Ambition statement on innovation in higher education

using fewer laboratory animals

Universiteiten *van* Nederland

NFU NEDERLANDSE FEDERATIE VAN UNIVERSITAIR MEDISCHE CENTRA

Content

Ambition statement on innovation in higher education *using fewer laboratory animals*

Management summary

Initiated by the Dutch Government in 2018, the Ministry of Agriculture, Nature and Food Quality has been managing an alliance aimed at accelerating the transition to animal-free innovation. In 2019, both UNL and NFU joined and started a project with an ambition statement aimed at using fewer laboratory animals in Dutch higher education (bachelor/master/postgraduate). UNL and NFU aim for shared responsibility regarding the use of laboratory animals in academic education, a reduction in the usage of these animals in education, and the creation of awareness on this topic among future scholars and professionals.

Dutch law and EU Directive 2010/63/ already state that laboratory animals can only be used in education (and in research) in cases with a convincing scientific justification and only when the objectives cannot be achieved using non-animal-based methods. Recently, the European Parliament called for urgent EU action to accelerate the transition to innovation without the use of laboratory animals in research, regulatory testing and education.

Annually, a total of approximately 9,000 animal experiments are performed in bachelor, master and postgraduate education in The Netherlands. Only a small minority of these experiments are performed in bio-medical education (e.g. medicine, medical biology), where several effective animal-free methods are already available and most institutes demonstrate that similar learning goals are achieved using animal-free methods. Both ethically, as well as legally, the full implementation of animal-free methods should be pursued here. Most animals are used in bio-veterinary education (UU and WUR), where studying animals is the primary focus. In recent years many laboratory animal-free methods have already been developed and implemented in the veterinary and animal sciences curricula. Further integration of simulations and models (skills lab) before approaching live animals and implementing earlier clinical teaching on real animal patients will directly decrease the number of laboratory animals.

In postgraduate education, most animals are used in the Laboratory Animal Science (LAS) courses (approximately 3300 animals per year) for practical training of those who actually perform animal experimentation themselves (approximately 2700 animals), and a minority for skills training of medical professionals. Most of the LAS courses in The Netherlands are organized as postgraduate education, but in a few specific cases they are also as part of a Master's programme. There is the ambition to abolish obligatory LAS courses at Master's level, which is logical, as most students in this phase of their career have not yet decided about their future. The LAS courses consist of a broad theoretical basis and a practical part, usually using live animals, which together lead to the required certification. The suggestion is to modernize the LAS courses by expanding the theoretical part and possibly including animal-free innovations (thereby also making this course more relevant to all biomedical Master's students) resulting in a new format that does not use live laboratory animals at all. The practical part should be made available as a more personalized course, only for those who are going to perform an actual animal experiment.

Further, the learning curve of researchers to perform animal procedures themselves can be avoided in part by transferring the practical animal work to dedicated personnel. Thus, there is a great potential to substantially reduce the laboratory animal usage in postgraduate education by organizing the programs differently.

Many new, animal-free teaching methods and innovations are being developed with great potential. For instance, (digital) models and virtual reality provide a safe and feasible teaching environment. But new teaching models that are already available still aren't being used sufficiently. It appears that where traditional animal use persists, this is most often due to uncertainty about the educational efficacy of humane alternatives and a lack of awareness of existing tools and resources. The outcome of animal-free teaching models should focus on learning goals and benefits, and should no longer be measured against the animal-based method as the traditional gold standard. In recent years, great advancements have been made in the development of new approach methods (NAMs). Higher education must fulfil its role as the driving force behind this technological change and the acquisition of new skills for many professionals.
The 2020 EURL ECVAM (European Centre for the Validation of Alternative Methods) status report on non-animal methods in Science and Regulation concluded that the actual status of educational activities and resources is not optimal. The higher education system has the duty to fill this gap by developing and implementing NAM courses/materials offered to students, researchers and professionals within and outside universities and in co-creation with industry, contract laboratories, and social partners. Funding opportunities for co-creational education projects among universities, universities of applied sciences, societal partners, industry, and public consortia are needed.

The ambition of the university boards to reduce the number of laboratory animals in academic education and favour animal-free methods needs to translate into policy measures.
This will enable deans, vice-deans, and course directors to implement this ambition at faculty, programme and course level. Many of the recommendations made in this document can be realised at this organisational level. Teachers and researchers should be provided with better access to knowledge regarding the development and application of animal-free methods in their daily work. To link all the primary stakeholders, we propose to establish a national "animal-free educational hub". This will be the first educational hub for non-animal testing innovations in the Netherlands and Europe and will therefore take a leading role in the creation and dissemination of knowledge about non-animal testing innovation.

Streefbeeld innovatie in het hoger onderwijs *met minder proefdieren*

Samenvatting

In 2018 heeft het ministerie van Landbouw, Natuur en Voedselkwaliteit, op initiatie van de Nederlandse overheid, een alliantie gevormd om de overgang naar proefdiervrije innovatie te versnellen. In 2019 zijn UNL en NFU aangesloten bij deze alliantie, en zijn deze organisaties een gezamenlijk traject voor een ambitieverklaring naar minder proefdieren in het Nederlandse hoger (bachelor/master/postgraduate) onderwijs gestart. UNL en NFU streven naar een gedeelde verantwoordelijkheid met betrekking tot het gebruik van proefdieren in het academisch onderwijs, een vermindering van het gebruik van proefdieren in het onderwijs en het creëren van bewustzijn over dit onderwerp bij toekomstige wetenschappers en professionals.

In de Nederlandse wet en EU-richtlijn 2010/63 staat dat proefdieren alleen in het onderwijs (en in onderzoek) mogen worden gebruikt bij een overtuigende wetenschappelijke onderbouwing, en alleen als de doelstellingen niet met proefdiervrije methoden kunnen worden bereikt. Onlangs riep het Europees Parlement op tot een EU-actie om de overgang naar innovatie zonder het gebruik van proefdieren in onderzoek, regelgevingstests en onderwijs te versnellen.

In het bachelor-, master- en postacademisch onderwijs in Nederland worden jaarlijks in totaal ongeveer 9.000 dierproeven uitgevoerd. Slechts een kleine minderheid van deze experimenten wordt uitgevoerd in het biomedisch onderwijs (bijv. Geneeskunde, Medische biologie), waar verschillende effectieve diervrije methoden al beschikbaar zijn en de meeste instellingen laten zien dat vergelijkbare leerdoelen met behulp van diervrije methoden kunnen worden bereikt. Binnen deze disciplines moet daarom zowel vanuit ethisch als juridisch perspectief de toepassing van diervrije methoden verder worden doorgezet. De meeste proefdieren worden gebruikt in het bio-veterinair onderwijs (UU en WUR), waar het bestuderen van dieren centraal staat. In de afgelopen jaren zijn er veel proefdiervrije methoden ontwikkeld en geïmplementeerd in de curricula van de veterinaire- en dierwetenschappen. Zo zal bijvoorbeeld het integreren van simulaties en modellen (skills lab) voordat levende dieren worden gebruikt, en het eerder implementeren van klinisch onderwijs op echte dierlijke patiënten, het aantal proefdieren direct verminderen.

In het postacademisch onderwijs worden de meeste dieren gebruikt in de Laboratory Animal Science (LAS) cursussen (ongeveer 3300 dieren), voor praktische training van onderzoekers die daadwerkelijk zelf dierproeven uitvoeren (ongeveer 2700 dieren) en een minderheid voor vaardigheidstraining van medische professionals. De meeste LAS-cursussen in Nederland worden aangeboden als postacademisch onderwijs, maar in enkele specifieke gevallen ook als onderdeel van een masteropleiding. Er is in Nederland een ontwikkeling gaande om de verplichte LAS-cursussen op masterniveau af te schaffen, omdat de meeste studenten in deze fase van hun carrière nog geen beslissing hebben genomen over hun toekomst. De LAS-cursussen bestaan uit een brede theoretische basis en een praktisch gedeelte, meestal met levende dieren, die samen leiden tot de vereiste certificering. In dit streefbeeld wordt voorgesteld om de LAS-cursussen te moderniseren door het theoretische deel uit te breiden en de mogelijkheid om “new approach methodologies” (NAMs) en innovaties op te nemen (waardoor deze cursus ook relevanter wordt

voor alle biomedische masterstudenten), resulterend in een nieuw format dat helemaal geen gebruik maakt van levende proefdieren. Het praktische deel moet alleen beschikbaar worden gesteld in de vorm van een meer gepersonaliseerde cursus voor mensen die een dierproef gaan uitvoeren. Verder kan het leerproces van onderzoekers om zelf dierproeven uit te voeren deels worden vermeden door het in de praktijk werken met dieren over te laten aan gespecialiseerd personeel. Er is dus een groot potentieel om het gebruik van proefdieren in het postdoctorale onderwijs aanzienlijk te verminderen, door trainingsprogramma's anders te organiseren.

Er worden veel nieuwe proefdiervrije onderwijsvormen en innovaties ontwikkeld met veel potentie; (digitale) modellen en virtual reality zorgen bijvoorbeeld voor een veilige en geschikte leeromgeving. Maar nieuwe onderwijsmodellen die al beschikbaar zijn, worden in de praktijk nog steeds onvoldoende gebruikt. Het lijkt erop dat waar traditioneel proefdiergebruik blijft bestaan, dit meestal te wijten is aan onzekerheid over de educatieve effectiviteit van humane alternatieven en een gebrek aan bewustzijn van bestaande middelen en hulpmiddelen. Het resultaat van proefdiervrije onderwijsmodellen moet bekeken worden in het licht van leerdoelen en -voordelen, en niet meer worden afgemeten aan de dierlijke methode als traditionele gouden standaard. De afgelopen jaren is er een grote vooruitgang geboekt in de ontwikkeling van zogenaamde new approach methodologieën (NAMs). Het hoger onderwijs moet een rol vervullen als drijvende kracht achter deze technologische verandering en het verwerven van nieuwe vaardigheden voor veel professionals.

In het EURL European Centre for the Validation of Alternative Methods (ECVAM)-statusrapport 2020 over dierproefvrije methoden in Wetenschap en Verordening werd geconcludeerd dat de feitelijke status van educatieve activiteiten en middelen niet optimaal is. Het hoger onderwijssysteem heeft de plicht om deze kloof te dichten bij het ontwikkelen en implementeren van NAM-cursussen en -materialen die worden aangeboden aan studenten, onderzoekers en professionals binnen en buiten universiteiten en in co-creatie met het bedrijfsleven en sociale partners. Er zijn financieringsmogelijkheden nodig voor co-creatie van onderwijsprojecten tussen universiteiten, hogescholen, maatschappelijke partners, het bedrijfsleven en publieke consortia.

De ambitie van de universiteitsbesturen om het aantal proefdieren in het (post)academisch onderwijs te verminderen en diervrije methoden te bevorderen, moet zich vertalen in beleidsmaatregelen. Dit stelt decanen, vicedecanen en cursusdirecteuren in staat om deze ambitie op faculteits-, opleidings- en cursusniveau te implementeren. Veel van de aanbevelingen in dit streefbeeld kunnen op organisatieniveau worden gerealiseerd. Docenten en onderzoekers moeten beter toegang krijgen tot kennis over de ontwikkeling en toepassing van proefdiervrije methoden in hun dagelijks werk. Om alle primaire stakeholders met elkaar te verbinden, wordt voorgesteldom een nationale "proefdiervrije educatieve hub" op te richten. Dit wordt de eerste educatieve hub voor proefdiervrije innovaties in Nederland en Europa, waardoor deze hub in het creëren en verspreiden van kennis op dit gebied een leidende rol zal spelen.

1. Introduction

1.1. Background and aims

Since 2019, VSNU and NFU have been partners in the Dutch national TPI ('Transitie Proefdiervrije Innovatie' – Transition to Laboratory Animal-Free Innovation) programme and committed to preparing a target image of animal-free innovation in education, particularly focused at academia (teaching Bachelor's and Master's, as well as postgraduate courses).

Laboratory animals in education and training are being used in:
1. Bachelor's and Master's programmes in (bio)medicine, biology, dentistry, neuropsychology, veterinary medicine and animal sciences, to improve and disseminate knowledge, in practical teaching and the development of new techniques.
2. Postgraduate education for scholars (including PhD students) and professionals, such as medical doctors, veterinarians and others, to teach new and/ or more advanced (bio)medical techniques, including training of researchers who need to use animals in their experiments.
3. Practical teaching in MBO/HBO (secondary vocational and higher professional education), such as to bio-technicians, para-veterinarians, etc.

This target image will focus on Bachelor's and Master's programmes and at postgraduate education in academia (1 and 2). For the practical teaching in MBO/HBO, a separate target image will be prepared.

The aims of this target image are:
1. To pursue a shared and mutual responsibility in animal-free innovation, and a 3R approach to the use of experimental animals in academic education.
2. To reduce the usage of experimental animals in (post)-academic education as much as possible whilst increasing, or at least retaining, the current level of quality.
3. To increase future scholars' and professionals' awareness of the use of laboratory animals in education.

1.2. Approach

The VSNU and NFU installed a steering group chaired by prof.dr. Wouter Dhert (VSNU, representative of VSNU in the TPI core team), with members: prof.dr. Hans van Leeuwen (until September 2021), who was succeeded by prof.dr. Annemie Schols as of September 2021 (NFU, representative of NFU in the TPI core team) and prof.dr. Merel Ritskes-Hoitinga (representative of VSNU in the TPI transition team), supported by policy officers, Sophie Dings (for VSNU) and Marjo Knapen and Dov Ballak (for NFU).

A working group covering academic and postgraduate education, chaired by prof.dr. Daniela Salvatori (Utrecht University) was installed. Members of the working group represented the participating universities and the chair/secretary of the working group consulted several experts in the field of image, on an individual basis.

Members of the working group represented the participating universities:

Rob Steenmans (Wageningen Universiteit)
Tineke Coenen (Leids Universitair Medisch Centrum) Martje
Fentener Van Vlissingen (Erasmus Medisch Centrum) Peter
Olinga (Rijksuniversiteit Groningen)
Hans Savelberg (Maastricht Universiteit)
Jolanda van der Velden (Amsterdam UMC)
Pieter Verbost (Radboud Universiteit)
Daniela Salvatori (chairperson, Universiteit Utrecht)

The NCad (Nationaal Comité advies) supported the preparation of the target image. On a regular basis, the progress of the draft target image was discussed between the chair of the working group and the steering committee. After approval of the final draft by the steering committee, the target image was submitted to the VSNU and NFU.

2. Current situation of laboratory animal usage in education and training in the Netherlands

2.1. Bird's eye view of the use of animals in education and training in the Netherlands

The annual number of animal experiments used for education and training in the Netherlands varied between approximately 15,000 to 20,000 in the period of 2014 to 2019, representing approximately 4% of the total number of experiments. Laboratory animals can be used multiple times in animal experiments. Therefore, the actual number of laboratory animals used is lower than the number of animal experiments. In this document, the terms animal experiments and laboratory animals will be used interchangeably.
Bachelor's, Master's and postgraduate teaching and training at universities and University Medical Centres (UMCs) account for a total of approximately 9,000 animal experiments annually, so this is the number relevant to the current target image (Figure 1). In 2019, these numbers were 2500 and 6500 for the Bachelor's/Master's programmes and postgraduate education, respectively (Table 1) [1-6]. Bachelor's/Master's degrees include biomedical sciences, as well as animal sciences (WUR) and veterinary medicine (UU) programmes, the latter two together mentioned as bio-veterinary education. Animals used in the programmes for veterinary medicine and animal sciences are so-called 'target animals' ("doeldieren") for teaching specific aspects of a species. The national registration of laboratory animals does not differentiate for this specific group; this will be mentioned separately whenever it is relevant in this document. Postgraduate education includes skills training programmes for (medical) doctors, Laboratory Animal Science (LAS) courses (mandatory training to become certified for designing/managing and performing laboratory animal experiments) and practical training for researchers to acquire and maintain competence (skills) in performing research procedures on laboratory animals (usually after the LAS course).

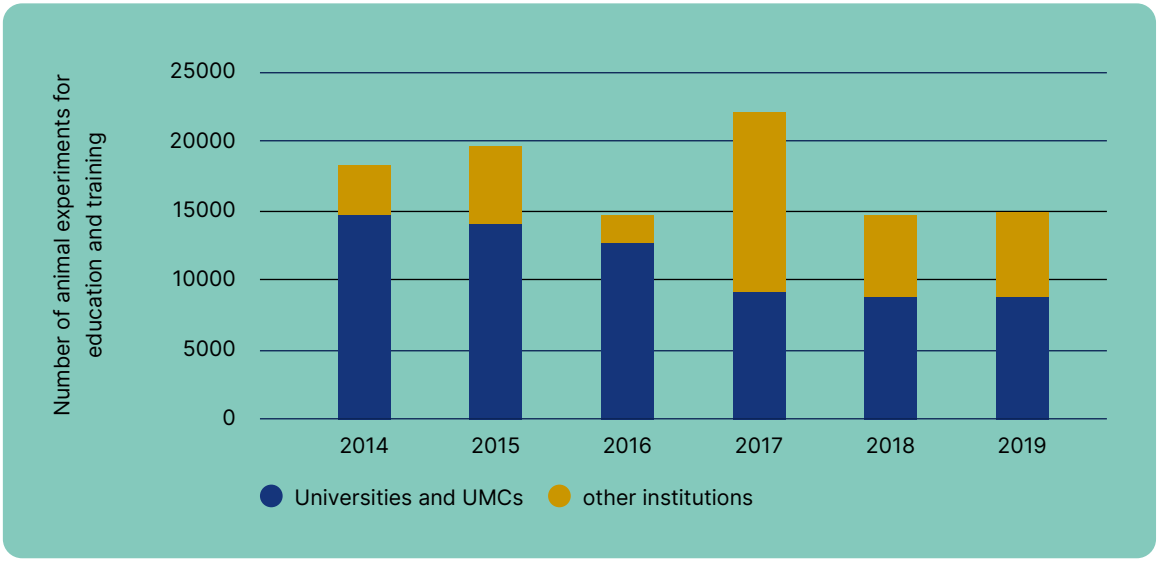

Figure 1: Total number of experiments on animals used for education and training registered by academic institutions (universities and academic medical centres (UMCs) and other institutions (called "Licensed user establishments") that have permission to perform animal experimentation, such as research institutes and pharmaceutical companies in the Netherlands from 2014 to 2019 (NVWA, Zodoende) [1-6].

Most LAS courses in the Netherlands are organized as postgraduate education, but in a few specific cases they are also part of a Master's programme. In this document, LAS courses will be discussed as postgraduate education.
So-called small animals represent 83.5% of experiments using animals for education and training; large animals represent 16.5% (Table 1).

2.2. The role of education to maximize the potential of new approach methodologies (NAMs)

Education and continuing education enable students, teachers, scientists and professionals to gain a solid grounding in the 3Rs. In recent years, great advancements have been made in the development of animal-free testing methods, such as organ on chip technology and in silico techniques. A third type of powerful test "model" that can complement others, includes testing on healthy or diseased humans [7]. By EU law, a researcher must be well informed about state-of-the-art developments in the field of investigation, and animals must only be used if all possible alternatives are considered to be inadequate [8].

In 2020, EURL ECVAM (European Centre for the Validation of Alternative Methods) led several activities in order to identify the availability of alternatives in basic, translational and applied research, making a review of available and emerging non-animal models in seven disease areas (respiratory tract diseases, breast cancer, immune-oncology, immunogenicity of advanced medicinal products, neurodegenerative disorders, cardiovascular disease, autoimmunity). These particular areas were selected based on disease incidence and prevalence, the reliance of related research on animal models and the amount of animal procedures conducted [9].

The 2020 EURL ECVAM status report on non-animal methods in Science and Regulation concluded that: "Raising the awareness of students and teachers of 21st century technologies and the European values related to animal welfare and animal protection in science, through

		bachelor/master education		postacademic training				
	Species	**Biomedical**	**Animal sciences and veterinary medicine**	**Laboratory animal science (LAS) courses**	**Practical training researchers**	**Skills training medical doctors**	**total # animal experiments**	**% of total**
SMALL ANIMALS	Mouse	76	0	2447	2075	24	**4622**	**51,5%**
	Rat	53	23	912	573	311	**1872**	**20,9%**
	Chicken	0	706	0	16	0	**722**	**8,0%**
	Other birds	6	129	0	0	0	**135**	**1,5%**
	Rabbit	0	32	0	18	0	**50**	**0,6%**
	Dog	0	44	0	0	0	**44**	**0,5%**
	Cat	0	11	0	0	0	**11**	**0,1%**
	Ferret	0	24	0	0	0	**24**	**0,3%**
	Fish	0	0	0	8	0	**8**	**0,1%**
	Guinea pig	0	0	0	4	0	**4**	**0,04%**
	total small animals	**135**	**969**	**3359**	**2694**	**335**	**7492**	**83,5%**
LARGE ANIMALS	Cow	0	1075	0	10	0	**1085**	**12,1%**
	Pig	0	125	0	5	89	**219**	**2,4%**
	Sheep	0	115	0	1	0	**116**	**1,3%**
	Goat	0	42	0	0	0	**42**	**0,5%**
	Horse	0	23	0	0	0	**23**	**0,3%**
	total large animals	**0**	**1380**	**0**	**16**	**89**	**1485**	**16,5%**
	total # animal experiments	**135**	**2349**	**3359**	**2710**	**424**	**8977**	
	% of total	**1,5%**	**26,2%**	**37,4%**	**30,2%**	**4,7%**		

Table 1: Number of experiments on animals and animal species used in Bachelor's/Master's degree courses and postgraduate training in the Netherlands in 2019.

specific education and training programmes, is a crucial endeavour towards the ultimate aim of abandoning animal testing" [9]. The report highlights that the actual status of educational activities and resources is not optimal. Section 3.4. continues on the subject of possible solutions and recommendations.

2.3. Legal framework

The EU Directive 2010/63/EU, the related EU 2020 implementing decision, the Experiments on Animals Act (or Wet op de Dierproeven, WoD 2014, in the Netherlands that is based on the EU legislation) and the EU working document on the development of a common education and training protect animals used for scientific purposes, including the laboratory animals used in education and training [8,10,11,12]. In the context of education and training, 'animal experiments' refers to 'animal uses' as defined in the EU Directive 2010/63 and inclusion in the scope of the EU Directive makes these 'regulated procedures', regulated in the sense that the animals are protected by this body of legislation, including provisions for ethical evaluation (permission based on harm-benefit analysis).

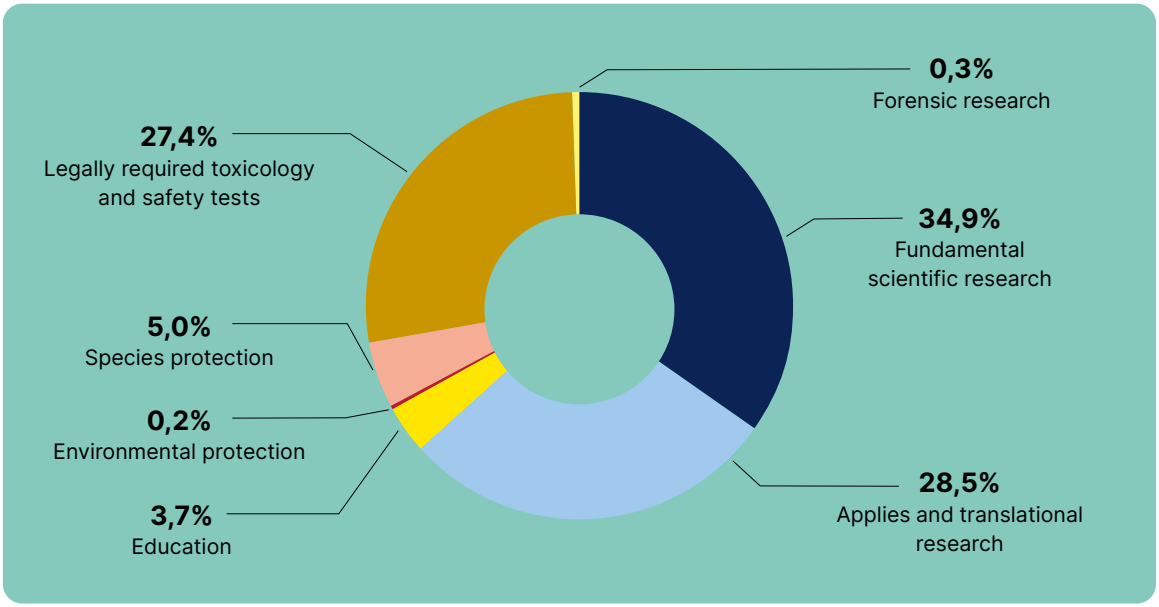

Figure 2: Overview of the categories/ purposes in which the use of experimental animals is legally allowed. Education (incl. training) represents 3.7% of total animal experiments (2019) [6].

According to the EU Directive, an animal experiment is "*any use, invasive or non-invasive, of an animal for experimental or other scientific purposes, with known or unknown outcome, or educational purposes, which may cause the animal a level of pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice" (Article 3. Section 1. Directive 2010/63/EU)* [8]. The animals covered under this directive are live non-human vertebrate animals, including independently feeding larval forms and foetal forms of mammals, from the last third of their normal development, and invertebrates. The purposes for the use of experimental animals are categorized, and include education and training, which is one of the categories that covers 3.7% of the total number in 2019 (Figure 2). Most animals are used in the categories called basic and applied research (63.4%, jointly. Figure 2).

It is recognized by law that: (a) animals have intrinsic value that must be respected, (b) animal welfare consideration should be given the highest priority and that (c) principles of replacement, reduction, and refinement (the 3Rs) should be systematically evaluated.

Furthermore, animals can only be used in research and education in cases where there is convincing scientific justification, where the expected benefits of usage outweigh the potential risks in terms of animal suffering, and when the objectives cannot be achieved using non-animal, alternative methods. Back in 1986, the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes in Strasbourg, already stated that "*procedures carried out for the purpose of education, training or further training of professionals shall be restricted to those absolutely necessary for the purpose of the education or training concerned and shall be permitted only if their objective cannot be achieved by comparably effective audio-visual or any other suitable method. (art. 25)*"

2.4. Approach to animal experimentation

Researchers/teachers who initiate a research or education project that involves live animals are required to apply for a project licence. Each project license must be submitted for approval

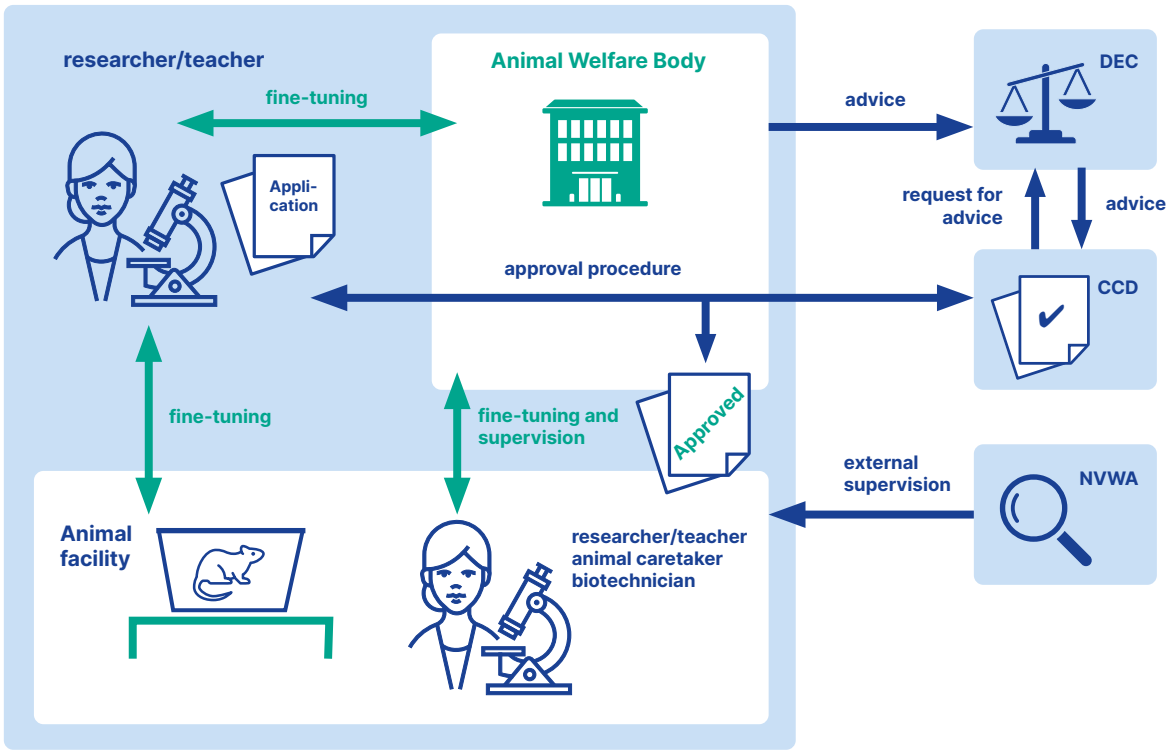

Figure 3: Graphical representation of the required procedures to obtain a project licence and approval to carry out an animal experiment (DEC=Animal Ethics Committee; CCD=Central Authority for Scientific Procedures on Animals; NVWA=Netherlands Food and Consumer Product Safety Authority). Adapted from infographic Animal Welfare Body Utrecht [13].

to the Central Authority for Scientific Procedures on Animals ('Centrale Commissie voor Dierproeven' – CCD) after consultation with the local Animal Welfare Body ('Instantie voor Dierenwelzijn' – IvD). The CCD asks the Animal Ethics Committee (Dier Experimenten Commissie – DEC) to evaluate whether the importance of the research/educational goal outweighs the animal's discomfort (harm-benefit analysis). If the Animal Ethics Committee gives positive advice, the CCD will grant a project license for a maximum of five years. Before the animal experiment can start, the researcher/educator must write a detailed plan (working protocol), including the number of animals required, based on the 3R principles and an estimate of the cumulative discomfort. The local IvD needs to approve this plan prior to the start of the experiment. All activities at the animal facility are subject to external supervision by the Dutch Food and Consumer Product Safety Authority (NVWA) see figure 3 [13,14].

2.5. Animal use in academic educational domains

2.5.1. Bachelor's and Master's Degrees

In 2019, a total of 2,484 experiments on animals were performed in the Netherlands for teaching Bachelor's and Master's degrees (Table 1). Most of these experiments (2,349 = 94.6%) were performed in animal sciences and veterinary medicine. Thus, the remaining 5.4% (135 animal experiments) were used in biomedical Bachelor/Master teaching. These numbers were traced down to course level at the different academic institutes.
Among the biomedical Bachelor's/Master's courses, the 135 animals were used in the following disciplines and related learning goals:
(a) anatomy and physiology (e.g. to gain knowledge about basic terms and principles of human physiology; about structural organisation and the functioning of vertebrate organ systems and

their interaction; learning to perform dissection, histology, microscopy, laboratory techniques and experimental set-ups for in vivo measurements); (b) nutrition and metabolism (e.g. gain insight into the digestion, absorption and metabolism of food; gain insight into the effect of nutritional intervention on animal growth, development and behaviour); (c) immunology (e.g. understand key immunological aspects of cell biological health problems in humans and in animals); (d) toxicology (e.g. identify toxic components in food relevant to health); (e) pharmaceutical sciences (e.g. gain insight into working mechanisms of the main classes of drugs, their agonistic and antagonistic interactions and how to quantify this in vitro and in vivo), and (f) neurobiology (e.g. gain insight into the planning, logistics and execution of pharmacological behavioural animal experiments). It appeared that animal experiments were performed at certain institutes, for certain specific courses, while other institutes did not perform animal experimentation for similar courses. The choice for the inclusion of animal experimentation in a course is usually taken at the course director/leader level.

The veterinary medicine and animal science courses account for the highest number of animal experiments in Bachelor's and Master's Degrees in the Netherlands, by far. These are also the courses where studying animals is the primary focus. Cows, pigs, sheep and chickens are the most used species in these specific subgroups. In animal sciences (WUR), the educational focus is to learn the biological functioning of domesticated animals and to tackle problems related to the management of livestock and companion animals. In the Netherlands, there is one school of veterinary medicine (UU). The goal of veterinary education at UU is to provide professionals with the necessary skills and knowledge needed to offer effective, safe and ethical animal care and treatment, and to safeguard public health. Clinical training is an essential part of the curriculum to prepare the student for the clinical skills required as a veterinarian. Most laboratory animals are used during the Master's phase of veterinary education, to teach clinical skills (from physical examination to surgical procedures). The registered discomfort ranges from mild to moderate and animals are frequently re-used. It is possible to use a laboratory animal more than once. Re-use predominantly happens in education and training. Around 50% of the number of animal experiments in which animals are re-used, are animal experiments for education and training.
Several animal-free methods have been developed and have been implemented in veterinary education, such as interactive videos and computer simulations, e-learning material, dummies, plastinated specimens, ethically sourced cadavers for surgery and clinical case-based practice (animal patients).

2.5.2. Postgraduate education

A total of 6,493 animal experiments were performed for postgraduate education in the Netherlands in 2019 (Table 1). This mostly includes animals used for training scientists that intend to use animals in their research projects, including LAS courses (6,069 animal experiments) and a smaller number of animal experiments that are registered for the postgraduate (surgical) skills training of (medical) doctors (424 animal experiments).

Scientists that intend to perform procedures on animals need to go through several steps of training. The first step is the laboratory animal science (LAS) course. LAS courses are mandatory courses for scientists that need to design and perform laboratory animal experiments. The certification obtained at the end of the LAS course or "Cursus Proefdierkunde" in Dutch, is also called the Art. 9 certificate. In 2019, a total of 3,359 animal experiments were registered in the Netherlands for the LAS courses (37.4% of the total of animal experiments used in education in academia). Mice and rats are the only species used within the LAS courses. After receiving the Art.9 certificate, a professional is authorised to develop projects (write project proposals and working protocols), but is not yet allowed to independently perform procedures on laboratory animals.

This requires further specific (practical) training. Such specific “post LAS” training accounted for 2,710 animal experiments in 2019. It allows the scientist to gain skills and become competent in the animal procedures described in their project proposal.

Each LAS course consists of a broad theoretical basis and a species-specific practical part (usually using live animals), which together lead to the required certification. The content of LAS courses at Dutch universities is similar and includes topics such as legislation, experimental design, ethics, animal welfare and the three R’s, anatomy, physiology, pathology and animal care, recognition and management of pain, euthanasia, basic handling, biotechnical procedures and systematic reviews courses. Several, but not all, LAS courses in the Netherlands are accredited at European level by the Federation of European Laboratory Animal Science Associations (FELASA Function B courses). This accreditation creates the harmonised content and easier mobility of researchers in Europe. In the FELASA guidelines, live animals need to be included for training on handling and restraints techniques. In certain Master’s programmes (e.g., biomedical sciences at some universities within the Dutch national programme for vocational postgraduate training in toxicology), the LAS course is obligatory. The LAS course coordinators at these universities have expressed the clear intention of abolishing compulsory LAS courses. Indeed, as of 2019, the Maastricht University LAS course is no longer compulsory for Master’s students, and the LUMC will soon follow.

It is required by law that ‘the staff employed by each breeder, supplier and user is adequately educated and competent and continuously trained and that they are supervised until they have demonstrated the requisite competence’ (Section 13(f)(3c) of the WoD and Article 24-1c of the European Directive 2010/63/EU) [8,11]. Therefore, post-LAS training needs to be specifically arranged for scientists that need to carry out animal procedures.

(Medical) specialists use animals to acquire and maintain skills for performing specific/complex (micro-) surgical skills, like end-to-end/side anastomosis, bypass operations, laparoscopy and resuscitation/trauma care. Rats and pigs are predominantly used for this type of training.

3. Reducing the number of laboratory animals in academic education and training

3.1. Bachelor’s and Master’s degree programmes in bio-medical studies

Around 135 animals, in total, are used per year for the bio-medical Bachelor/Master’s courses (Table 1). Three universities use laboratory animals in their Bachelor’s/Master’s courses. Similar bio-medical courses at other universities do not make use of laboratory animals. We further analysed the learning goals and non-technical summaries (NTS) related to the bio-medical programmes for the courses using laboratory animals. Each NTS (non-technical summary for lay people) must include information on objectives, predicted harms and benefits, the number and species of the animals to be used, and consideration of the 3Rs principles.
NTS documents are available via the CCD website. The NTS is part of the approved project proposal for performing an experiment on an animal [14]. Animals in this category are primarily used to gain knowledge of the anatomy and physiology of organ systems, and as a source of material for training molecular/cell biological techniques.

In general, the justification for using live animals, found in the NTS, refer to either a lack of an adequate alternative that is as effective as using animals in providing the intended learning outcomes; or the necessity of using a living animal for 'proper' learning and for attitude forming and competence. Specific arguments were given to reinforce the need to use animals during education. Some examples include:

- *Introducing students to animal experimentation in an early phase is important, as they are likely to encounter animal research in later stages of their career and therefore this experience will help them make future career choices and decisions;*
- *Education using laboratory animals connects students to daily practice in biomedical sciences and teaches them to design, plan, perform and analyse animal experimentation;*
- *Experiencing animal experimentation will not only make future researchers competent but also addresses effective learning goals by teaching them to act in a responsible and deliberate manner;*
- *In course evaluations, students indicate that working with animals and animal tissues increases the learning yield and gives discussions more depth, something which cannot be achieved by alternatives, like watching video material.*

However, for the disciplines mentioned above, and their learning goals, many effective animal-free methods are already available [15-17]. Despite this, the NTSs of the biomedical courses where animals are still used reveal a bias towards the use of living animals instead of implementing alternatives and give the impression that animal-free methods are inferior to the use of live animals for reaching the same learning goals.

Also, in our opinion, it is not necessary to kill animals to build knowledge and critical-thinking skills that will allow students to make an informed choice in their future careers. It also appears that some educators find the experience with animal experiments formative, but it should be realised that to date there are other methods to achieve a positive formative experience [18]. Moreover, it has been shown that students who are forced/required to practise painful techniques and terminal surgery have demonstrated signs of stress and "compassion fatigue". Compassion fatigue results in reduced empathy for others (co-workers and loved ones) and can diminish the quality of medical care delivered to animals [19]. This pedagogical approach could even harm the student. Additionally, if students are regularly confronted with using animals during their studies, they might not be able to develop a balanced attitude toward the use of animals during their research career [20-23].

The main interest for the students is to achieve the best competency level using the methods that show efficacy (evidence-based approach). Animal-based methods should not be founded in tradition and students have the right to use animal-free methods.

Recommendation

In the Bio-Medical Studies Bachelor's and Master's programmes, if the same learning goals can be achieved using animal-free methods, it is ethically responsible and should be legally mandatory to implement animal-free methods.

3.2. Bachelor's and Master's Degrees in Bio-Veterinary programmes

As mentioned, clinical training is essential to prepare veterinary students for their future profession. The main goal is to provide the clinical skills necessary to give optimal animal care and treatment. Teaching clinical skills can be done using a variety of means: from text books to e-learning, from low fidelity models to high fidelity models, to live animals. Many animal-free methods have already been developed and organised in skills labs. Skills labs are modern, technology enriched environments where models, mannequins and simulators can be combined with multimedia computer simulations, including virtual reality. The opportunity to practise on models has a direct influence on reducing the use of laboratory animals. Teaching clinical skills in a safe environment allows for mistakes and the repetition of complex procedures without harming a living animal and, importantly, reducing anxiety and stress for the student [23,24]. It has been shown that training students with animal-free skills before going to work with live animals directly promotes animal welfare [25].

To improve the educational benefits of a skills lab, the underlying educational theories, as well as a properly designed learning environment, need to be part of the approach [25-28]. Managing the cognitive loads of the learners when they go through a series of models from low to high fidelity, then eventually to live animals will boost confidence and efficacy while greatly diminishing the number of animals that have to be used.

In veterinary and human medicine, clinical training has relied on simulators for many years. The number of simulators currently available to veterinary educators has proved to enhance student skills and usually received positive feedback from the students who use them [28]. Further research is required to increase the range of available simulators for use in veterinary education, in order to improve the practical skills of veterinary students and reduce the use of live animals and cadaver material for teaching purposes [29].

All Dutch medical schools have already transitioned to non-animal teaching, using skills labs, human patients and volunteers for their Bachelor's and Master's programmes. The replacement of laboratory animals for vocational training can be achieved by involving students directly in the diagnosis, treatment and care of real patients instead of using laboratory animals. Examples of such an approach are students helping patients who are brought to the educational facility/ hospital or students working under supervision in farms or animal shelters.

Recommendations

Develop a step-by-step approach based on animal-free methods before approaching the live animal in bio-veterinary programmes.

Create animal-free skills labs, based on, but not limited to, models and simulators.

Implement more, and earlier, clinical teaching on real patients in clinics/ hospitals or farms in bio-veterinary education.

3.3. Postgraduate education

3.3.1. LAS courses

As mentioned previously, a significant number of mice and rats are used for the LAS courses. LAS certification is required to develop projects with laboratory animals, but further training is required to perform an experiment on an animal. To date, laboratory animals are being used in the practical part of LAS courses, to learn basic handling and behavioural aspects, for instance. Usually this is done on mice and rats, which may not necessarily be the species the participant will be using during their research. It can be questioned whether this is a desirable approach in the lead-up to the reduction of animal use, particularly as many researchers need to do more targeted training prior to starting their experiment anyhow. A future action point could be to target practical LAS and post-LAS training only on actual, practical work, focused on the relevant species.
A revision of the theoretical and species-specific/practical part of the LAS course could then be possible, even going as far as restructuring the LAS into a theoretical part, open to all life sciences students, with a stronger focus on the 3Rs, and a transition to animal-free methods and ethics without using laboratory animals. A tailored, practical part will be offered only to those professionals who really need targeted practical training. The advice is to modernize the LAS course, resulting in a new format that does not need to use laboratory animals.
This separation of the theoretical part and the practical part has already been positively tested during the Covid-19 situation. The proposed changes would mean that the LAS course coordinators would have to initiate the discussion with the FELASA accreditation board for those LAS courses that are accredited.

Recommendations

Restructure the LAS course into a two-step approach: a) a theoretical part relevant to all biomedical students with emphasis on the 3Rs, animal-free methods and ethics, and b) a species and procedure specific practical part that is only for those who are going to perform an actual experiment themselves.

Discuss a wider, regulatory implementation of this two-step approach with the FELASA accreditation board.

3.3.2. Practical training of researchers prior to animal experimentation

When animal experimentation, usually requiring living animals, is still necessary, an appropriate training course must be discussed with the researcher (e.g. for practising the surgical procedure prior to the start of a study). Thus, laboratory animals are also used for training researchers in specific animal procedures. Frequently, these animals are registered as part of the research project itself (see figure 2). This course of learning could involve an appropriate embedding of animal-free methods (e.g. simulators for surgical training) before approaching the idea of using live animals. This will reduce the number of animals required when developping adequate skills to perform the actual study of the animal.

A researcher's entire and complex route when learning about how to perform animal procedures can, in several cases, also be avoided by transferring the practical animal work to specially skilled personnel (animal technicians, veterinarians). We emphasise that performing procedures on laboratory animals is not a simple matter. For instance, a veterinarian is allowed to perform surgery on an animal patient not earlier than after completing a Master's programme in veterinary medicine. This is in sharp contrast to the current requirement which rules that in order to work with laboratory animals, having completed the LAS Course, any researcher only needs a compact, practical training course, under supervision. Moreover, when researchers have temporary/short term contracts, it is a challenge to ensure continuity and a high standard for animal procedures. If these tasks are transferred to specialised personnel, it can be expected that both the quality (highly skilled professional) and efficiency (fewer animals as there will be no complex individual learning route) of animal experimentation will be improved.

In line with the requirements for continuous professional education in the healthcare sector, continued education of personnel will also be needed to achieve a professional laboratory animal science environment. A guide for the implementation of this has already been given by the national IvD platform and the Utrecht Life Sciences 3R centre [30]. It is of great importance that universities offer employees who are involved in animal experimentation opportunities to participate in lifelong learning activities which include animal-free methods. The Dutch Association for Laboratory Animal Science (DALAS) has already started a course based not only on the 3Rs principles, but also on the application of the transition to animal-free methods (https://www.uu.nl/onderwijs-voor-professionals-dalas).
In the transition to animal-free innovation, several professional figures need to interact together. Because of this we advocate more connections and collaborative initiatives in which MBO, HBO and/or WO students can work together.

Recommendations

Wherever feasible, transfer practical animal work that includes surgical procedures from the individual researcher (with an individual learning requirement) to dedicated highly skilled personnel.

Ensure that the researchers and staff at animal facilities are enrolled in continuous education programmes that also include animal-free innovation.

Develop and implement animal-free innovation based courses/materials in the Bachelor, Master and in the continuing education programmes offered to students, researchers and professionals within and outside universities and in co-creation with industry and contract laboratories and social partners.

Create funding opportunities for industry and public consortia aimed at positioning projects in the field of education and the training of professionals.

3.3.3. Skills training of medical professionals

For skills training of medical professionals, the majority of animals are used to learn new ((micro)surgery) procedures, and for training in intensive care. Although literature shows that microsurgery training on live animals is currently still relevant, non-animal models that include low/high fidelity and robotic systems are rapidly bridging the gap [31]. Animal-free physical training models are becoming rapidly available, especially for microsurgery procedures. Studies into the efficacy of non-animal models as learning tools indicate that these devices measure what they are intended to measure, and that they can improve performance relative to traditional learning methods [32]. Basic training in microsurgery is mostly about instrument and microscope handling. These aspects can very well be trained in an animal-free setting. Training initiatives in the area of intensive care has shown a positive implementation of simulators and replacement of laboratory animals [33].

Recommendation

Invest in further development and implementation of animal-free models for skills training of medical professionals.

3.4. Training students,researchers and professionals in new approach methodologies (NAMs): the driving force of higher education

As new approaches and methodologies are continuously developing, there is a continuous need for education and training in all aspects of animal-free science in order to disseminate the new methods.
NAMs are vulnerable to many of the same problems with animal studies, such as standardisation, the need to improve reporting, in vitro to in vitro extrapolation, data interpretation, and possible ethical issues [34]; because of this, it is of great importance to make educational plans aimed at developing critical thinking, supporting the choice, creation, development, validation and the use of animal-free methods.
EURL ECVAM has produced a report to stimulate and facilitate the uptake of the 3Rs and non-animal based science education content in schools and universities [35]. EURL ECVAM has also created freely accessible eModules for: 1) Searching for (existing) non-animal alternatives (EU-52), and 2) Developing in vitro methods and approaches for scientific and regulatory use (EU-60). This can be found on the Education and Training Platform for Laboratory Animal Science (ETPLAS) platform (https://etplas.eu/learn/).
Education and training are necessary, not only for academic researchers but also for professionals working in industrial and contract laboratories. The key will be to adopt a new education model based on the alignment of continuing education programmes with regular Bachelor's and Master's programmes. By this we mean the mutual tuning of educational innovation within the existing organisational and financial frameworks of the funded (Bachelor and Master) and non-funded (continuing education) programmes, in such a way that the implementation of these programmes can interlock at different times without getting mixed up. This will translate into closer collaboration with the professional fields and in the active creation of a learning community.
By offering education in co-creation with external stakeholders, a rich learning environment arises that benefits both businesses and students [36]. Accreditation, the introduction of "Open badges and micro-credentials", will be necessary to support the quality of education and to prove that the recipient possesses certain knowledge or skills [37].

Investments will be needed to create knowledge resources for education and the training of students and professionals. To inform the public and all relevant stakeholders in a transparent and non-polarising manner is also an educational duty. The National 3Rs Centre could have a leading role in these activities.

Recommendations

Develop and implement NAM courses/materials offered to students, researchers and professionals within and outside universities and in co-creation with industry and contract laboratories and social partners.

Create funding opportunities for industry and public consortia aimed at positioning projects in the field of education and the training of professionals.

3.5. Animal welfare bodies

Animal welfare bodies independently advise on, and critically review, the justification of animal use. This includes advice to professionals on the application of the 3Rs. A rigorous assessment of how well the 3Rs, and in particular 'replacement', should be pursued and the animal welfare bodies should strongly steer away from animal use in their review process. The incorporation of experts in animal-free methods in education within animal welfare bodies can help to facilitate this approach.

Recommendations

Animal Welfare Bodies should incorporate experts in animal-free methods in education to strongly steer away from animal usage in a proactive way during their review process of project proposals with an educational aim.

3.6. Innovations in animal-free education

In the previous sections, we have described several possibilities, advances and opportunities in animal- free teaching and education as part of the existing academic education. In this section, we will further discuss some promising innovations in animal-free education and teaching. Many teaching models for higher education have been developed and are currently available, see the InterNICHE Alternatives Database for examples [16]. The total spectrum of animal-free modalities in teaching encompasses models, mannequins and mechanical simulators, computer and virtual reality simulations, videos, self-experimentation, observational studies, studies on cell lines and organotypic cultures in vitro, the application of ethically sourced animal cadavers, and supervised clinical practice [18]. We will further discuss several - but not all - of these modalities below.

3.6.1. Promising innovations in animal-free education

Models, mannequins, and mechanical simulators, as well as computer-based simulators, are already widely available and are being used for teaching anatomy and physiology and clinical procedures such as blood collection, intubation, or urinary catheterization. For example, it is possible to mimic an artificial pulse with a pump and practise injections. Low fidelity models like cuddly toys are frequently used in curricular (veterinary) basic skills training. High fidelity models, like life-size latex models, are dedicated for specific procedures like vascular anastomosis [24]. Plastinated models based upon ethically sourced cadavers are currently primarily used for basic anatomy although there is a trend towards clinical skills training [38]. Further down the spectrum are the technology enhanced models for skills training, which prove to have big effects on skills development [39]. Models can be coupled to computer simulations in order to practice skills for critical care or to study the effects of drug administration/dose dependent response.

The challenge of obtaining basic and applied knowledge from a real animal is the high level of cognitive load caused by the complex interaction of structures and behaviours. A stepwise, increasing complexity in learning, without losing the 3-dimensional context, can be achieved by Virtual Reality (VR) simulation. VR simulation is a rapidly developing technology referring to computer technologies promoting generation of virtual environments, allowing the user to interact with them. Adding principles of interaction design, e.g. gaming scenarios, further aids to improve the efficacy of learning strategies [40]. In the medical field, VR is an already well-established tool to train surgical skills as well as to further improve knowledge in general [41]. VR tools have been proven useful to learn anatomy, procedures such as intubation and the interpretation of radiological images, and more in general, to improve diagnostic problem-solving skills. Following the positive experience in the medical field, VR is now being introduced in the Bachelor's and Master's bio-medical and bio-veterinary programmes. Thus, VR technology forms a very useful tool in animal-free learning. In VR simulation, haptic feedback, i.e. adding a sense of feeling, can be provided to the virtual learning environment by adding mannequins or plastinated models, for example, onto which digital models can be projected. A next step is that haptic feedback can be provided electronically through computer simulation as well (see for instance https://www.senseglove.com). *Robotic simulators* are used for skills training, such as for laparoscopic interventions [42]. At the end of the spectrum of VR simulations, fully digital models are applied for 3-dimensional training [43]. A specific type of VR is Augmented Reality, in which the physical surroundings are visible and can be integrated into the experience; for example, by digitally augmenting or overlaying the models with information, e.g. anatomy, clinical imaging or lab results [43,44].

The added value of using (digital) models is that they provide a safe teaching environment in which users can repeatedly practise and safely make mistakes until the required competence level has been reached. For example, to prepare for surgical procedures, students and professionals can refresh the technique at their own preferred time and location, and activate the right knowledge domain (3D vs 2D from a book or computer screen). This complies with modern educational frameworks, such as self-directed learning and flipping the classroom, and meets societal demands, like traffic limitations, continuous education, and the freedom to schedule activities.

It should be realised that the development of these learning modalities, especially those using advanced computing technologies, can be expensive. However, these modalities are generally sustainable, can be used repeatedly, and often save time and reduce stress for both the teachers and the students. Since computer and VR based simulations are not location or time dependent, dedicated facilities can be shared with many partners nationwide.

Recommendation

Invest/establish funding for innovation in animal-free teaching methods and technology according to the principle of sharing high-tech and/or complex facilities between academic partners.

3.6.2. Efficacy of animal-free methods

Animal-free models can be considered as a spectrum of technologies ranging from basic to advanced, which support stepwise learning and managing the cognitive load during that process. A systematic review published in 2021 concluded that animal-free teaching methods produced learning outcomes superior (30%) or equivalent (60%) to those produced by the traditional usage of live animals [18]. Similar, earlier reviews reached the same conclusion: animal-free methods are effective in achieving the desired learning outcomes [45]. Nevertheless, a recent analysis of non-technical summaries related to projects using live animals for education, published in Europe in the period 2017–2019, concluded that there is a deeply established perception that animal-free methods are less effective than live animal methods [46]. Of course, all methods have strengths as well as limitations but scientific evidence of efficacy of animal-free methods should not be easily dismissed.

In studying efficacy of animal-free methods, most studies focus on the comparison between animal-free methods and animal-based methods. For example, in comparing live training on live animal models with simulators, most authors discuss the question of whether simulation-based training is as effective as, or more effective than using the animal model, and whether the simulator might render the animal model obsolete [47]. Thus, the animal model is positioned as the "gold standard" and the focus is on searching for evidence of the educational outcomes of simulation-based training. Following this line of thought, replacing animal models by simulation-based training is only justified if there is sufficient evidence that the animal-free method provides a more effective learning experience.
We propagate that taking into consideration the currently available refined simulation/animal-free methods, these should be the new reference method. How can the training on live animals still be justified? Thus, when testing efficacy, it should not be necessary to compare learning outcomes of animal-free methods with those achieved by animal use; we should focus on the achievement of relevant learning benefits, and success should be determined by the definition of adequate learning goals.

Recommendation

Position animal-free models as the reference model in teaching and abandon the dogma that laboratory animals are indispensable tools.

Make learning objectives and context the guiding principles for choosing and designing the best animal-free method.

4. How to proceed - implementation

This section focuses on how to proceed in order to further embed animal-free methods into education. In our current era, there is urgency. On 16 September 2021, the European Parliament called for urgent EU action to accelerate a transition to innovation without the use of animals in research, regulatory testing and education [48]. Through this call, a clear role is assigned to education and training, pointing out that academic institutions have an essential role to play in terms of promoting alternatives to animal testing in scientific disciplines and disseminating new knowledge and practices, which are available but not always widely used. It should be realised that most scientists operate within cultural norms that are reinforced by education and training. Thus, education and training should be considered as drivers, able to influence how research questions are approached in the future. The key principles guiding such a roadmap are innovation, quality of education, and evidence-based intervention.
We propose an integrated top-down and bottom-up approach involving the primary stakeholders. Ownership of this transition will be required by everyone of influence on this roadmap, and animal-free education and innovation should be part of the core ambitions of the academic community.

4.1. Stakeholders

Among the primary stakeholders in this target image, we list the animals, the academic organisations, teachers and researchers, the students and professionals and the animal welfare bodies.

Animals
Animals are the primary stakeholders in this aim. Humans and animals are bound in a complex interplay of relationships, which demands a re-evaluation of the status of animals [49]. Animals are sentient beings that can experience pleasure and discomfort and that have a high level of intelligence. Taking on board that animals are sentient has a direct influence on all areas of human-animal interaction, including the use of animals in education; the fact that animals have feelings means that both their physical and mental welfare necessities must be considered in everything we do. This is relevant with respect to laws, policies and people's behaviour relating to animals and their welfare.
In this perspective of care ethics, we have moral obligations to animals when we take any action that makes them dependent upon us for their survival, functioning, and well-being. In other words: we assume moral duties to animals when we make them dependent upon us, because we are the ones who actively brought them into this relationship [50].

Academic organisations (e.g. university boards, deans, vice deans of education)
There is an important role for the boards of universities and faculties in the implementation of this aim to reduce the number of animals in academic education. A first and important step will be taken when university boards embrace this ambition and make this an integral part of their strategy and related policy. This will ultimately enable deans, vice deans of education and programme directors to implement this aim at faculty, program and course level.
Many of the recommendations made in this document can be realised at this organisational level. Examples are to stop using animals in bio-medical Bachelor and Master programmes, stimulate the establishment of skills labs, and to propagate to abandon the dogma that laboratory animals are indispensable tools.

This is specifically true for how universities have organised their training for working with laboratory animals, and the subsequent practical implementation. Academic organisations are pivotal in initiating the restructuring of the LAS courses and follow-up targeted training with laboratory animals. Closely related to this is the recommendation is to transfer animal work to highly skilled personnel, where feasible.

Teachers, researchers and students
Despite the resources that are currently available to teachers and students, it is difficult to obtain information regarding animal-free methods that can be used in education. It has been shown that awareness of existing tools and resources among educators is limited and that the introduction of animal-free methods into a course occurs on a voluntary basis [51]. This also counts for researchers and the dissemination of animal-free methods. In fact, recent surveys among Dutch and European researchers indicate that innovations that are already available could be used more efficiently and that researchers should be made more aware of animal-free methods [52]. Academic professionals hold the creative capacity to develop new methods, models and innovative technology, and in particular, teachers play a central role in defining the learning objectives and introducing the animal-free methods [53]. Teachers and researchers should be provided with easy access to knowledge regarding the development and application of animal-free methods in their daily work.

4.2. An interdisciplinary approach

Animal-free innovation is a broad and complex concept both in research as well as in education. It includes a wide range of disciplines, such as animal science, basic biology, assay development, pharmacology, toxicology, regulatory practices, as well as ethics, public policy and communication. Multidisciplinary and interdisciplinary aspects directly translate into cooperation with different areas to develop comprehensive teaching programs. Interdisciplinary topics will help students not only to develop knowledge but also to encourage connections with other disciplines and overarching systems. Sharing latest research achievements through education and training play a central role in the shift to animal-free research [52]. Advice given in the EU JCR report is to develop a closer collaboration between Master's programmes and research centres for optimal knowledge sharing [35]. To have optimal communication between education and research, data sharing is pivotal. In fact, the lack of data sharing has been recognized by the research community as one of the main roadblocks for the implementation of animal-free innovations. Animal-free innovations (niche level) need to be embedded in regulatory practices (regime level) and become accepted by society (landscape level) [54].

4.3. Animal-free educational HUB

We propose the establishment of a national "animal-free educational HUB". This Hub will have the mission: to facilitate the creation and spread of knowledge of animal-free innovation in education and research. It will aim to fill the gap between research and teaching practice. Furthermore, it will work as a collaborative, structural point where education professionals share and build new knowledge and expertise. The hub will give the possibility to share and scale-up successful animal-free approaches, beyond the faculty/university in which they have been developed. We envisage that the "animal-free educational HUB" will be directly linked to the Utrecht National 3Rs Centre but also with the professionals associations, with industry and with all relevant societal parties at a national and international level. In addition, institutions, including the universities of applied sciences, should establish a stable network for sharing resources and best practices, and to combine forces to favour research and publication. It is a priority to share and write about strategies for implementing the animal-free methods in courses and within the

several disciplines. The implementation of animal-free methods should be based on educational theories; the efficacy of model introduction should also be investigated and reported. Training with animal-free methods should also become an integral part of professionalisation plans for teachers.

4.4. Open science

The “open science” principles based on a more open, collaborative and transparent way to conduct, publish and evaluate scientific research can also be extended to education by sharing and reusing online educational resources. Sharing technologies and applications among institutions could be of great benefit to accelerate the embedding of animal-free methods into graduate and postgraduate curricula. Added value is a higher chance of being able to make an informed decision, based on evidence, about the efficacy of educational innovations and animal-free transition.
In addition, methods and models are not always published in peer reviewed journals. This is due to the current granting and publishing climate which does not favour behavioural sciences, in addition to the fact that proving efficacy of (novel) training methods is difficult and time consuming. Research into the efficacy of animal replacement strategies in education should be stimulated.

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