

STUDYGUIDE

Species specific module:

Rodents and Rabbit

Introduction to Laboratory Animal Science



Universiteit Utrecht

Organisation:

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English pages: www.uu.nl/lascourse

Dutch pages: www.uu.nl/art9cursus

Species specific courses: www.uu.nl/LASspecies

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Objective of the module

The objective of this module is to present basic and appropriate biology, care, health and management of rodents and rabbits, recognition of pain, suffering and distress in these animals and minimally invasive procedures without anaesthesia to be applied on these animals. This course meets the standards for the species-specific education and training requirements for persons designing projects and procedures for rodents and rabbits.

Competence

For the function ‘designing procedures and projects’ the Dutch government requires competency.

On December 18, 2014 the new legislation regarding animal experimentation was implemented. Due to this implementation the course on Laboratory Science has been adapted. The course contains now two parts, a basic course (Introduction to laboratory animal science) and a species-specific module. The basic course certificate and, at least, one species specific certificate will give the required competence.

From August 1, 2015 the competence is limited. You are not allowed to perform any procedure on animals, unless there is supplementary education. From now you are competent when you are skilled (competence profile, species and skill(s) stated).

After successful completion of the new basic course and after successful completion of the present module on rodents and rabbits, you will be competent to design procedures and projects and to execute simple procedures on these animals. Further skills have to be obtained by working under supervision until competence is demonstrated. Only then are you allowed to work with animals independently.

Workload

The number of credits that can be obtained after successful completion of the course is 1 ECTS (European Credit Transfer and Accumulation System). The length of the course is one week (fulltime, 09.00-17.30 hrs). Participation in all parts of the course is mandatory.

Course material

During the course the book Principles of Laboratory Animal Science, revised edition, 2001, L.F.M. van Zutphen, V. Baumans and F. Ohl (eds.) (ISBN 13: 978-0-444-50612-2) will be used. Further material will be provided on OneDrive and Teams.

Program

Title	1. Introduction rodent & rabbit specific course
Content	During this interactive lecture an overview of all topics to be presented during the entire course period will be given. The current national legislation governing the use of rodents and rabbits in research will be introduced. The natural history of the most common laboratory rodents and rabbits will be presented. In dependence on the natural social structure of these animals' implications for housing and testing of these animals will be discussed. Special attention will be paid to welfare related questions.
Key Text	<ul style="list-style-type: none"> a) Movie: The Laboratory Rat: A Natural History (http://www.ratlife.org) b) Origin of the Laboratory Mouse and Related Subspecies. Chapter 1 in (The Laboratory Mouse; Edited by: professor Hans J Hedrich and Professor Gillian Bullock; ISBN: 978-0-12-336425-8). c) History, Strains and Models. Chapter 1 in (The Laboratory Rat A volume in Handbook of Experimental Animals; Edited by: Georg J Krinke; ISBN: 978-0-12-426400-7). d) On usb-stick 'Laboratory animals and animal experiments': BIOLZOOT-12 translation v2. ppt: 3. The laboratory animals: general part.
Form	Lecture
Testing your competence	<ul style="list-style-type: none"> 1. Name the differences in social structure between wild house mice and mice kept in the laboratory. 2. How would you decide on enrichment items for laboratory rats? 3. When would you decide on mice as model organism?

Title	2. Anesthesia
Content	This lecture attempts to provide a basic level of knowledge in anesthesia for research workers with special emphasis on those areas that are of practical importance when anesthetising laboratory animals. The general principles of peri-operative care, anesthetic techniques and anesthetic management are discussed including injection- and inhalation anesthesia. The pathophysiology of pain and knowledge concerning different techniques providing analgesia are reviewed.
Key Text	Van Zutphen, L.F.M., Baumans, V., Beynen A.C. (2001) Principles of Laboratory Animal Science: chapter 15, Anesthesia, analgesia and euthanasia
Form	(Interactive) lecture
Testing your competence	<ul style="list-style-type: none"> 1. What is pre-emptive analgesia 2. Describe the pillars of anesthesia 3. Name the advantages and disadvantages of inhalation anesthesia.

Title	3. Practical Rodent & Rabbit Handling & Behaviour
Content	In this practical first of all you will learn procedures for handling and restraining mice, rats, Guinee pigs and rabbits. This practical prepares

	<p>you for the practical on basic techniques. Important to understand that 95% of a procedure is restraining the animal in the right way. Working safely and humanely with laboratory animals requires a core competency in handling and restraint methods. Proper restraint and handling techniques are essential for clinical examination and injections while limiting the amount of stress and/or discomfort to the animal and to the handler.</p> <p>Then we will move on to the practical part on mouse and rat behavior. Behaviour is frequently studied in laboratory mice and rats and is one of the most important read-out parameters for the welfare of these animals.</p> <p>In this practical you will carry out simple behavioural investigations in mice and rats focusing on social behavior and animals' preferences.</p>
Key Text	<ul style="list-style-type: none"> a) Handbook "Principles of Laboratory Animal Science" (course book), chapter 3 "Biology and husbandry of laboratory animals". b) Videos on handling/restraining c) http://film.oslovet.norecopa.no/ d) Handbook "Principles of Laboratory Animal Science" (course book), chapter 4 "Behaviour, stress and well-being". e) Whishaw, Ian Q., ed. The Behavior of the Laboratory Rat: A Handbook with Tests: A Handbook with Tests. Oxford University Press, 2004. f) Film 'The laboratory rat: a natural history' (http://www.ratlife.org/)
Form	Lecture and practical
Testing your competence	<ul style="list-style-type: none"> • Every species and even different strains (can) have their own specific way of handling and restraining. • Restraining is handling an animal in such a way that nor you neither the animal will be harmed when performing a technique. • Name possible consequences (for the animal and for the handler) if animals are not handled and/or restraint properly. • How would you train yourself in handling when using a certain species and/or strain for the first time in an experiment? • What is an ethogram? • Which behavioural test can be used in order to draw conclusions on animal needs? • Name parameters that might influence animal behaviour in the laboratory.

Title	4. Diseases of laboratory animals (Gezondheidsbewaking bij proefdieren)
Content	<p>Diseases in animals can be a consequence of experimental setup or occur as an unintended effect during the study. This lecture will focus on how to handle when animals die or are diseased as an u. In particular, the risks of disease at different levels will be discussed as well as how to recognize disease and come to a diagnosis.</p> <p>Furthermore, the most common infectious diseases of laboratory animals are given, with a special focus on zoonosis. Measurements to</p>

	reduce the infection risks as well as how to handle in case of infection the potential effects on the studies. ...re.
Key Text	<ul style="list-style-type: none"> • Natural Pathogens of Laboratory Mice, Rats, and Rabbits and Their Effects on Research; Baker, Clin. Microbiol. Rev. 1998 • Confronting Zoonoses, Linking Human and Veterinary Medicine; Kahn, Emerging Infectious Diseases, 2006 • Code of Practice: Welzijnsbewaking van proefdieren • Robbins & Cotran Pathologic Basis of Disease, 9e (for reference only) • http://dora.missouri.edu/
Form	Interactive lecture
Testing your competence	<ol style="list-style-type: none"> 1. How to handle when laboratory animals are ill or diseased? 2. What are the different (levels of) risks when animals are diseased? 3. What are actions with regard to pathology, clinical and microbiological diagnostics that can be considered? 4. What can be consequences of diseases in laboratory animals? 5. What is the importance of collection of samples and how can they be used to diagnose disease? 6. Give an example of how a natural pathogen in lab animals can interfere with research. 7. Give an example of how rodents might be used as model to study human disease. 8. List the transmission routes of pathogens and indicate what measurements can be taken to reduce the risks of spreading.

Title	5. General Anatomy for LAS, with special focus on mice, rats, guinea pigs, hamsters and rabbit
Content	<p>‘One of the prerequisites for responsible use of animals in biomedical research is a thorough knowledge of the biological characteristics of the species to be used. The choice of animal species, sex, age and strain largely depend on whether their anatomical characteristics are suited to the research demands’.</p> <p>In this lecture the general anatomy of mammals, birds and, fish will be discussed shortly, after which special attention will be given to the anatomy of mice, rats, rabbits, guinea pigs and hamster in relation to biomedical research, in order to provide a basis for the creation of the decision tree for finding the optimal animal model.</p>
Key Text	Principles of laboratory animal science, chapter 3 ‘Biology and husbandry of laboratory animals’. Handboek Proefdierkunde, hoofdstuk 3; Biologie en Zoötechniek
Form	Lecture
Testing your competence	<ol style="list-style-type: none"> 4. What feature places a rabbit outside the order of rodents? 5. Is it possible to withdraw/retrieve gall from a rat? 6. Which locations can be used in mice to withdraw blood? 7. What are the differences between the wall of the forestomach parts and the ‘real’ stomach?

Title	6. Physiology
Content	<p>Stress, defined as any deviation from homeostasis, induces a behavioural and physiological response that may impact on a wide array of animal experiments. In this lecture, the basic principles of homeostasis and physiological response to stress will be discussed. Specific topics that will be addressed are:</p> <ul style="list-style-type: none"> - Autonomic nervous system and sympathetic and parasympathetic response - Impact on cardiovascular system - Neuroendocrine response to stress - Impact on animal studies
Key Text	a) Handbook “Principles of Laboratory Animal Science” (course book), chapter “Behaviour, stress and welfare”, Environment and Physiology.
Form	Lecture
Testing your competence	<p>8. How is stress defined?</p> <p>9. Which physiological systems are affected in response to stress?</p> <p>10. What is the impact of a sympathetic and neuroendocrine response to stress?</p> <p>11. Why is it important to consider stress in animal experiments?</p>

Title	7. Gnotobiology and Microbiological standardization
Content	<p>Gnotobiology is the study of organisms or conditions that are either free of microorganisms or associated only with known or specified microorganisms.</p> <p>Just as other aspects of environmental standardization, microbiological standardization is necessary to prevent unwanted and unknown interference with experimental results. Moreover, microbiological contamination can lead to disease and even death of the animals. Other risks are the contamination of humans, or biological products made with the use of animals.</p> <p>Procedures and techniques to obtain laboratory animals of the desired microbiological quality and to maintain this quality (e.g. by using barriers) will be discussed.</p>
Key Text	<ul style="list-style-type: none"> • Handbook “Principles of Laboratory Animal Science” (course book), chapter 8 “Microbiological standardization”. • Hardy, P. “Gnotobiology and Breeding Techniques”. Chapter 4.6 in “The Laboratory Mouse” (Second Edition). Academic Press, 2012.
Form	Lecture

Title	8. Preventing avoidable discomfort in laboratory animals
Content	<p>In this interactive working group assignment students and lecturer will discuss housing and care of laboratory animals, assessment of discomfort, clinical signs indicating the humane endpoint and the best method to kill animals (least distress and not interfering with experimental results). On the basis of three hypothetical experiments the above-mentioned topics will be discussed: 1. Accommodation of</p>

	the animals; 2. How to assess discomfort? and 3. Selection of the most appropriate method of euthanasia?
Key Text	<ul style="list-style-type: none"> • “Principles of Laboratory Animal Science; chapter 4 (Behaviour, stress and wellbeing) • Council of Europe Convention ETS 123 for the protection of vertebrate animals used for experimental and other scientific purposes. Appendix A: Guidelines for accommodation and care of animals. • EU Working Party Report: Recommendations for euthanasia of experimental animals Parts 1&2 • FELASA Working Group Report: Pain and distress in laboratory rodents and lagomorphs • Environmental enrichment for laboratory rodents and rabbits: requirements of rodents, rabbits, and research. V. Baumans, ILAR Journal Vol. 46.2 (2005) • EU Directive 2010/63/EU on the protection of animals used for scientific purposes; Annex IV: Methods of killing animals.
Form	Interactive working group assignment
Testing your competence	<p>For each of the three hypothetical experiments</p> <ol style="list-style-type: none"> 1. What is the most appropriate way to house the laboratory animals? 2. How do you assess distress, pain in the laboratory animals? 3. What is the most appropriate method to euthanize the laboratory animals? 4. Which clinical symptoms should be used to define the (humane) endpoint of the animal experiments? 5. In general: how do you prevent avoidable discomfort in laboratory animals?

Title	9. Genetic standardization
Content	The extent to which genetic standardization of laboratory animals is needed depends on the goal of the animal experiment. Some experiments require a more uniform responsive laboratory animal population, while for other experiments a certain variation is preferred. Besides genetic standardization, the genetics and breeding of the major classes of laboratory animal populations are discussed as well as the way in which one can verify that the test animals still fulfil the necessary genetic standards.
Key Text	<p>Chapters 7 (2001) from <i>Principles of Laboratory Animal Science. A Contribution to the Humane Use and Care of Animals and to the Quality of Experimental Results</i>. Revised (2nd) Edition. Edited by Van Zutphen LFM, Baumans V & Beynen AC, Elsevier Science Publishers, Amsterdam, The Netherlands.</p> <p>Chapter 7 (2009) from <i>Handboek Proefdierkunde. Proefdieren, dierproeven, alternatieven en ethiek</i>. Vijfde druk. Onder redactie van: Van Zutphen LFM, Baumans V & Ohl F, Reed Business, Amsterdam, The Netherlands.</p>
Form	One lecture
Testing your competence	We advise the animal researcher to go through module 8 (Strains of mice and rats) from the interactive website http://www.3rs-reduction.co.uk/ developed and launched by Michael F.W. Festing. Module 8 is (like all the modules of this website) mostly self-explanatory, with a lot of feedback, and there are a couple of ‘test yourself’-questions. For a (Dutch) review of this website see ‘Van

	Lith HA (2013). Voor u getest: de nieuwe interactieve website ‘www.3Rs-reduction.co.uk’. Biotechniek 52(4), 9-12’.
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Title	10. Demonstration Basic Techniques
Content	In this demonstration a brief description of some basic procedures concerning sampling of blood, feces and urine will be discussed.
Key Text	<ul style="list-style-type: none"> a) Handbook “Principles of Laboratory Animal Science” (course book), chapter 16 “Experimental procedures”. b) Videos on handling/restraining
Form	Lecture and demonstration
Testing your competence	<ul style="list-style-type: none"> • Which methods of blood sampling do you know? • How do you decide on a certain sampling technique? • When would you anesthetize your animals for sampling and when not? How would you sample urine and feces of mice? How would you do that when animals are kept in groups?

Title	11. Practical Basic Techniques
Content	This practical contains a brief description of some basic procedures concerning the administration of drugs. Basic principles of surgery and some administration procedures will be shown. Administering substances to animals, for whatever reason, can have a significant impact on their welfare. If carried out incorrectly, not only can animal welfare be compromised, but the scientific goals of study can be affected. In practice participants will be instructed in the administration of substance (injections (ip, sc, iv), oral) to mice and rats. Basic principles of suturing and iv-injection will be practiced on an artificial model.
Key Text	<ul style="list-style-type: none"> a) Handbook “Principles of Laboratory Animal Science” (course book), chapter 16 “Experimental procedures”. b) Videos on handling/restraining c) http://film.oslovet.norecopa.no/
Form	Lecture and practical
Testing your competence	<p>Which methods of administration do you know? Which routes of administration do you know? How do you decide on a certain method of administration? Understanding a surgical procedure and the different steps needed.</p>

Title	12. LAS assignment
Content	As a group you have to analyze a given article with help of a questionnaire that is based on the ARRIVE guidelines: (Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG (2010) Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research.). Based on every aspect you learned about during the course you have to describe in detail how the experiments described in the article are performed. You will report this in a small presentation (10-15 min) at the end of the course and discuss your choices with the critical audience- the other students.

Key Text	<ul style="list-style-type: none"> • Van Zutphen, L.F.M., Baumans, V., Beynen A.C. (2001) "Principles of Laboratory Animal Science: A Contribution to the Humane Use and Care of Animals and to the Quality of Experimental Results" • Additional literature (sought by the participants themselves)
Form	Working group assignment

Final examination

As a group you have to analyze a given article with help of a questionnaire that is based on the ARRIVE guidelines: (Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG (2010) Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research.). Based on every aspect you learned about during the course you have to describe in detail how the experiments described in the article are performed. You will report this in a small presentation (10-15 min) at the end of the course and discuss your choices with the critical audience- the other students.

Each student gets a mark ranging from 0-10 points (0= unsatisfactory, 10=very good) depending on the quality. The examination involves the handbook, the lectures, discussions, demonstrations and practicals.

Certificate

If the participant has met all legal requirements and has successfully passed the exam at the end of the course, the participant will receive a certificate for this species-specific module Rodents and Rabbit.

If you do not meet all legal requirements, like not holding a Master degree (yet), you will receive a written confirmation stating that you followed the module and successfully passed the exam. Together with the certificate for the basic course, after obtaining your Master degree, you can request the final certificate confirming that you meet all legal requirements of the Dutch legislation to be registered for the function “designing projects and procedures for rodents and rabbits”.

More information

Learning outcomes in accordance with the EC Training and Education Document relating to Directive EU/2010/63,

http://ec.europa.eu/environment/chemicals/lab_animals/pdf/Endorsed_E-T.pdf