and remind the MEB of their duty to encourage the use of alternative methods whenever possible.*

The guidelines regarding medicines for humans and registration of these medicines do not explicitly prescribe the use of cats and dogs. In general, the use of a second species of mammal in addition to a rodent is prescribed. The decision regarding the second species is made based on the purpose of the study and/or the characteristics of the species in order to maximise the likelihood that the test is translatable to humans. For example, mini pigs are particularly used for research in which skin permeability is a decisive factor.

In 2014, 450 procedures required by law were carried out on dogs (and 0 on cats) within the scope of research into medicines for human use. Dogs were used in five safety-testing procedures relating to the regulated production of blood products. The other 445 procedures on dogs predominantly researched carcinogenicity in repeated-dose studies.

[13] 3.2.6. Medicines
- Enable the exchange of confidential information to facilitate more collective assessment of new medicines.
- Harmonisation of the approval requirements for 'biosimilar medicines': products that are almost identical to biological medicines that have already been licensed.
- Streamlining of licensing systems for generic medicines.
- Cooperation to adjust international guidelines for the testing of paediatric medicines.

[14] According to the European Pharmacopoeia, the safety test is no longer necessary for the routine release of medications.

The choice of a particular animal model is also made based on past experience of what the registration authorities will accept. Based on the requirement that the best animal model must be selected and taking technological progress into account, the selection of an animal model must be made based on the very latest scientific knowledge. If there is a habit to select a particular animal model (e.g. cats or dogs), then the registration authorities can take this opportunity to encourage reconsideration of this choice.

At the moment, an animal-model shift is in progress from dogs to mini pigs. The NCad does not want the efforts to reduce procedures on dogs to result in animal procedures usually conducted on dogs being carried out on mini pigs instead, unless the mini pig is a better animal model for the particular research question. With regard to finding alternative models, the NCad would prefer to see effort and time invested in reducing duplications and implementing in-vitro models.
After all, the regulatory bodies are able to actively maintain contact with companies regarding the selected animal model in order to reduce duplications and collectively examine whether *in-vitro* or – as a second choice – *in-vivo* alternatives are available. The continued collection and sharing of data plays a crucial role in this process.

4.2 Education

1. *Appeal to the AOC Council to abolish the use of live cats and dogs as laboratory animals during paraveterinary programmes.*

In the Netherlands, there is a range of possibilities to pursue a paraveterinary programme at the MBO (secondary vocational education) and HBO (higher professional education) levels. The content of these programmes differs somewhat between the various institutes. At some institutes, techniques are learned using live animals, which by law constitute animal procedures. Other institutes use no live animals, only alternative methods. Both types of training result in the same qualification being awarded upon completion of the programme.

The NCad does not favour having these different approaches and thinks that the AOC Council could play a key role in abolishing the use of live cats and dogs as laboratory animals during paraveterinary programmes. In compliance with the law, the NCad believes that if alternative approaches are available, then these must be used.

2. *Assign Utrecht University a facilitative and coordinating role via the implementation of skills labs.*

Utrecht University has extensive experience with skills labs, in which people can practice a variety of techniques without the need to use live animals. At the moment, a number of programmes are taking advantage of this opportunity. To get more programmes to use the skills labs, Utrecht University can play a facilitative and coordinating role.

Considering the opportunities that are already available, the NCad does not believe it is necessary for live cats and dogs to be used as laboratory animals during paraveterinary training.

3. Ensure optimal use of donor cards.

In 2014, 501 animal procedures were conducted for educational purposes (392 on dogs and 109 on cats). In 319 of these procedures, animals were used by academic institutes (227 on dogs, 92 on cats). Table 27 from the 2014 Zo Doende report showed that these were conducted exclusively by Utrecht University. The other licence holders conducted 182 animal procedures for educational purposes (165 on dogs, 17 on cats).

In the past, animals were killed at Utrecht University for use in the Anatomy and Surgery courses taken by students of Medicine, Biomedical Sciences and Veterinary Science. At the moment, the donor card scheme obtains 300 cadavers per year, primarily from animal shelters and veterinary practices. That is more than enough for the surgery practical sessions, although it is only half of the number of fresh cadavers required for the anatomy classes.

The cats and dogs confiscated by the NVWA are offered to private individuals by animal shelters and pounds. For this kind of service, donor cards should be made compulsory. An appeal should also be made to other institutes, such as the police, hunting associations, veterinary practices and animal protection organisations to promote donor cards.

4. Facilitate optimal use of plastinated specimens.

Within educational institutes, training and practice can be conducted using plastinated specimens. However, it has proved difficult to obtain animals viable for preservation. This is because the cadavers must be delivered to the mortuary within three hours of death. The expertise and routine required for plastination is currently only available at the Faculty of Veterinary Medicine at Utrecht University. Due to the relatively short viability period (three hours) and the concentration of expertise in Utrecht, the effect of the donor card scheme is currently limited to this region. However, due to the rapid developments in the field of preservation techniques, older cadavers may be viable for preservation in the near future. It may also be possible to introduce the technique in multiple places, enabling plastination to be conducted elsewhere.

Plastinated specimens can last for 10 to 20 years depending on the nature and intensity of use. By using plastinated specimens, both education institutes and research centres that train staff can reduce the required number of cats and dogs. At the moment, there are no financial obstacles involved in the use of plastinated specimens, as they are offered by Utrecht University at cost price.

In order to obtain a sufficient number of both cadavers and plastinated specimens, pets that are euthanised for health and welfare reasons should be issued with donor cards in order to satisfy the needs of the education sector.

4.3 Fundamental research/ applied and translational research

In 2014, fundamental scientific research involving the use of cats and dogs was performed only within academic institutes. A total of 107 animals were used for fundamental research, of which 68 were dogs and 39 were cats.

All of the dogs were used for fundamental scientific research on behalf of humans; 21 cats were used for the same purpose. The other 18 cats were used for fundamental scientific research in the field of ethology, animal behaviour and animal biology.

Also in 2014, a total of 150 animal procedures was conducted within the scope of applied and translational research; 83 of these (33 on dogs and 50 on cats) were conducted by academic institutes and 67 (59 on dogs, 8 on cats) by other licence holders.

1. *Stimulate the use of new technologies and non-invasive techniques.*

In the past ten years, various research groups have conducted studies from a variety of perspectives to investigate opportunities for innovation that require no laboratory animals, as well as the domains, technologies and strategies that offer the greatest opportunities in this regard. Likely areas include imaging, omics telemetry, systems biology, organ-on-a-chip and organoids. It is expected that the implementation of these technologies will result in a reduction in the use of animal procedures involving cats and dogs.

2. *Stimulate the exchange of tissue, organs and blood to enable optimal use of each animal.*

In addition to live animals, tissue, blood and organs are also required in order to perform tests. Both universities and other research institutes have a need for certain types of tissue, such as skin for determining in-vitro dermal absorption. Specific animals are not obtained for these purposes. If information is available regarding material that institutes have at their disposal, then this will promote more effective use of animals, which could reduce the required number of laboratory animals.

Due to Utrecht University's experience in exchanging tissue, it can play a central role in the process of requesting cat and dog tissue. In this way, optimal use of tissue is promoted, and both universities and research institutes can better coordinate supply and demand.

4.4 Communication

The recommendations from this opinion by the NCad must be brought to the attention of all stakeholders involved in the use of cats and dogs for scientific research and education in order to promote its implementation. When clients, implementing bodies, the education sector (research universities, higher education and vocational education) and the MEB make their contributions visible to a larger audience, they demonstrate that the greatest of care is taken with regard to using cats and dogs in research. This is done not only to comply with the law, but also stems from proactive efforts by the profession and the MEB to address society's concerns regarding this issue. For people outside the field of animal procedures, it is usually

difficult to gain insight into the scale and purpose of the use of cats and dogs for research. It is important that all parties are open about all matters. The basic premise must be to account for all actions performed and ensure that all parties support them. This is in line with the Openness Agreement for Animal Procedures *(Convenant Openheid Dierproeven)* that the Royal Netherlands Academy of Arts and Sciences (KNAW), the Association of Universities in the Netherlands (VSNU) and the Dutch Federation of University Medical Centres (NFU) offered to the Dutch House of Representatives' Parliamentary Standing Committee for Health, Welfare and Sport on 10 June 2008. The purpose of the code is to ensure compulsory openness and dialogue regarding animal procedures by means of self-regulation.

The NCad believes that openness provides the right context, which is important for the debate on the use of cats and dogs. This does not necessarily have to result in opponents of animal procedures changing their minds; the purpose is to give the general public insight into the proportion of and the benefits and need for animal procedures involving cats and dogs, as well as the efforts being made to reduce the number of such procedures.

Specific points for attention for each actor:

- Clients and implementing bodies: Focus on making the reasons for the need to use cats and dogs more transparent. This can be done by focusing more attention on, for example, non-technical overviews on the CCD website when a licence is issued. For this purpose, the Synthesis of Evidence, which must be included in the project application, must be emphasised within the NTS. The importance of this could be underlined in communication from the government and affiliated parties such as the NCad and CCD.
- Research universities, higher education and vocational education: Focus on exchanging best practices and on carefully examining whether procedures involving live animals are absolutely necessary. In this communication, cases in which cats and dogs are no longer used can be cited as inspirational examples.
- MEB: Focus on the role that the MEB can play in harmonising legal obligations with regard to procedures involving cats and dogs. The MEB could also include information on this issue on its website.

Annex 1 *Overview of Licence Holders*

In 2014, nine licence holders, of which five were academic institutes, performed procedures on cats and/or dogs.

Procedures on	Dogs	Cats	Total
1.*	45		45
Fundamental scientific research	37		37
Applied and translational research	8		8
2.*		58	58
Fundamental scientific research		8	8
Applied and translational research		50	50
3.*	271	113	384
Fundamental scientific research	19	21	40
Education	227	92	319
Applied and translational research	25		25
4.*		10	10
Fundamental scientific research		10	10
5.*	12		12
Fundamental scientific research	12		12
6.	143		143
Education	143		143
7.	154	33	187
Legislation, TOX/WV, quality control	96	8	104
Education	22	17	39
Applied and translational research	36	8	44
8.	23		23
Applied and translational research	23		23
9.	450	30	480
Legislation, TOX/WV, regulated production	5		5
Legislation, TOX/WV, other	445	30	475

** = Academic institute (6 is not an academic institute, but does use dogs exclusively for educational purposes.)*

Annex 2 *Recommendations arising from the consultation of community groups*

On 24 March, the consultation of community groups was conducted in The Hague. During this meeting, the following organisations put forward their opinions:

- NVP
- Train
- NV DEC
- IvD-platform
- NFU
- WILresearch

The NCad reviewed the sound recordings from the meeting and summarised the recommendations, which were then submitted to the relevant groups for approval.. The recommendations as approved by the participating organisations are listed by topic below, and each is followed by an indication of whether the particular recommendation was included in the NCad's advisory report. When a recommendation was not included, a brief explanation is provided.

Focus on cats and dogs

NVP	- With regard to quick wins, most of the low-hanging fruit has already been picked. The production process is frequently designed to minimise the number of animals used. *Duly noted* - Researchers do not use cats or dogs if a suitable alternative is available. People are under the impression that cats and dogs are used even if an alternative animal model is available, but this an inaccurate impression and has never been the case. If cats or dogs are used, then this means that no alternative animal model is possible for that particular research question, especially in the case of translational research. *Duly noted*
Train	- You must also take the moral/ethical aspect into account: what would be an acceptable alternative? Is it acceptable to exchange one dog for multiple rabbits or rats? No researcher would use a cat or dog unless it is truly necessary. *Included in opinion: Yes*
NV DEC	- What arguments exist for making an exception in the case of cats and dogs? The special status of cats and dogs has been abolished in this law. *Included in opinion: The request for advice only relates to cats and dogs. The NCad has therefore focused on cats and dogs in this opinion.* - By making a distinction between cats and dogs on the one hand and other animals on the other, the NCad is creating a double standard. *Duly noted*
IvD-platform	- Why focus on cats and dogs? The Experiments on Animals Act *(Wet op de dierproeven)* is based on a European Directive that is in turn based on the intrinsic value of animals. In principle, the intrinsic value of each species is equal. Legally, we are not allowed to discriminate between species. Only non-human primates occupy a special position in the European Directive, and the Commission has obliged itself to engineer a reduction. The Netherlands has not implemented the law that requests attention be paid to other species, so paying special attention now is illogical. *Included in opinion: The request for advice only relates to cats and dogs. The NCad has therefore focused on cats and dogs in this opinion.*
WILresearch	- Limit the number of dogs kept. *Included in opinion: Yes*

Registration authority

NVP	- There is freedom of choice regarding toxicity tests with large animals, but dogs are frequently chosen. Examination could be conducted into why this choice is made. It is possible that what the registration authority finds acceptable could be a factor. If selecting an alternative could result in the registration authority delaying the procedure (and therefore causing extra costs), then this can influence the choice of an animal model or alternative. *Included in opinion: Yes* - Extra pressure can be applied, but you have to be careful when introducing new standards. If someone in the Netherlands says that you cannot produce medicines for Japan because they operate different standards, then this can also have negative side effects such as relocation of the industry or the animal procedure sites. *Included in opinion: Attention was paid to this aspect during formulation of the opinion.*
Train	- The parties that regularly conduct animal procedures must also report this to the Animal Experiments Committee (DEC). The DEC must then critically assess whether a cat or dog is absolutely necessary for this kind of procedure. By this point, this issue must already have been discussed. *Included in opinion: Yes* - If the argument in favour of using a dog is that the application process will take less time, then a change must be made. *Included in opinion: Yes* - Australia and Japan have operated different requirements for years. The government could make efforts to harmonise these requirements. *Included in opinion: Yes*
WILresearch	- Amongst other factors, the choice of animal model is dependent on the test that will be conducted on the animal. *Duly noted* - Acceptance within the registration authority also plays a major role in the choice of the animal model. *Included in opinion: Yes*

Donor cards and plastinated specimens

NVP	- If vets are properly informed about the logistical problems and the requirements with which the animals must comply, then they can play a role in the provision of fresh cadavers. *Included in opinion: Yes*
Train	- It may be possible to realise the required number of fresh cadavers for education by examining conservation techniques. If other conservation methods are available, then time will be a less restrictive factor. *Included in opinion: Yes* - Use of plastinated specimens is made partly for safety reasons. Amongst other reasons, they are used to avoid formalin allergies in students and employees. *Included in opinion: No* - In the past, cooperation with animal shelters to supply fresh cadavers has been very difficult to establish, as even though the animals are dead, the shelter does not want the animals to be dissected. This was a very sensitive issue for them. *Duly noted*
IvD-platform	- The need for frozen cadavers – which are used for practical surgery sessions – can be satisfied. For this purpose, collaboration is being conducted with various veterinary practices in the region. The cadavers used for anatomy training must be fresh. It is therefore necessary that these animals are supplied to the faculty within an hour of euthanasia being conducted. *Duly noted* - Better collaboration with owners and vets within the region in which the donor card scheme is active could help increase the supply of fresh cadavers. *Included in opinion: Yes* Another option for increasing the supply of fresh cadavers is more intensive collaboration with animal shelters in the region. When they euthanise animals, we could use these animals for anatomy training. Supply via these channels is not as high as it could be, so there may be an obstacle that is holding animal shelters back. It would be extremely welcome if the government could make an effort to get animal shelters to cooperate on this initiative. *Included in opinion: Yes* - The donor card scheme has been set up and rolled out in collaboration with the Dutch Society for the Replacement of Animal Testing (Proefdiervrij). Thanks to its donations, we have been able to improve and implement plastination technology. As a result, we have been able to create and supply more material for education. Plastinated specimens can be stored for 10-20 years, and they can be used both for dissection and for the lesson packages provided to students. *Duly noted*

Communication

NVP	- With regard to accommodation, the Netherlands goes much further than the minimum applicable standards. The soft side – playing with and training the animals – is difficult to convey to the public. *Duly noted*
Train	- The method for registering the use of laboratory animals in fields such as education results in confusion, as it seems that more cats and dogs are used for educational purposes than is actually the case. These animals usually function as laboratory animals for years, but have to be repeatedly and separately registered. For example, one dog may be used by students hundreds of times for less invasive or non-invasive procedures such as learning to apply bandages. The NVWA should clarify this issue. *Included in opinion: Yes* - It is often not clear to the general public that cats and dogs used in veterinary research are also used as target animals in order to cure illnesses in cats and dogs and to create vaccines for these animals. *Included in opinion: Yes* - Communication with the public is essential. The collection-box organisations play a role in this regard. They don't want to be associated with animal procedures, but at the same time, they fund research that is conducted on animals. *Included in opinion: Yes* - The conditions in which cats and dogs are kept is also an issue that the public finds objectionable. There is an impression that these animals are kept in sub-standard accommodation. In most cases, this is simply not the case, as the accommodation of cats and dogs is subject to European legislation. In contrast, people keeping animals as pets are not subject to this legislation! *Included in opinion: Yes*
NV DEC	- Communicating concrete examples results in greater understanding. *Included in opinion: Yes*

Communication *(continuation)*

IvD-platform	- Due to the amended definition of what constitutes an animal procedure and the different registration method, the number of animal procedures has reduced on paper, while in practice, nothing has changed. *Included in opinion: Yes* - All kinds of parties, including the government and the NVWA, are giving incorrect information. One of the tables in the 2014 'Zo Doende' report is titled 'Number of animals on which animal procedures have been conducted', while the figures in the tables actually represent the number of animal procedures conducted using a particular species. This frequently made error gives the general public the wrong idea about animal procedures. The government has an important responsibility to ensure correct communication. In the past, the number of animals used was 2-3 times fewer than the number of animal procedures performed, but due to the new registration method, this gap has been reduced. *Included in opinion: Yes* - Utrecht University's IvD has a communications officer who conducts both internal and external communication regarding what the IvD does. This communication also includes sensitive subjects such as the use of cats and dogs in animal procedures. In this communication, we clarify our vision on animal procedures in general, explain how we – if necessary and permission has been granted – conduct animal procedures, and address the dilemmas involved in this issue. This is a way of making it clear to society that researchers who conduct animal procedures and all other parties involved are people who want to help solve social problems by preventing diseases and treating patients. *Duly noted*

Other

IvD-platform	- Although reuse can reduce the number of animals used, it can also result in increased distress. The question is therefore what situation does the government prefer: a greater number of laboratory animals with a lower level of distress, or a lesser number of laboratory animals with a higher level of distress? *Duly noted*
NFU	- With regard to the choice of animal model, the researcher is at all times accountable to various bodies, such as the DEC and the CCD. If these bodies approve the selected animal model, then this means that a cat or dog is the most suitable animal model. *Duly noted* - Utrecht University works together with WILresearch If an animal has to be euthanised in Utrecht or at WILresearch, then UU contacts fellow researchers and attempts to make as much material as possible available to as many researchers as possible. This enables more researchers to make use of the animal's tissue. The use of tissue in this way can reduce the number of animal procedures. *Included in opinion: Yes*
WILresearch	- Non-rodent: The choice of animal model also depends on the test in question. Rabbits or mini pigs could also be chosen. *Duly noted*

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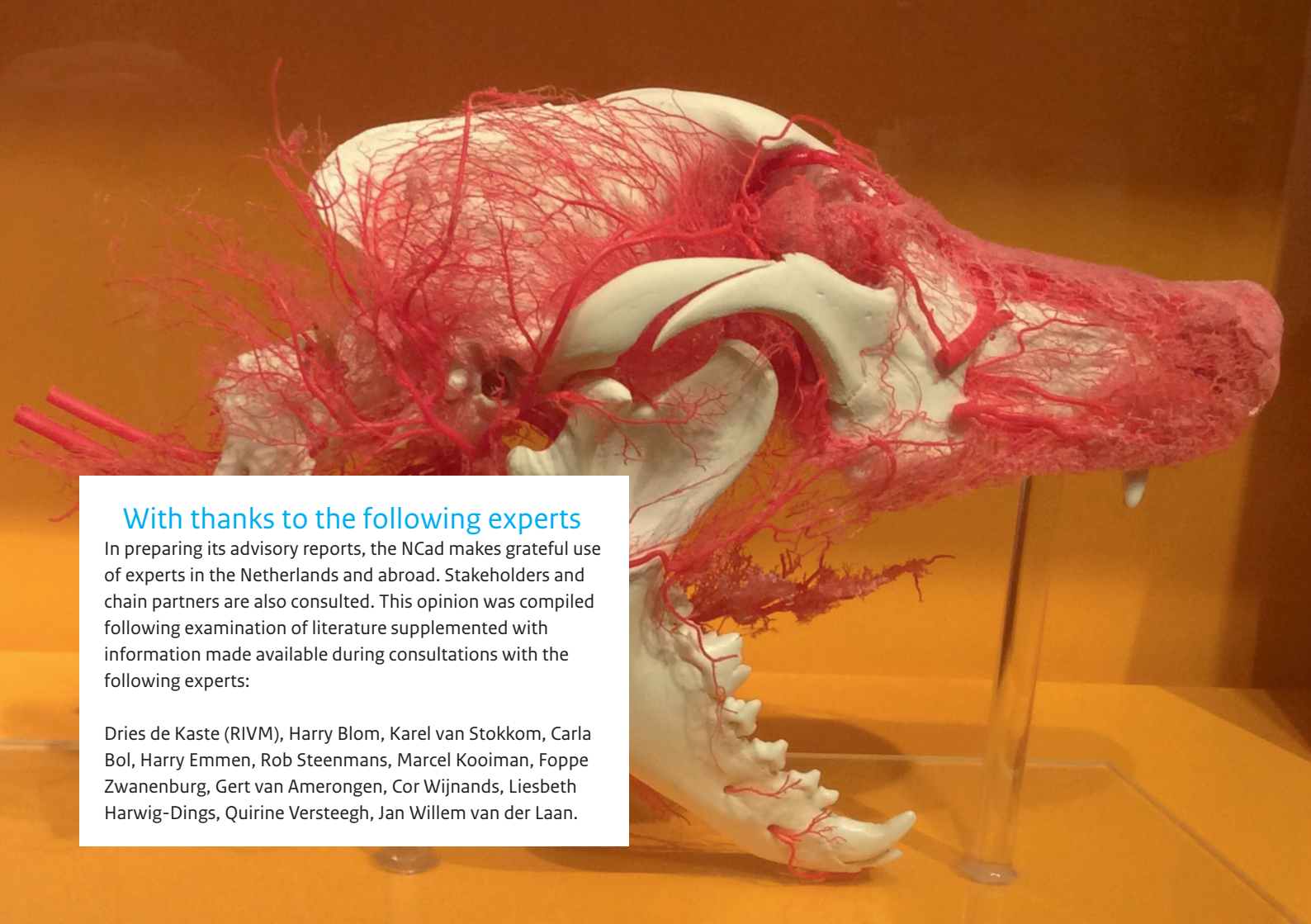

With thanks to the following experts

In preparing its advisory reports, the NCad makes grateful use of experts in the Netherlands and abroad. Stakeholders and chain partners are also consulted. This opinion was compiled following examination of literature supplemented with information made available during consultations with the following experts:

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This is a publication by the NCad (Netherlands National Committee for the Protection of Animals Used for Scientific Purposes).
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Publication date: August 2016
Publication number: 201609
Photos taken by Thomas Dobber, UMC Utrecht

The NCad was appointed for the protection of animals used for scientific purposes and for education. The NCad achieves visible improvements in the Replacement, Reduction and Refinement (3Rs) of animal procedures and the ethical review thereof in order to minimise the use of laboratory animals, both nationally and internationally. The ethical review of animal procedures is of pivotal importance in this regard, as are the 3Rs.