

Specialist Information Planning and Organization of Laboratory Animal Housing Units and Laboratories

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1. Introduction

This booklet no. 1 of GV-SOLAS is a revision of earlier texts. The revision became necessary for a variety of reasons. The new animal welfare legislation at European level (Directive EU/2010/63, (1)) and, at national level, Germany's new animal welfare act (2) and ordinance on the protection of laboratory animals (3) gave rise to a number of new aspects that impact the planning and operation of laboratory animal facilities. Aside from the legislation, new scientific findings have been made in the meantime that have to be taken into account in any such recommendations to improve not only aspects of animal welfare, but also the value of results from animal experiments. For one thing is clear: animal experiments remain an essential and very important means of finding answers to scientific questions both in basic biomedical research and in clinical settings. The planning and operation of laboratory animal facilities therefore remain key to providing a framework for meaningful animal experiments and their correct interpretation and their potential for standardization according to a control of variables from the environmental domain of the animals that is as far-reaching as possible. The standardization of husbandry and experimental conditions makes an important contribution to the 3Rs, in particular to reduction and refinement.

The values and descriptions given in these recommendations are not categorical requirements. They are intended rather as values for the planning and design of facilities in order to exclude any problems as far as possible during subsequent operations. Deviations are possible in justified individual cases after careful assessment and in consultation with the head of the animal house responsible for operations. It is crucial that the conditions required for the appropriate breeding and housing of the animal species concerned and for the research projects are both established and complied with.

The main focus of the booklet is unequivocally on rodents, which account quantitatively for the largest proportion of laboratory animals by far. In addition, other animal species, such as pig, sheep, rabbit, frog and fish, will also be considered with regard to certain individual aspects.

These recommendations are intended primarily for:

- · directors of laboratory animal facilities,
- scientists performing animal experiments,
- planners.
- producers of equipment and fittings,
- · grant authorities and
- approving authorities.

Further information on the various topics can be found on the homepage of GV-SOLAS (<u>www.gv-</u>solas.de).

- (1) Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes.
- (2) TierSchG Animal Welfare Act in the version of the notification of 18 May 2006 (BGBI. I p. 1206, 1313), which was last amended by Article 4 Paragraph 90 of the act of 7 August 2013 (BGBI. I p. 3154) (in German).
- (3) TierSchVersV Directive on the protection of laboratory animals of 1 August 2013 (BGBl. I p. 3125, 3126), which was amended by Article 6 of the ordinance of 12 December 2013 (BGBl. I p. 4145) (in German).

2. Organization of laboratory animal facilities

Laboratory animal facilities have to cover a broad range of tasks, the most important of which are listed under the following points. To ensure that these tasks can be fulfilled, a comprehensive organization is required, which is discussed under section 2.2.

2.1 Tasks

- To make sure the requirements set forth in national and European legislation are met (animal welfare, protection against infection, animal diseases, occupational safety and biological safety officer).
- To ensure that animal housing is species appropriate and advice is provided in the event of differing requirements in the experiment.
- To assign, instruct and inspect the scientific and technical staff deployed in animal husbandry and supervision of stock.
- To undertake the duties of an animal welfare officer.
- To provide medical care for the animals.
- To supervise the veterinary dispensary.
- To provide required laboratory animals from breeding unit or through acquisition.
- To make sure environmental conditions (husbandry, accommodation, stock density, care, feed/water, feeding technique, bedding, climate and lighting) are standardized.
- To ensure that rooms and equipment are properly cleaned, disinfected and sterilized.
- To conduct diagnostic tests aimed at charactering the hygiene status of the laboratory animals (conventional, SPF, gnotobiotic and germ-free laboratory animals).
- To make sure the internal and external transport of animals is conducted properly and expertly.
- To assist in experimental procedures.
- To provide for expert euthanasia of laboratory animals.
- To advise scientists performing animal experiments with regard to the selection of suitable laboratory animals.
- To mediate the dialogue between scientists performing animal experiments and animal welfare organizations or persons interested in animal welfare issues.
- To make sure all those involved in animal experiments receive training and continuing education.
- To advise on the planning and construction of laboratory animal facilities.

(The sequence of the above list does not imply any weighting.)

2.2 Organization

A modern laboratory animal facility that meets scientific requirements and the demands of animal welfare is one of the most complex areas of biomedical research. In the modern laboratory animal facility, equal consideration must be given to the species-specific needs of the animals and the scientific requirements stipulated by the research project. For this reason and also out of economic considerations, the choice of the most appropriate form of organizational for a laboratory animal facility is of fundamental importance. This also includes the early involvement of the animal facility's management.

A distinction is to be drawn between centralized and decentralized facilities, mixed forms and external sub-facilities.

2.2.1 Centralized facilities

A centralized laboratory animal facility is understood to refer to the spatial and organizational concentration of animal housing facilities for a group of several institutions/working groups. The management should include a GV-SOLAS veterinary specialist/scientific expert in laboratory animal science.

The following factors speak in favour of this type of organization:

- Efficient <u>supervision</u> of the research project within the meaning of animal welfare legislation (animal welfare officer, animal welfare committee, supervisory authority).
- Lower costs for structural and technical expenditure and for maintenance of air-conditioning systems and of supply and waste disposal installations.
- Professional, business-like mode of operation, e.g. central procurement, shared use of stock and scientific apparatus and more intensive use of ancillary and adjoining rooms.
- Efficient use of resources (animal housing capacity, equipment, premises, technical installations and personnel).

2.2.2 Decentralized facilities

Decentralization may be required for the following reasons:

- Direct access, use of non-mobile and complex diagnostic installations, avoidance of lost time on clinical diagnosis or on series of experiments in which the animals frequently have to be monitored by institute staff. Optimum adaptation to in-house research.
- Greater opportunity for strict isolation of infected animals. In the case of larger institute
 complexes, the rooms for infected animals may also be accommodated min the area of a
 central facility. However, the rooms for infected animals must be provided with separate
 access, separate ventilation systems (negative pressure!), antimicrobial exhaust air filters
 and other hygienic installations that reliably prevent contamination with disease pathogens.

 It may be easier to house relatively small animal groups of special laboratory animal species that have specific housing requirements (e.g. fish, amphibians, reptiles, birds, bats or also single larger animals) under decentralized conditions than to integrate them into a central laboratory animal unit.

2.2.3 Mixed forms

Mixed forms of laboratory animal housing can be found at many research sites today. The installation of laboratory animal rooms within areas of the institute where animals are housed to a limited extent for acute studies has proved useful in many cases. In each case, a central personnel and organizational supervision of the entire animal facility is necessary in a central building complex. In this way, the advantages of centralization can be usefully combined with those of decentralization – taking into account of course the local circumstances.

2.2.4 External sub-facilities

Laboratory animals are to be kept at the central facility as far as possible. In exceptional situations, the operation of an external sub-facility is necessary. This form of housing primarily concerns the breeding, housing and long-term accommodation of large laboratory animals, such as dogs, pigs and sheep.

There are a number of advantages arising from the structure and situation of such facilities:

- Less investment in building compared with facilities in densely populated regions.
 Lower land prices permit the acquisition of larger areas, as a result of which it is easier to achieve an economically optimum design and to take into account legal requirements for housing large laboratory animals (German Directive on Animal Welfare for Dogs, 2001).
- Less risk of microbial contamination by humans and animals.
- Reduction in noise and odour pollution of the environment.

The same legal requirements apply to the external sub-facility as to a central animal facility.

Literature

Militzer, K., Büttner, D. "Die Bedeutung zentraler und dezentraler Tierversuchsanlagen für Forschung und Tierschutz" in: *Der Tierschutzbeauftragte* 2, p. 84-87, 1996.

3. Planning

Laboratory animal facilities, especially those with strict hygiene and safety requirements, are among the most cost-intensive research buildings. Compared with conventional laboratory facilities, the price per square meter of gross floor area is about 20 to 30% higher.

The planning of such facilities has a substantial impact on subsequent operations, because it determines to a large extent, for example,

- the wellbeing of the animals and their breeding behaviour,
- the quality of experimental results,
- the working conditions of people employed there,
- the operational processes,
- · the investment and operating costs and
- the possibility of subsequent changes of use (see chapter 8.1, Flexibility).

These requirements necessitate a higher degree of technical installation than with other research facilities to provide for trouble-free care of animals and complex barrier installations to comply with hygiene specifications. The system of supply and waste disposal pathways for the housing areas and the cleaning zone with rinsing systems for husbandry systems such as cages and racks results in a larger circulation area as well as additional equipment costs.

Misjudgements at the start of the planning process can often no longer be corrected or, if they can, then only at disproportionately high cost. It is therefore very important to invest sufficient time and expertise in the planning phase – this applies in particular, but not only, to the building services engineering (see chapter 8).

The rule of thumb that planning generates about 10 to 15% of the costs of a building but determines 90% of the overall costs clearly shows how important the planning process is for the construction and subsequent operation of the facility. Yet the possibilities for influencing construction costs are by their very nature highest at the beginning and fall very sharply with all subsequent planning phases.

3.1 Catalysts for a building project

The following cases may serve as a catalyst for a planning project:

- Change in the concept of the laboratory animal facility for scientific reasons.
- Adjustment of the laboratory animal facility to new structural and technical standards.
- Amendment of the legal framework conditions.
- Need for increased capacity.

3.2 Ideal type of process for a building project

A building project should ideally be broken down into three steps in terms of content and timing:

- Master or requirement planning, including feasibility study.
- Planning of the building with all technical installations and systems.
- Construction, including commissioning, trial operation and handover to the user.

3.3 Requirement planning, including feasibility study

3.3.1 Requirement planning

The requirement planning brings together all the parameters and data in a list of requirements and thus serves as the basis for the rest of the entire planning process. Its importance cannot be overstated and is therefore also described in a standard of its own, namely DIN 18205 for Germany.

The requirement planning both for a new building and for the renovation of an existing building can only be put together in close collaboration with the user institution and the management of the laboratory animal facility. To achieve continuous participation within the entire planning process with ongoing communications to preserve the interests of the user, a trusted person - if possible with construction experience - should be named or a small committee formed on the user side. In this way, a contact partner can accompany the planning team during the entire planning and construction phase. One essential task of this contact partner is to identify any diverging interests of the building's other user group and, where necessary, to filter and coordinate these in order to create clear framework conditions for the planning.

The requirement planning for building design (master planning) must basically include the following elements:

- Analysis of the scientific programme for the coming years with regard to animal holding requirements.
- Definition with respect to:
 - Species,
 - Hygiene status of the animals,
 - Safety levels according to the regulations of genetic engineering or handling of bio substances and, where necessary, other guidelines,
 - Number and hygienic status of each holding areas (experimental holding, breeding, quarantine holding etc.),
 - Requirements of different holding areas regarding size and capacity, type of barriers, principle of material or personnel flow etc.,
 - Type of housing and housing systems,
 - Scientific facilities such as laboratories, position in relation to holding areas etc.,
 - Necessary infrastructure, such as storage facility and cage preparation zone.
- Analysis of any laboratory animal holding unit present with respect to possibility of compliance with requirements, especially regarding the aspects of building substance and technical installations in relation to the building's age and need for renovation.

- Analysis of property with respect to:
 - Erection of provisional buildings in the event of renovation of the existing laboratory animal facility.
 - Possibilities for structural extension of existing laboratory animal facilities.
 - Other laboratory animal facilities with spare capacity as fall-back option.
 - Infrastructure development such as supply and waste disposal transport, staff and visitor traffic, security measures and surveillance options.
- In the case of a new building, analysis of the potential building site with respect to building regulations and the technical development of the site infrastructure.
- A room programme/plan of required space that has been developed on the basis of the
 analyses and defines the area and, where applicable, any special spatial, technical or climatic requirements for each room to be used (= usable floor space; areas to be distinguished from this are circulation areas, such as corridors and stairwells, and the technical
 function areas, such as technical centres or shafts).
- Human resources plan of the laboratory animal facility for the coming years.
- Cost budget for building and operation, which essentially includes:
 - Purchase of land,
 - Building construction and building services with the necessary ancillary costs, such as for planning fees etc.,
 - Initial equipment, such as housing systems and other devices,
 - Scientific instruments,
 - Personnel.
 - Operation of building services systems, such as energy, maintenance,
 - Consumables.

Further aspects, such as depreciation, allocation of overheads and also income, are to be considered individually (see chapter 12).

3.3.2 Feasibility study

To review the possibility of fulfilling the above requirement planning for the building design under the given technical and economic circumstances, it is advisable to have a feasibility study carried out. For this, it is essential to commission a planner experienced in laboratory animal facilities.

A feasibility study should include the following points:

- In the case of renovation:
 Evaluation of structural substance and technical infrastructure with identification of the renovation measures required.
- In the case of conversion/extension:
 Investigation of extension options, including connection to existing facilities.

- In the case of a new building:
 Analysis of options for building development on the building site taking into account building regulations and the technical development of all access possibilities for traffic and media supplies, and the identification of any problems, such as emissions and immissions etc.
- Test design of new building or also of existing buildings for review of the feasibility of the room programme with schematic floor plans of important floors and sectional plans.
- Identification of potential risks, such as foundation soil, safety etc.
- Review of cost budget based on test design.
- Rough timetable for realization of the building project.

To increase planning certainty, a detailed description of building requirements and, in particular, of room requirements can already be drawn up at this point. This is usually done in the form of a building space utilisation book in which all use-specific parameters, such as climatic conditions, other requirements of building physics - e.g. protection against vibration and shock, radiological protection or electromagnetic shielding - scientific equipment and installations are described for each group of rooms or each room relevant to its use. Also useful for the further planning steps is an operational description that covers all procedures and their constructional requirements, as well as a functional diagram with a chart of the various pathways.

Once the master planning is completed and both the cost budget and the building site are secured, the architect and the special engineers can be commissioned.

3.4 Planning team for building services planning

The client usually installs a project management to take over the tasks of the building owner in the long and complex planning process for a laboratory animal facility. In the case of public building works, this is often a public building authority or a regional construction agency, a university building authority or a department of building within the research institution. In the industrial or commercial sector, the company's own building department is involved and project steering offices often commissioned. What is crucial here is that the project management remains in constant contact with the user representatives and passes on their concerns to the planning team.

Project management will then carry out the tendering procedure for the selection of the planning team. For the public sector, this is strictly regulated by the ordinance governing the award of contracts for professional services. In the performance of this procedure, care must be taken to ensure that the suitability criteria for the architectural and specialist planning offices to be selected include sufficient experience in the planning and construction of laboratory animal facilities in view of their very specific requirements.

The planning team (design team) usually comprises the following:

User representatives:
 Management of laboratory animal facility, person of trust or committee of scientific working groups using the facility and, if necessary, other persons commissioned by the user, e.g. for workplace safety.

• Project management:

Authorized representatives of the landlord/owner/principal/client.

Architect:

The architect or architectural office is responsible for planning the building construction, designs the building and coordinates all further planners. The architect is also the main contact partner for the user representatives.

Structural engineer:

The structural engineer develops the static system of the building, essentially working in collaboration with the architect.

Landscape architect:

This planner is responsible for designing the open spaces around the building. As a rule, this also includes the supply and waste disposal zones with their access routes.

Planner for building services:

Building services include heating, sanitation and media, cooling and ventilation installations. This planning is heavily influenced by the climatic and media-related requirements of animal housing, which is why it is absolutely essential that the planner has experience and an understanding of the user's concerns.

Planner for electrical engineering:

The electrical engineering planner handles the mains power system with socket outlets and all lighting installations, as well as low-voltage systems such as fire alarms, intruder alarms, access control systems and also IT network and data transmission.

A further area is the building control system with the entire measurement and control technology for all building installations.

Laboratory planner:

The laboratory planner plans the equipment of the laboratories with furniture and sometimes also the animal housing systems and the equipment of animal rooms and the lock installations of the hygiene barriers (autoclaves, material and personnel airlocks), the cleaning systems and logistics. Since this area of planning has a major impact on the operation of the laboratory animal facility, this work must be entrusted to a very experienced planner who has also dealt intensively with operational procedures within a laboratory animal facility.

• Other planners/experts:

Other planners handle specialist areas, such as fire safety, building physics, ground assessment, survey work, radiological protection etc.

The following diagram shows the complex relations between the parties involved in the building project:

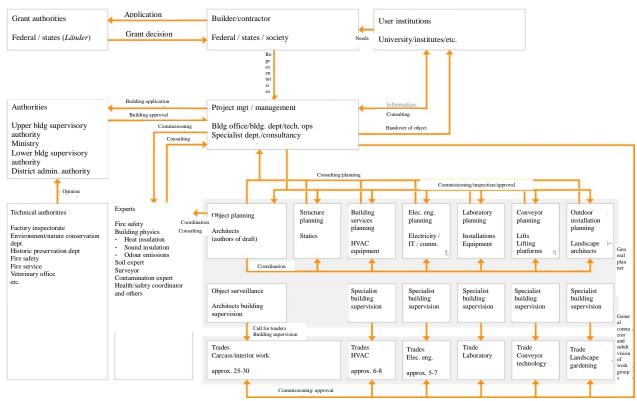


Fig. 3/1: Parties involved in planning and construction (in German speaking countries)

3.5 Building planning process

Addressing all scientific and operational requirements early on, as far as possible by requirement planning, is crucial for the success of planning and of the building project per se. As a basis for schematic and final design planning, the risk assessments on individual workplaces must at all events be presented by the users early on in accordance with the Safety and Health at Work Act, the Occupational Safety Act and also the Ordinance on Safety at Business Premises, so that structural and technical safety measures can be considered in the planning from the outset.

In the early phase of planning, it is recommended to contact the local police. This is necessary so that a risk analysis can be undertaken and safety measures thus included in the planning (requirements for windows, doors, video surveillance if necessary etc.).

Continuous communication within the planning team throughout the planning and execution process helps to define requirements more precisely and to clarify any questions. As a rule, any changes in the plans result in added costs and delays. The later in the planning process these changes are made, the greater their impact.

The normal planning process in a building project is broken down into nine phases, which in Germany are regulated by law through the Ordinance on Fees for Architects and Engineers (HOAI) - in Switzerland, they are regulated by the Swiss Society of Engineers and Architects (SIA); in Austria formerly by the HOA, now unregulated).

The individual planning steps are summarized in the following chart:

Project sequences

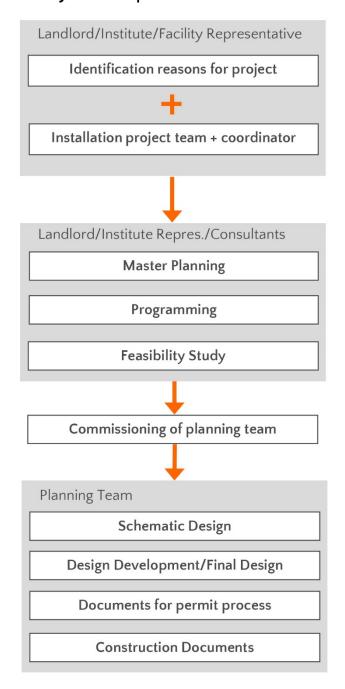


Fig.3/2: Planning steps

More details on the individual planning phases can be found in the appendix.

Appendix: Planning phases HOAI

The text in italics is taken from the German lists of services for the respective planning phases according to the Ordinance on Fees for Architects and Engineers.

Planning phases:

1. Basic evaluation

Clarification of the assignment on the basis of the requirements or the design brief of the client; site inspection; summary, explanation and documentation of the results.

In the case of public sector clients, this planning phase is usually carried out by the building department itself and hence is not assigned to the planning team.

2. Preliminary or schematic design planning

Analysis of fundamentals; coordination of services with those professionally involved in the planning; coordination of objectives; indications of conflicting objectives; elaboration of preliminary planning; examination, presentation and assessment of variants according to the same requirements; scale drawings according to nature and size of building; clarification and explanation of essential interdependent aspects, requirements and conditions (e.g. urban, design-specific, functional, technical, financial, ecological, physical, energy-related, social, public law); provision of work results as a basic framework for the other specialists involved in the planning as well as coordination and integration of their services; preliminary negotiations on approvability; cost estimate; drafting of timetable with the essential procedures of the planning and construction process; summary, explanation and documentation of results.

With the conclusion of this phase, the building is actually fixed in its dimensions and its structural and technical form. The scale of the plan is 1:200.

The costs are estimated on this basis, making this the crucial phase for future users, because any changes in the further planning process will lead to added costs. For this reason there should be intensive communication between the planning team and the user representatives in this phase under the project management's leadership, so that all operational and scientific requirements are taken into account in the schematic design. The time allowed for preliminary design planning should therefore not be too short, but instead should allow time for the examination of planning variants.

3. Design development

Development of schematic design with further consideration of essential interdependent aspects, requirements and conditions (e.g. urban, design-specific, functional, technical, financial, ecological, physical, energy-related, social, public law) on the basis of preliminary planning and as a basis for further planning phases and the requisite public-sector approvals using the contributions of other specialists involved in planning; drawings according to nature and size of building to the requisite scale and degree of detail, taking into account all specific requirements, e.g. with buildings on a scale of 1:100, e.g. with inner rooms of a scale of 1:50 to 1:20;

provision of work results as a basic framework for the other specialists involved in the planning as well as coordination and integration of their services; description of building; negotiations on approvability; calculation of costs according to DIN 276 and comparison with cost estimate up to second level or first level with details of other work involved, e.g. concrete work, carpentry work etc.; updating of timetable; summary, explanation and documentation of results.

The design development refines the preliminary design and technical concept with all the systems, installation routes and shafts. The plan is presented on a scale of 1:100 and for model rooms such as animal housing rooms or laboratories also up to 1:50. The costs are calculated on the basis of individual items, i.e. each building component is recorded in terms of dimensions and cost to arrive at the greatest possible cost certainty.

In the public construction procedure, the budgetary framework, design documents and building or construction documents are drawn up on the basis of the design development plans with a large number of additional forms, in which the project management is then assigned by a parent institution following a review.

The possibility of the planning being influenced by the user, except on questions of detail, thus ends with the conclusion of this phase. The selection of materials (bearing in mind chemical resistance) and also all details on the equipment and installation of the rooms should therefore be considered jointly with the user and ideally formally approved by the user.

4. Documents for permit process

Elaboration and collation of submissions and verifications for permissions or approvals by official public bodies, including applications for exceptions and exemptions, as well as requisite negotiations with authorities using the contributions of other specialists involved in the planning; submission of presentations.

The documents applying for building permits include all requisite plans, descriptions and forms to obtain approval for the construction of the building from the building permit authority of the municipality or the city.

The user must usually submit an operational description for the laboratory animal facility.

5. Construction documents

Elaboration of the construction documents with all the specifications (both in drawings and text) needed for execution of the project on the basis of the final design and documents for the permit process through to the executable solution as a basis for the further work phases; construction, detail and design drawings according to the nature and size of the building to the requisite scale and degree of detail, taking into account all specific requirements, e.g. with buildings on a scale of 1:50 to 1:1, e.g. with inner rooms of a scale of 1:20 to 1:1.

The technical construction plans are prepared in this phase as a basis for inviting tenders for the work and implementation on the construction site.

During this phase, the user only remains involved for the clarification of specific details.

6. Documents for tendering

Establishment of a procurement timetable; preparation of specifications with lists of services according to work packages; determination and listing of quantities based on execution plans using the contributions of other specialists involved in the planning.

The bills of quantities are drawn up according to the different work packages involved with a large number of individual items of building components along with their pertinent quantities, so that the companies can tender their bids on this basis.

The bills of quantities for the installations specific to animal housing, such as housing systems, lock installations, cleaning systems and laboratory equipment, should be scrutinized by the user and, if applicable, amended to ensure user requirements are fulfilled.

7. Tendering

Invitation for bids; review and evaluation of bids, including the establishment of price comparisons according to individual items or partial services; review and evaluation of bids regarding additional and modified services of the executing companies and the appropriateness of their prices; negotiations with bidders; drafting of procurement proposals; documentation of procurement procedure.

In public building procedures, the review of bids and the procurement procedure are strictly regulated and are usually conducted by the building department/project management.

8. Site management

Management of project execution for compliance with the permit or approval by public authority, the contracts with executing companies, the execution documents, the pertinent regulations and the generally accepted rules of technology; organizing inspection of construction work together with other specialists involved in the planning and monitoring of the building; determination of defects; recommendation for the client following inspection; request for inspection by public authorities and participation in inspection; systematic collation of building documentation, drawings and calculations; handover of building; monitoring of the elimination of defects found during inspection.

This phase, which is crucial for the success of the entire building project, includes the organization and monitoring of the building work by construction management and specialists. As a result of the ever declining quality of building work, care must already be taken on the construction site to ensure that the execution is as free of defects as possible, which leads to increased expenditure in construction management. Elimination of defects after the building has started operations, especially behind the barrier, are not possible. After completion of the actual construction and assembly work, therefore, a sufficiently long period is absolutely essential for inspections, commissioning of all systems, verification that they operate well together, instruction of the user in the specific animal housing systems along with a test run that concludes with a smooth and stable operation of all systems for at least 4 weeks.

The planning of these various procedures up to the handover of the building to the user includes a large number of individual processes and, in their complexity, can only be undertaken by an experienced office.

When the cleaned building is handed over to the user, the various housing compartments are decontaminated, after which the building's operations are started up. Workmen or other outside staff are then no longer allowed to enter the animal housing facility or only subject to certain conditions. The user and operator of the building must also be handed the full documentation of all technical systems and equipment providing instructions for the immediate elimination of any faults that may occur in the systems and for the regular performance of all necessary maintenance operations.

9. Supervision of building

Technical evaluation of the defects found within the limitation periods for warranty claims, but not for more than five years after acceptance of the work, including any necessary inspections; inspection of the property for the identification of any defects before the limitation period for claims against the executing companies elapses.

The inspection of the building for subsequently occurring defects is usually undertaken by the client's institutions.

4. Functional areas and types of room

The structural design and equipment of the rooms and functional areas of an animal laboratory as described in this chapter must satisfy a lot of legal requirements in order to be authorized and approved by the authorities. These essentially include the Animal Welfare Act with its pertinent ordinances, EU Directive EU/2010/63 on the housing of laboratory animals, the Gene Technology Act with its corresponding ordinances, the Ordinance on Biological Substances, various Technical Rules on Hazardous Substances, Technical Rules for Biological Agents, the Animal Diseases Act its corresponding ordinances, the Ordinance on Dangerous Substances and the Workplace Directive, which also take into account the aspects of occupational safety and ergonomics.

4.1 Basic principles for determining required space

Planning for any animal laboratory facility and its functional areas goes through several decisionmaking steps depending on the focus of research and the associated animal experiment methods specific to the institution (see chapter 3 Brief for building design):

- 1. What animal species are to be housed on what scale and with what hygiene requirements? How are the animals to be housed (isolator, IVC, housing conventional etc.)?
- 2. To what extent (number of people, frequency, equipment, experimental materials) and within what timeframe do scientists need access to the laboratory animals?
- 3. To what extent is the integration of laboratory and operating rooms necessary for procedures and treatments within the laboratory animal facility?
- 4. Up to what safety level (e.g. with regard to the Gene Technology Act and Ordinance on Biological Substances) is work to be conducted in the rooms in future?

The concept of an animal laboratory developed on this basis must usefully combine three areas with each other in terms of their functions:

- Building technology (size and arrangement of rooms, passageways),
- Building services (installation of water, gas, steam, compressed air and electricity supply lines; data network; air conditioning; cleaning and sterilization technology),
- Equipment technology (cage systems, transport systems, animal room and laboratory equipment etc.).

The main requirements for the technology of an animal laboratory arise from hygiene safety, biosafety, security of supplies and operational safety.

<u>Hygiene safety</u> means that, subject to compliance of the established operational processes, any entry or escape and spread of pathogens is excluded as far as possible.

<u>Biosafety</u> means that, subject to proper handling, biological agents (BAs) and genetically modified organisms (GMOs) must not endanger personnel and that measures are taken that reliably prevent the escape of BAs and GMOs.

<u>Security of supplies</u> means that, even if a part of the building services or equipment technology fails, the required standard conditions are maintained and the supply of laboratory animals with air, the required temperature and relative humidity, food, water, clean bedding material etc. is guaranteed. The security of supplies requires the planning of redundancies for technical systems and equipment, including a risk assessment for any possible disruptions.

<u>Operational safety</u> in this context means continuous assurance of that building services and equipment technology remain functional.

The above requirements determine the concept and the operation of an animal laboratory. The starting point for all considerations is the research concept. The plethora of possible solutions arises from the individual weighting of the particular requirements.

The investment and operating costs to be expected are determined by the animal species, the number of animals, the hygiene standard, safety levels and research-specific access rights. Careful planning (see chapter 3) is therefore indispensable. The scale and degree of demands and wishes (species diversity, access diversity, hygiene standard and air conditioning) have a direct impact on the cost of the facility and its operations.

The coordinated interaction of all corresponding parts of the facility is especially important and effective, because the compatibility of the facility installations is a relevant factor for production costs, operating costs, personnel costs, operating procedures and the functionality of an animal laboratory. It therefore makes sense for the animal house managers, authority representatives (state department for the environment, veterinary office and fire department), architects and technicians to agree on joint solutions in advance.

4.2 Overview of functional areas

The following functional areas are usually necessary in an animal laboratory facility:

- Animal housing area with:
 - Animal housing rooms in differing designs depending on the species being housed,
 - Preparation area for filling any bottles, administration work etc.,
 - Laboratories within the barrier area.
 - Storage facility within the barrier area,
 - Supply corridors and any separate waste disposal corridors,
 - Airlocks as part of the barrier.
- Infrastructure area with:
 - Cleaning and preparation area.
 - Storage rooms for supplies and waste disposal with delivery area for trucks,
 - Technical rooms for operation of the cleaning and supplies/waste disposal systems,
 - Cleaning rooms.
- Social area with:
 - Recreation rooms,
 - Central changing area,
 - Toilets.
- Administration area with offices.

- Research area with laboratories outside the barrier.
- Technical area with rooms for:
 - Ventilation systems,
 - Water conditioning,
 - Generation of heat, steam and/or cooling,
 - Gas production,
 - Data technology and electrical engineering supplies.

4.3 Room layout in the animal housing area

The room layout and thus the organization of an animal housing area as a hygienic unit (barrier) may proceed according to two principles, namely the "one-corridor principle" or the "two-corridor principle" (see following figures).

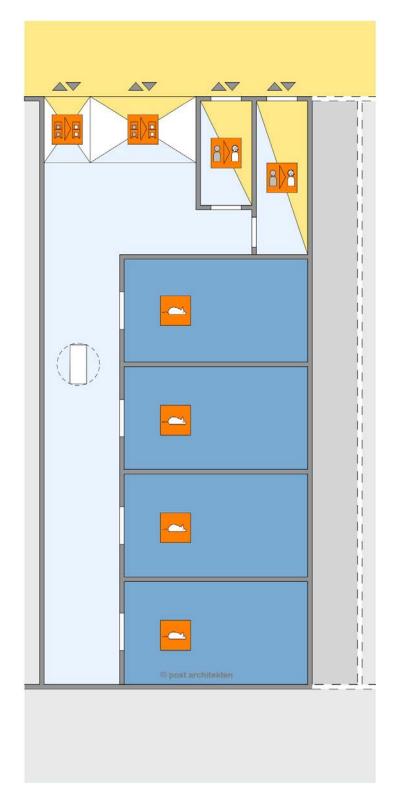


Fig. 4/1: One-corridor principle: here the supplies and waste disposal for the animal rooms take place only on one corridor, i.e. all personnel and material access routes cross before reaching the animal rooms.

	Supply corridor
)	Animal room
	Material airlock
	Personnel airlock

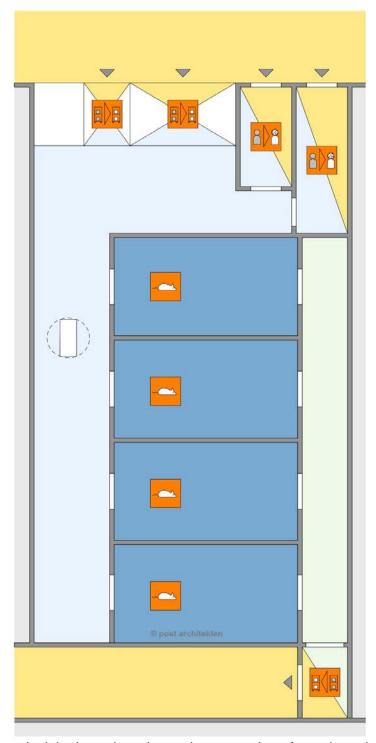


Fig. 4/2: Two-corridor principle: here there is a strict separation of supply and waste disposal pathways.

	Supply corridor
1	Animal room
	Material airlock for supplies
8	Personnel airlock
	Waste disposal corridor
	Exit airlock for material and personnel

Every animal housing unit needs an airlock zone through which both personnel and materials enter behind the barrier into the supply corridor, which should have sufficient storage area directly after the airlock installations. The animal rooms line this supply corridor.

With the <u>one-corridor principle</u> the supply and waste disposal systems for the animal rooms are located only on one corridor, i.e. all personnel and material access routes cross before reaching the animal rooms and thus pose a potentially higher risk of cross-contamination. "Unclean" material may be removed via the supply airlocks or ideally via separate material airlocks arranged in the reverse direction.

With the two-corridor principle (or three-corridor principle, if the animal rooms are arranged in a mirrored layout on both sides of the supply corridor) the supply and waste disposal systems are strictly separated. In this arrangement, the animal rooms feature two doors located opposite each other, through which the clean material enters the animal room on one side and the unclean material leaves on the other side, after the transfer of the animals, and passes into the waste disposal corridor. In this way, the risk of cross-contamination is substantially reduced. This principle is mainly used in housing facilities with specific pathogen-free hygiene status (SPF housing units). The relatively large proportion of circulation area resulting from the additional corridor means that this solution is associated with higher investment costs.

As few technical facilities or building components that have to be maintained or set up by outside personnel should be installed in animal housing areas as possible. This can reduce the entry of technicians with the tools/materials needed and the associated risk to hygiene.

The animal housing area should be supplied with media (air, water, gas, electricity) over a short distance directly from the technical control centre. This is especially applicable for air-conditioning if the rooms are also to be gassed through the ducts. Further explanations on this can be found in chapter 8.

4.4 Types of rooms

4.4.1 Animal rooms

There is no standard animal room for all purposes and laboratory animal species, because the specific requirements of the animal room vary widely depending on the species (laboratory rodent, fish, primates etc.).

An animal room with a floor space of about 20 to 25m², as was often described in the past as the "standard animal room", still has many advantages today, even if larger animal rooms are sometimes desirable for a variety of reasons. Larger species in particular (pigs or dogs) are sometimes housed in other room sizes.

The following <u>advantages</u> speak in favour of relatively small animal rooms with a floor space of about 20 to 25m²:

• Each room can be seen to some extent as one hygiene unit, which considerably reduces the risk of any infection spreading.

- Each room offers the possibility of installing a dedicated climate and time zone and separate access control.
- It is easier to house different species separately. (Classic case: mice and rats not in the same room!)
- The same modular design of the rooms allows standardization effects in their equipment and operation.
- With the right choice of room geometry (minimum width 3 m; length about 6 m), which allows an arrangement of one-sided housing systems (e.g. cage racks) in parallel with a wall, it is possible to achieve a clear set-up that can make the work a lot easier and reduce the deployment of personnel.
- Any disturbances in a room only have an impact on the (relatively few) animals in this room, i.e. the overall system is more tolerant of errors.

Animal rooms of this kind have the following disadvantages:

- Higher construction costs are inevitable.
- Higher equipment costs might also have to be expected for example, when there is a wish to have certain components, such as transfer benches, in each room.
- The greater technical complexity results in higher service and maintenance costs.
- Some special technical solutions, e.g. sliding shelf systems parallel with the wall, cannot be usefully deployed with small room sizes.

The above advantages and disadvantages of relatively small rooms can of course be conversely applied to argue the case for or against relatively large rooms (often 40 m² and in some cases even bigger). With carefully considered room planning, the same cage densities (number of cages per square metre) are achieved for large and small rooms.

The dimensions of the animal rooms and their ancillary spaces are determined by the dimensions and number of the housing systems (e.g. cage racks), the means of transport and the space for the animal attendants to move around in. When planning the shelving set-up within the rooms, attention must be paid to ensuring a good use of the rooms (many cages per square metre) and adequate space for an ergonomically correct work environment. Whether work is to be conducted with one-sided shelves (then usually arranged parallel with the wall) or with double-sided racks (then usually in a comb-like set-up, i.e. at right angles to the longitudinal wall) essentially depends on the room geometry. One-sided shelves are usually used in elongated rooms (minimum width 3 m!) and double-sided racks more in relatively large, often square-shaped rooms. What is important in all cases is that there is sufficient space for the procedure from the transfer stations to the shelves, because otherwise the animal attendants would have to cover very long distances when transferring animals.

When determining room heights, it is necessary not only to bear in mind the ordinance on work-places, but also to consider the space needed for the requisite media (e.g. air-conditioning ducts, electricity and data transmission, fire alarms, water supplies) as well as for the selected air-conditioning concept and, where applicable, also for laboratory furniture (e.g. height-adjustable work-benches). These considerations usually result in ceiling heights between 2.80 m and 3.50 m.

The animal room equipment (i.e. animal shelves, cages, work benches, work and transport trolleys etc.) must allow for easy cleaning and disinfection of the room. It should therefore be kept to a minimum and be mobile (e.g. rollers) for easier floor cleaning. According to the Gene Technology Safety Ordinance (GenTSV), handwashing and disinfection facilities must be provided close to where animals are kept. These facilities should ideally be located in the corridor or in the access airlocks, but not in the animal room.

The doors must be designed so that the animal rooms can be disinfected using liquid and/or gaseous disinfectants. Any leakage of gaseous substances into the environment must be avoided. This can be achieved e.g. by means of "gas-tight" doors (cost-intensive) or by taping over the doors before treating with gas. Doors must have an observation window and open outwards (GenTG/Occupational Safety). To prevent light from entering the animal rooms during the dark phase, panes are covered with a red foil.

4.4.2 Barrier and airlock installations

A barrier is the sum of the structural technical installations (usually in the form of airlocks) and of the hygienic and organizational screening measures for microbiological and hygienic protection of laboratory animals from the environment and/or vice versa. With any such barriers, all potential carriers of contamination must be considered, such as laboratory animals (procurement), personnel (animal attendants, scientists), materials (feed, bedding, laboratory animal technology), media (water, air), biological materials (e.g. substances, cell cultures and sera), special instruments for experiments, wild rodents and insects.

The decision about the type and number of barrier units and airlock systems influences operational processes and hence the operational cost of an animal house. The greater the number of barrier units, the higher the investment costs and both work and operational costs. While relatively large barriers are more economical, the larger number of animals make the negative consequences of any infection outbreak more serious than they would be with smaller units.

Material airlocks (see chapter 8.13):

All materials needed in the clean animal housing areas must be handled in a way that ensures the animals and the research projects conducted with these animals are not compromised by undesirable pathogens. Depending on requirements, disinfection or sterilization may be necessary.

Material airlocks are prefabricated components with a chamber and gas-tight doors or room areas that are separated by structural elements and feature reciprocally interconnected door elements which are loaded from the unclean side and then are emptied from the clean side once the programme is completed. Technical solutions for such installations are, for example, chambers accessible at floor level (e.g. pass-through autoclaves, H_2O_2 airlocks), which are ideally

large enough to take transport trolleys or racks. For other disinfection goods there are also smaller material airlocks that can be immersed, sprayed and gassed.

In the case of biological materials (cells, antibodies, sera etc.), it is necessary to make sure they do not contain any undesirable pathogens themselves. It is therefore advisable to regard biological materials (also those of human origin) as contaminated in principle and to use them only for experiments if their freedom from pathogens (viruses, bacteria, parasites) is proven (Mouse Antibody Production Test, Rat Antibody Production Test, Polymerase Chain Reaction) and documented in corresponding certificates.

Personnel airlocks:

To preserve the microbiological quality of laboratory animals, a hygienically controlled access is also necessary for personnel. It is absolutely essential that personnel change their shoes and clothes and/or cover the body to avoid bringing unwanted pathogens into animal housing areas.

Personnel access to barriers is usually organized via a <u>three-chamber gowning area</u>: 1. Removal of clothing, 2. Mandatory shower (wet or air shower), 3. Donning of sterile scrub clothing. The sequence of the three chambers may vary.

In addition, there are also <u>one and two-chamber gowning areas, with or without a "sit-over"</u> (e.g. for large animal housing units). All persons, including experimenters, are required to use these gowning areas. With their interlock doors, the gowning areas also allow the (air) pressure difference to the animal housing area to be maintained when personnel pass through the gowning area. These doors also impede the entry of insects and wild rodents into the clean area.

Wet shower:

This involves a chamber in which a compulsory shower is taken. The clothes are removed in an antechamber, and the scrub clothing is donned in a room behind the wet shower.

- Air shower:

In gowning areas with an air shower, there are two different variants in the arrangement of the room for the removal and donning of clothes:

<u>Variant 1</u> follows the standard sequence in industrial cleanroom technology:

1. Removal of clothing, 2. Donning of scrub clothing, 3. Air shower cabin, in which the person is "blow cleaned".

<u>Variant 2</u> follows a sequence analogous to that of the wet shower:

1. Removal of clothing, 2. Air shower, 3. Donning area.

The active principle of an air shower consists in the application of airflow to remove any pathogens adhering to particles. The cleansing effect depends on the airflow and the clothing that is worn.

For <u>all</u> variants of these shower airlocks the complete change of (outer) clothes is absolutely integral to preventing the entry of microbes into the animal housing unit!

Animal airlocks:

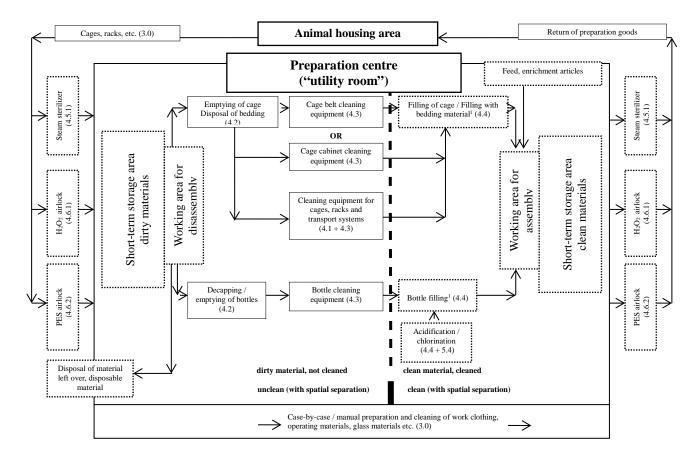
A variety of set-ups is used to transfer animals in or out of a barrier system. In most cases, separate (transfer) airlocks are used. As with material airlocks, various technical installation are available for this. Depending on the hygiene requirement, this may take place in the disinfected transport container or by repacking under laminar flow conditions into a special transfer box that can be disinfected. There are also systems in which a laminar flow workbench can be connected directly to a (transfer) airlock. For the admission of animals, a separate room is often planned that features a (transfer) airlock to the animal housing area. Comparable installations are used for removing animals.

4.4.3 Preparation area

It is imperative that the cages, water dispensers, racks and accessories are prepared outside the animal rooms. If the ("dirty") material from the animal rooms that has to be prepared is transferred to the preparation centre ("utility room") through the airlocks, the contamination of the animal rooms themselves can be minimized, which benefits hygiene in the animal rooms.

Depending on the nature and quantity of the goods to be prepared, varies technical solutions are available to ensure that the mechanical preparation that always has to be strived for is ergonomic, hygienically impeccable and cost-effective. These are described in detail in the <u>brochure on the correct procedure for preparing cages ("Käfigaufbereitung in der Tierhaltung richtig gemacht")</u>, published by the Working Group for Cage Preparation (AK KAB), an impartial working group with members from both industry and research. This brochure also describes the most common mistakes made in preparation and possible ways of avoiding these mistakes.

The individual process steps and the process loop in a preparation centre are shown in the following figure, which is taken from the brochure by the kind permission of the AK KAB. (The numbers that appear alongside the various preparation functions refer to the respective chapters in the brochure.)



Note: Boxes with dotted lines may be included in the process loop as shown, but do not have to be.

Fig. 4/3: Process loop of preparation centre

(Source: Käfigaufbereitung in der Tierhaltung richtig gemacht. Brochure of the AK KAB, Working Group on Cage Preparation, 4th edition, 2013.)

4.4.4 Storage rooms/ancillary rooms

Central storage rooms <u>outside</u> the animal housing areas must be present in sufficient size. Different storage goods, such as cages, feed, bedding material, disinfectants and other consumables, should be stored in different rooms to ensure that any delivery-related contamination remains locally confined. The storage room should be large enough to stockpile supplies for 3 to 4 weeks, which has proved a good length of time in practice. A longer period for stored goods, such as feed and bedding material, would make it difficult to identify and remedy any contamination. Rooms for storing feed should be capable of refrigeration. Safety cabinets are required for the storage of hazardous goods and gas cylinders. If work with radioactive isotopes is carried out in the laboratory and animal housing areas, separate decay rooms must be provided. The delivery point should provide for access by trucks (possibly with a loading bay) and as far as possible a seamless transition with flush thresholds to the storage facilities for delivery of supplies and removal of waste.

Ancillary rooms <u>within</u> the animal housing area for temporary storage of feed, bedding, cages and other materials should be large enough to cover a brief outage or shortfall of preparation components (such as the autoclave). The structural design of these rooms should correspond to that of animal rooms to allow for easy cleaning and disinfection. However, the air change rate may be lower.

Animal cadavers must be stored in chest freezers or cold-storage rooms, depending on the size of the animal housing facility, before they are properly disposed of. In principle, animal waste must be stored and refrigerated or deep-frozen separately.

4.4.5 Social and staff rooms (outside the barrier)

Staff rooms, such as recreation and dining rooms, cloakrooms and changing rooms, as well as sanitary facilities, must be provided outside the animal housing area for animal laboratory staff and experimenters. While the animal rooms have only artificial lighting as a rule, the staff recreation rooms must be provided with natural daylight and visual contact to the outside.

Changing, showering and sanitary rooms:
 Special work clothing should generally be worn within the animal laboratory, i.e. also outside the actual animal housing area. It is therefore a good idea to provide all users and staff with sufficient changing, cloakroom, washing and showering facilities, where outdoor clothing is removed, close to the main entrance.

Toilets:

Toilets should always be provided close to the central changing area (see above).

<u>Note</u>: If it is decided to provide toilets within the barrier, special hygiene measures should be observed:

- Thorough cleaning and disinfection of the hands,
- Disinfectant solution as rinsing solution,
- Repeated daily disinfection,
- Regular hygiene checks (toilet seat, door handles).

· Recreation and dining rooms:

These are located outside the animal housing areas as a rule.

<u>Note</u>: If it is decided to allow consumption of food within the barrier, the installation of an additional recreation room would be required according to the workplace directive. Bringing in food and storing it within the barrier must be strictly regulated in compliance with special hygiene measures to avoid hygiene risks.

4.4.6 Administrative rooms

For staff members who perform management and administrative work in an animal laboratory, appropriately furnished rooms must be provided. These should be located outside the actual animal housing areas, but within the animal laboratory building.

4.4.7 Laboratory rooms

The following laboratories may be required:

- Operating rooms,
- Microinjection labs,
- Irradiation rooms,
- Rooms for imaging procedures,
- Rooms for behaviour studies,
- Dissections, pathology and histology rooms,
- Diagnostic labs (bacteriology, virology, parasitology, clinical chemistry, haematology, calorimetry),
- · Laboratories for genetic quality control,
- Cryopreservation rooms.

For these and other specialist laboratories that might be necessary, special requirements and regulations must be observed. It is therefore recommended that appropriate specialists be involved in the planning.

In view of the cost and complexity of ensuring the compliance of the hygiene status, it makes sense to locate laboratories for animal experiments outside the barrier area as far as possible. Work in laboratory rooms within the barrier area only make sense when the hygiene status of the laboratory animals needs to be maintained in order for the animal experiment to continue (e.g. not in the case of terminal experiments).

All laboratory rooms within an animal housing area must be integrated in the hygiene management of adjacent animal rooms. This means that hygienically important work processes, such as personnel access, the entry of materials and the performance of cleaning and disinfection measures, must be designed according to the same principles as for the other barriers. The temporary stay of laboratory animals in such laboratories must not alter their hygiene status, if they are then returned to the animal rooms of origin, where they continue to be housed and possibly raised.

<u>Note</u>: If this cannot be guaranteed, the animals must then be housed in a separate area. In these cases, a "one-way street" principle has proved effective: working "from clean to unclean".

Installation objects and consumables of these special laboratories are to be kept to a minimum and must on principle be thoroughly cleaned and disinfected. Therefore, the installation of laboratory rooms in the animal housing area should be strictly limited to laboratories in which animal experiments are intensively carried out.

4.4.8 Technical and server rooms

Technical and server rooms supplying animal housing areas are to be set up as far as possible so that they are only accessible from the unclean side. Only the end devices required for their given function are installed in the animal housing rooms. This largely avoids the need for technical equipment to be serviced within barrier areas and the animal housing area thus entered by technical maintenance staff. Server rooms are to be specially secured, because the data has a high level of security relevance. Attention must be paid to ensuring there is adequate ventilation/cooling for dissipation of the heat generated by the equipment.

4.4.9 Quarantine areas

The same basic principles apply to quarantine areas as to the other animal housing areas. Depending on the required size, number of animal rooms and complexity, they may take the form of anything from individual animal rooms to autonomously operated animal housing areas. The introduction of procured laboratory animals into animal housing areas with a high standard of hygiene always poses a high risk to hygiene. This risk can be reduced by means of various measures.

Hygienically consistent and reliable methods are:

- Transfer of animals from external housing units into their own housing areas via embryo
 transfer or hysterectomy. Work with infected laboratory animal strains should be carried out
 in completely separate infection/quarantine stations until successful elimination of the pathogens has been proven.
- 2. Separate housing of procured animals in strictly isolated areas or housing systems for their entire lifetime. Handling of these animals requires appropriate hygiene measures to avoid infecting populations of different origin.

The classical, temporary quarantining of laboratory animals is fraught with many disadvantages and is not an appropriate means of excluding the risk of pathogens being introduced. It leads to loss of flexibility resulting from the animals being kept in a temporary period of compulsory detention (change in age and weight). It is also associated with high costs resulting from the need for additional space, high organizational and personnel costs, high laboratory capacity and costs for examination of the animals during the quarantine phase. The examination of the animals during quarantine must take into account in the sample size, sample type and sampling time the different lengths of pre-patency periods (parasites), latency periods (antibody formation after infection) and the distribution rate of pathogens (prevalence) so that reliable conclusions can be drawn.

Literature

2007/526/EC Commission Recommendation of 18 June 2007 on guidelines for the accommodation and care of animals used for experimental and other scientific purposes ("Appendix A of ETS 123").

Käfigaufbereitung in der Tierhaltung richtig gemacht, Brochure on the correct procedure for preparing cages, published by AK KAB, Working Group on Cage Preparation, 4th edition, 2013.

5. Housing systems

Laboratory animals may be shielded against environmental influences with differing degrees of intensity. This may take place at the level of an animal facility department, a housing room, a group of cages within a housing room or the individual cage.

The monitoring of physical factors requires ventilation installations for air-conditioning in the room (air temperature, humidity, pressure, air change rates and air filtration) as well as technical installations for regulating light intensity, light rhythm and, if applicable, also for noise reduction (see chapter 8).

For the hygienic shield, not only is the above-mentioned air-conditioning installation required, but also airlock systems and disinfection devices for materials and personnel, as well as clear regulations (SOP) for the handling of animals on locking into the facility, on provision of supplies and on how to perform experiments.

Basically a distinction is drawn between hygienic open respectively conventional animal housing systems and barrier housing systems. Thanks to the combination options of various cage systems with diverse organizational measures – especially for the housing of rodents – a plenty individually different forms of housing are possible.

GV-SOLAS has published separate brochures on various species, such as mice and rats (see GV-SOLAS homepage). Therefore, only general aspects of the housing systems are described here.

5.1 Conventional housing systems

In a conventional housing system, hygienic measures are reduced to the donning of overshoes and lab coats or not even provided at all in favour of easy access. There is no strict hygienic isolation of the animals from the environment outside the housing area. As a rule, there is no provision for special barrier measures and hygiene airlocks. The animals are often kept in open cages with wire mesh closures or in open-top boxes, depending on the species. The handling of the animals does not require any special hygienic measures. Pathogens can be transferred between all cages relatively unhindered via dust particles and aerosols, unless other additional measures are taken (e.g. static filter tops on the cages). Allergens also spread within the room by the same routes. The proportion of dust in the bedding material has a great influence on the spread of allergens in open cage housing in particular. Ventilation in the area occupied by the animals essentially depends on the airflow in the room. Based on many years of experience, 15 to 20 air changes per hour are recommended in the animal rooms for the most commonly used species (see chapter 8).

5.2 Barrier systems

5.2.1 Room barriers

As in conventional housing, the regulation of air-conditioning in the room is standardized. In addition, the animals are subject to hygienically strict isolation from the environment outside the housing room. To this end, the rooms are ventilated via high-efficiency particulate air (HEPA) filters. Depending on the intended purpose, the system may be run under positive pressure vis-à-vis the environment (immissions barrier: avoiding the entry of pathogens) or negative pressure (emissions barrier: avoiding the escape of pathogens). Personnel access happens via personnel airlocks with or without showers (air or wet showers), but always after a change of clothes and disinfection measures. Material is brought in through material airlocks (sterilizers for thermostable goods; im-

mersion tanks, H_2O_2 chambers and disinfection locks for heat-sensitive goods). Doors to the unclean area, which are only needed for revision purposes, are gas-tight or sealable and must always be kept closed during barrier operation.

For housing in <u>open cage systems</u> (cage + wire mesh lid without any other top) there are no hygiene barriers between the cages of a room within the barrier system.

5.2.2 Animal housing cabinets

For the housing of rodents, animal housing cabinets are also used. They are suitable for accommodating small numbers of animals in rooms that are otherwise not designed as animal housing rooms because the air change rate is too low. They are well suited to the accommodation of animals close to the laboratory during experiments. Usually, animal housing cabinets suck the required air from the air-conditioned room and pass it through HEPA filters. After it has flowed through the cabinet, the air is fed back into the room either filtered or unfiltered. Animal housing cabinets with integrated regulation of temperature, humidity and light rhythm are likewise available, but are designed rather for experimental use. The air change rate in the cabinet is substantially greater than the air change rate in the room. An animal housing cabinet can be seen as a hygienic unit if the intake air is HEPA-filtered and the opening of the cabinet and the handling of the open cages are conducted under laminar flow conditions. If cages with filter tops are used within the cabinet, the cage is the hygiene unit. In combination with the use of the cabinet under laminar flow conditions, a hygienic shield comparable to IVC can then be achieved between the individual cages in the cabinet.

5.2.3 Individually ventilated cages (IVC)

IVC systems are frequently used in particular for the breeding and housing of rodents. IVC housing means that the cage is closed by means of a special top and, linked to a special IVC rack, is supplied via a blower unit with air that is sucked from the air-conditioned room and also HEPA-filtered. As a rule, the cages are supplied with 60 to 90 air changes per hour. The advantages of IVC housing lie in the very good hygienic shield provided for the animals, the markedly reduced exposure of personnel to allergen and dust and the possibility of using it also in rooms whose ventilation capacity is insufficient for open cage housing. Its disadvantages over open cage housing are the higher investment costs and the relatively time-consuming cage-change routines, which, as outlined below, can only be offset to a limited extent by longer cage-change intervals. From the perspective of the cage occupant, the IVC cage also differs from the open cage by the fact that the animals are largely shielded from the acoustic and olfactory stimuli of the outside world.

The air exchange in IVC cages can be technically solved in such a way that no draughts occur. As a result of the high air change rates in the IVC cage, humidity and noxious gases can be much better evacuated than in the open cage. This would permit longer intervals between cage changes, but a weekly change of cages should be observed as a rule for reasons of hygiene and animal checks. When monitoring the hygiene of animal stocks in IVC housing systems (Compton et al. 2004a, Compton et al. 2004b) account must be taken of the fact that every cage in principle is a hygienic unit in its own right. The study of a sample of animals from the entire population does therefore not have the validity of a sample of identical size from an open housing system. Relatively large animal populations in IVC can also only be inadequately monitored by means of the sentinels that are kept on bedding samples from different cages. Everyone involved must be aware

of the lower diagnostic reliability of this method (see GV-SOLAS brochure on "Monitoring the hygiene of mouse and rat stocks in different housing forms").

There are big differences between the IVC systems of different manufacturers when it comes to the design of the cages, the airflow, safety technology, operation of the blower units, practical handling procedures and many technical details. Careful system selection is therefore urgently advised. A good aid to selection is the checklist developed by TIZ-BIFO, Munich (Part II of the *Leistungsbewertung von IVC-Systemen* [Performance assessment of IVC systems], see homepage of GV-SOLAS and TIZ-BIFO).

5.2.4 Isolator

Housing in isolators is the most complex form of housing. Isolators are force-ventilated compartments usually with a capacity of 1 to 2 m³, whose outer shell is made of a transparent, flexible, airtight plastic film. For the provision of supplies and removal of waste, special sterilization containers ("supply cylinders") and special connecting airlocks are required, which have to be chemically disinfected each time something enters or leaves the isolator. For the breeding of pathogen-free rodents, positive-pressure isolators are the system of choice. Negative-pressure isolators are essentially for housing e.g. experimentally infected animals. There is no olfactory delimitation of the cages within the isolator. For many applications with less stringent hygiene requirements, especially in the experimental area, IVC housing is a practical and economic alternative. The microbiological safety of isolator housing, however, is still higher, unless IVC systems are used that have been specially developed for this purpose.

6. Housing units

6.1 Cages

Cages with largely standardized dimensions are used for housing laboratory rodents (mice and rats). The GV-SOLAS brochures on housing mice and rats describe the standard cage types for rodents in detail.

Various plastics have proved suitable for cages:

Cages and water bottles may be made of polycarbonate (PC), polysulfone (PSU), polyphen-ylsulfone (PPSU), polyetherimide (PEI) or other plastics. The disadvantage of PC is that it becomes milky and brittle with frequent autoclaving as a result of the unavoidable hydrolysis with this material. The newer materials PSU, PPSU and PEI are thermally, chemically and mechanically more resistant. The most robust are PPSU and PEI. PSU lends itself to frequent autoclaving - and PPSU or PEI even more so; with autoclaving procedures at temperatures of > 121°C, these high-performance plastics are absolutely required. When cages are autoclaved after use together with the bedding, urine and faecal droppings, the destruction of PC cages is accelerated by combination with the high temperature. When filled PC water bottles are autoclaved at 121°C (and therefore the temperature of the inflowing steam is necessarily > 121°C), local temperature increases above 121°C may destroy the PC water bottles, as PC has its thermal limit at 121°. PPSU and PEI have the added advantage of being inert to all standard detergents and rinsing aids. Cages made of each of the four materials mentioned should not be gassed with hydrogen peroxide, because H_2O_2 binds to these plastics and residual concentrations are still detectable in the gassed cages days later.

PEI is approximately half as permeable to light as PC, PSU and PPSU, which do not substantially differ in this respect. (GV-SOLAS publication: *Tiergerechte Haltung: Labormäuse 2014* [Animal-suitable housing: laboratory mice 2014])

For some rodents (e.g. rats and gerbils) cages in an elevated design are also available. For all cage sizes, there are matching cage tops made of stainless steel, some of which are likewise obtainable in an elevated design. In the case of systems for supply rodents with food (water bottles with drinking nipples, wire mesh tops with feeders) care must be taken to ensure they are at the right elevation (above the cage floor). To make sure young animals also have access to food and water, the distance of the feeder and the drinking nipples from the floor must not be too great. On the other hand, drinking nipples that are too low can lead to the bottle spilling, when the animals pile up bedding material under the nipple.

Guinea pigs and rabbits are kept in different stainless-steel or plastic cages. Plastics of differing hardness and scratch resistance are available, which vary in temperature resistance.

6.2 Housing installations for relatively large animals (pens, stalls, kennels)

As a rule, the species-appropriate housing of relatively large animals requires installations whose dimensions cannot be usefully represented with (mobile) cages. Species such as pigs, sheep, goats, dogs, cats, ferrets or also poultry are therefore usually housed on the floor of the animal room in pens, boxes or kennels.

Pens:

Pens are housing units with fixed half-height walls (height about 120 cm) and a floor space of 6 to 20 m². They should allow partitioning, so that the animals can be kept in groups or also singly while maintaining contact with the group. The floor must be non-slip and thermally insulated or heated in the lying area.

Stalls:

Stalls are housing units in closed buildings with a floor space of at least 2 m² and a maximum size of 6 m² as a rule. Stalls should have dividing walls that can be removed to allow group housing which is appropriate for most animal species. Unlike pens, stalls are usually floor-to-ceiling installations or at least 2 m high and are fitted with a wire mesh cover so that jumping or climbing animals such as dogs, cats or ferrets can be kept in them. The stall enclosures are predominantly made of metal grids.

Kennels:

This term is used in the German ordinance on keeping dogs, which also applies to laboratory dogs. Kennels inside buildings must be at least 6 m² in size and high enough to ensure that the dogs cannot reach the upper part of the enclosure with their paws. No side of the kennel may be shorter than 2 m.

The corridors outside of pens, stalls or kennels should be non-slip and easy to clean. They should also serve as a security gate. Connecting doors in long corridor areas are useful for this purpose.

Runs:

Runs are fenced enclosures, usually outside buildings, to which animals can be brought to meet their need for exercise or to make it easier to clean the housing areas.

Flexibility of housing forms:

Since the demand for relatively large animals can fluctuate in terms of number and species, the pens, stalls and kennels should be designed in a modular form of construction that allows a wide variety of animal species to be housed in groups or also singly but with contact to the group. With a basic format of 3 m in depth and 1 m in width, it is possible to keep cats, ferrets or poultry in small groups. If two such stalls were combined, this would provide the size necessary for a single dog kennel. Three combined units provide a pen area of 9 m² and hence the minimum space for six sheep weighing up to 60 kg. It is sufficient if only the front two thirds of the dividing walls are removable. The rigid last third allows lying spaces to be installed with bedding materials. Here the floor should also be thermally insulated. It is a good idea if the upper part of the wall (above 120 cm) can be removed for species that jump very little. With all the above-mentioned housing installations, water and diet dispensers must be adapted to the needs of the animal species concerned.

6.3 Housing areas for rarely used animal species

If rarely used animal species are deployed, the required housing conditions must be discussed and defined with the relevant experts. Further information is contained in the background information to Appendix A of ETS 123.

7. Guidelines for housing laboratory animals

7.1 Legal directives

Regulations on the care and accommodation of vertebrate animals used for experimental and other scientific purposes in keeping with animal welfare are set forth in Annex A of the European Convention of 18 March 1986 for the protection of vertebrate animals used for experimental and other scientific purposes, supplemented by the protocol of amendment of 22 June 1998. Annex A was revised in 2007 and, together with Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010, forms the European legal requirements for the accommodation of laboratory animals. With the ordinances of Germany's Federal Ministry of Food and Agriculture dated 15 November 2007 (Annex A) and 1 August 2013 (Directive 2010/63/EU), both European regulations have been transposed into national law in the form of the animal welfare act and the ordinance on the welfare of laboratory animals, both from the year 2013. General requirements on the housing of laboratory animals are defined in §1 of the ordinance on the welfare of laboratory animals and in §2 of the animal welfare act. Annex A defines concrete housing standards for individual animals of various species if they are used for scientific purposes. Further more specific ordinances to date include the ordinance on the welfare of dogs (2001), the ordinance on the welfare of pigs housed indoors (1994), the ordinance on the welfare of calves during housing (1997) and the ordinance on the welfare of laying hens housed in cages (1987). Further information on the housing of laboratory rodents are provided in the publications of GV-SOLAS. Details on other species used for scientific purposes can be found in Annex A.

Various scientific studies on enrichment for laboratory animals (see also The COST Manual of Laboratory Animal Care and Use: Refinement, Reduction, and Research, 2010) show that the question which enrichment measures are possible or necessary always depends on the animal species/strain/line concerned, the form of housing and the scientific purpose. This publication can therefore offer no detailed information on this question.

The housing rules given here conform to the minimum requirements of Annex A. Recommendations that deviate from these requirements are identified as such and the reasons for the deviation are explained. Differing recommendations in older GV-SOLAS publications are no longer valid.

7.2 Guidelines for important laboratory animal species

The cages should be made of a material which is easy to clean and the construction of which allows adequate monitoring of the animals without disturbing them.

7.2.1 Mouse

The laboratory mouse is derived from the wild house mouse (*Mus musculus*) and subspecies (Festing & Lovell 1981, Wade & Daly 2005). Mice are timid flight animals. Nocturnal activity and preference for environments that offer protective structures, such as caves or bolt holes, are to be seen as adaptations to their marked exposure to predators in the open (Jennings et al. 1998). During the domestication of laboratory mice, all behavioural elements and the underlying pattern of social organization of the wild forms remain intact. Territoriality of both sexes with markedly greater incompatibility between males is the underlying patterns of social organization in the wild. When

space is limited in the laboratory housing environment, these underlying patterns manifest themselves in a despotic hierarchy between males and the formation of stable cage groups between the females (Mackintosh 1981). It is notable that there are marked differences between the different strains of laboratory mouse as regards the frequency of almost all behaviour patterns and the tendency for triggering these behaviour patterns. This applies also to the compatibility of mice (Mondragon et al. 1987, Guillot & Chapouthier 1996).

The area of 330 cm² specified in ETS 123 is the minimum space for housing an individual animal or a breeding pair. Cages with an area of more than 500 cm² should be the standard for the group housing of mice. This permits the housing of up to 6 Mice (up to 30g b.w.) in type II long and up to 10 mice in type III cage (up to 30g b.w.), according to ETS 123. A floor space of 500 cm² facilitates the use of enrichment measures (e.g. nesting material or possible places of refuge). Although group housing is basically preferred, individual housing for male mice that are often in-

Although group housing is basically preferred, individual housing for male mice that are often incompatible is the more appropriate alternative. Mice should always be offered nest-building material.

Table 7/1-1: Guidelines for cage housing of mice in stock, during procedures and breeding

	Body- weight	Minimum cage size cm ²	Minimum enclo- sure height	Floor area per animal
	g		cm	cm ²
In stock and	≤ 20	330	12	60
during proce-	21-25	330	12	70
dures	26-30	330	12	80
	> 30	330	12	100
Breeding		330 for a monogamous pair or a trio; for each additional fe- male + litter a further 180 cm ² should be added	12	
Housing in breeding cages* Cage size 950 cm ²	< 20	950	12	40
Cage size 1500 cm ²	< 20	1500	12	30

^{*} Post-weaned mice may be kept at these higher stocking densities, for the short period after weaning, in case that the animals are housed in larger enclosures with adequate enrichment. These housing conditions should not cause any welfare deficit, such as increased levels of aggression, morbidity or mortality, stereotypies and other behavioural deficits, weight loss, or other physiological or behavioural stress responses.

(Source: ETS 123 Appendix A 2007)

Since daily weighing of the animals is not practicable, it is recommended that maximum stock densities per cage type be defined on the basis of the background strains of mice used.

An example of this is given in the following table.

Table 7/1-2: Standard cages in Europe for housing and breeding mice with a max. stock density (according to Directive 2010/63/EU)

Cage type	Cage floor area ¹ Approx. figures in cm ²	Max. number of mice (≥30g b.w.)²
I long	335	3
II	370	3
I super long	435	4
Type 500	510	5
II long	540	5
III	820	8
IV	1820	18

The minimum cage height is 12 cm.

7.2.2 Rat

Laboratory rats are derived from the brown rat (*Rattus norvegicus*) in its wild form. Rats are very good climbers, swimmers and burrowers and have highly developed olfactory, acoustic and tactile senses. These sensory elements are characteristic of wild and laboratory rats in equal measure. Wild rats live territorially in social communities with a promiscuous mating system, shared rearing of young and marked incompatibility with members of other communities. Laboratory rats have been bred and kept for scientific purposes for about 100 years. Today there are more than 400 conventional inbred and outbred strains and a large number of transgenic lines available.

Appropriate housing of laboratory rats requires the possibility of group housing. Species-specific social behaviour must be developed in social groups during the rearing phase, and subsequent housing must also be provided in social groups to avoid "isolation stress". The optimum group size is 3 to 5 rats. Cages with a floor area of about 1800 cm² (this size corresponds to a type IV cage) should be the "standard cage" for housing rat groups (max. 1500 g total bodyweight of rat group). This cage also allows a minimum of enrichment measures (e.g. nesting material or possible places of refuge). The cage should not exceed a height of 18 cm. An elevated cover should be used for full-grown rats (cage height then 24 cm). Housing in smaller IVC cages (1450 to1500 cm²) is also possible. Type III cages should only be used for experimental purposes (study-related individual housing).

¹⁾ The calculation of the cage floor area may vary from one manufacturer to another, because the transition from sloping cage wall to flat cage floor gives rise to different possibilities for the definition of the floor area.

²⁾ The stock density is based on the bodyweight of the mice. In the case of young mice, the end weight of the animals should always be taken into account.

Table 7/2: Guidelines for cage housing of rats in stock, during procedures and breeding

	Bodyweight g	Minimum cage size cm ²	Minimum cage height cm	Floor area per animal cm²
In stock and during proce- dures*	≤ 200 201-300 301-400 401-600 > 600	800 800 800 800 1500	18 18 18 18 18	200 250 350 450 600
Breeding		800 Mother + litter; for each additional adult animal permanently added to the cage add 400 cm ² .	18	
Housing in breeding cage** Cage size 1500 cm ²	≤ 50 51-100 101-150 151-200	1500 1500 1500 1500	18 18 18 18	100 125 150 175
Housing in breeding cage** Cage size 2500 cm ²	≤ 100 101-150 151-200	2500 2500 2500	18 18 18	100 125 150

^{*} In lifetime studies, animals should be provided with cages of a suitable size to enable the animals to be socially housed. As stocking densities towards the end of such studies may be difficult to predict, there may be occasions where the provided space per individual animal may fall below those indicated above. In such circumstances, priority should be given to maintaining stable social structures.

(Source: ETS 123, Appendix A 2007)

This guideline allows a type III cage to be used for housing an individual rat, for housing 3 to 4 young rats or for housing a lactating dam with her litter. However, for housing rats, Appendix A recommends in general the use of larger cages that allow a sophisticated use of space.

7.2.3 Mongolian jird/gerbil

Jirds or gerbils (*Meriones unguiculatus*) live in family groups in the wild. Housing in groups requires correspondingly large cages. The groups should be formed and keep stable before the animals reach sexual maturity. In the event of incompatibilities, the animals must be separated. Pair housing or the housing of one male with 2 females (trio) is appropriate.

A minimum area of 1800 cm² (MIV) is recommended for each breeding pair. According to Appendix A ETS 123 (2007) an area of 1200 cm² is permitted. But this does not do completely satisfy the need of these very active animals for locomotion. Only correspondingly large cages can be divided into sleeping, feeding, and "toilet" areas by the animals. The cage height must be at least 14 cm to

^{**} Post-weaned rats may be kept at these stocking densities, for the short period after weaning until issue, provided that the animals are housed in larger enclosures with adequate enrichment. These housing conditions should not cause any welfare deficit, such as increased levels of aggression, morbidity or mortality, stereotypies and other behavioural deficits, weight loss, or other physiological or behavioural stress responses.

allow the animals to stand upright.

To satisfy the animals' need for activity, various structures must be provided for gnawing, burrowing and building, such as gnawing wood, deep bedding, pipes, nesting material etc. Intensive use is also made of sand baths. Grains may also be distributed in the bedding provided this does not conflict with the feeding regimen. If gerbils are not provided with the opportunity for nest-building behaviour, they develop very often stereotypies (Wiedenmayer 1997).

Table 7/3: Guidelines for cage housing of gerbils in stock, during procedures and breeding

	Bodyweight q	Minimum cage size cm ²	Minimum cage height	Floor area per animal
			cm	cm ²
In stock and dur-	≤ 40	1200	18	150
ing procedures	> 40	1200	18	250
Breeding		1200	18	
		Monogamous pair or trio with offspring		

(Source: ETS 123, Appendix A 2007)

7.2.4 Hamster

A few different species of Hamsters are used in animal experiments. Some of them are socially compatible, other species lead solitary lives. Their level of activity is not as high as that of the gerbil. The cage areas can therefore be somewhat smaller, but should be at least 800 cm² (type III) for a breeding pair or a female with a litter (ETS123, 2007). The by the GV-SOLAS recommended size is 1800 cm² (type IV), because this type of cage also allows group housing and enrichment to reduce aggression (opportunities to retreat and hide). The cages must be at least 14 cm in height.

Young animals, some golden hamster lines (*Mesocricetus auratus*) and a few dwarf hamster species (*Phodopus sungorus* and *P. campbelli*) can usually be kept in groups. Chinese dwarf hamsters (*Cricetulus griseus*) are considered less socially compatible.

Hamsters prefer a completely darkened sleeping area. Therefore, a hiding place and/or nesting material must be provided. The opportunity for burrowing should be provided with a thick layer of bedding and pipes. Sand baths are extensively used by dwarf hamster species in particular. If the feeding and hygiene regimen allows, gnawable material and grains that can be hoarded should also be provided.

Table 7/4: Guidelines for cage housing of hamsters in stock, during procedures and breeding

	Bodyweight	Minimum cage size	Minimum	Floor area per
	g	cm ²	cage height	animal
			cm	cm ²
In stock and dur-	≤ 60	800	14	150
ing procedures	61-100	800	14	200
	> 100	800	14	250
Breeding		800	14	
		Mother or monoga-		
		mous pair with litter		
Housing in breed-	< 60	1500	14	100
ing cage*				

^{*} Post-weaned hamsters may be kept at these stocking densities, for the short period after weaning until issue, provided that the animals are housed in larger enclosures with adequate enrichment. These housing conditions should not cause any welfare deficit, such as increased levels of aggression, morbidity or mortality, stereotypies and other behavioural deficits, weight loss, or other physiological or behavioural stress responses.

(Source: ETS 123, Appendix A 2007)

7.2.5 Guinea pig

Domestic guinea pigs (*Cavia aperea f. porcellus*) have a considerable need for security, which has to be taken into account with a sufficient number of possible hiding places. The provision of large quantities of hay is also suitable for this. Wide, open floor areas are hardly used. Guinea pigs like to sit on their hiding places. These should therefore not be too high and should have a flat roof.

The minimum cage size for full-grown animals or breeding pairs is 2500 cm² (ETS123, 2007). Small groups of one male and 2 to 5 females is recommended for breeding. However, floor housing in larger groups (3 to 10 males and 15 to 20 females) would be preferable. For young animals, growing up in a colony is crucial for the development of normal social behaviour and for successfully dealing with stress (Sachser & Lick 1991).

Every cage and every enclosure should have at least 2 feeding dish and water bottles to ensure that all animals have access to them at all times. Since guinea pigs like to play with water bottles and tend to empty then in the process, attention must be paid to ensuring there is adequate water supply and that the bottles do not run dry. In the case of the diet care must be taken to ensure there is adequate provision of vitamin C and hay.

<u>Table 7/5: Guidelines for accommodating guinea pigs in stock, during procedures and breeding in cages or ground level enclosures</u>

	Bodyweight	Minimum cage size	Minimum	Floor area per
	g	cm ²	cage height	animal
			cm	cm ²
In stock and	≤ 200	1800	23	200
during proce-	201-300	1800	23	350
dures	301-450	1800	23	500
	451-700	2500	23	700
	> 700	2500	23	900
Breeding		2500	23	
		Pair with litter. Add		
		1000 cm ² for each ad-		
		ditional mother animal.		

Floor arrangement: Solid floors with bedding or perforated floors are preferable to lattice floors.

(Source: ETS 123, Appendix A 2007)

7.2.6 Rabbit

The domestic rabbit is the domesticated form of the European rabbit (*Oryctolagus cuniculus*) and belongs to the order of lagomorphs (*Lagomorpha*).

Territorially, wild rabbits live in small mixed-gender groups. These basic forms of social organization are also to be assumed for the domesticated rabbit.

Rabbit cages must allow so-called bunny jumps and relaxed lying. The rabbits must be able to sit upright in the cage. A raised lying area with a hiding place must be provided as minimum enrichment. Gnawing opportunities with soft wood, hay and straw also lend themselves to use as further enrichment factors.

The minimum cage area for rabbits according to ETS 123 is 3500 cm² for an individual animal or 2 compatible animals with a bodyweight of less than 3 kg. A mother animal in this weight category can also be kept in this cage area with her litter, although a separate nest box of at least 1000 cm² must be added. The cage height for rabbits up to 5 kg bodyweight must be at least 45 cm. The relevant weight-specific tables from ETS 123 (2007) are shown below.

In the case of young animals, the cage area should be based on the final bodyweight so that the animals are provided with the appropriate space for movement and play also in long-term studies.

Wherever possible, rabbits should be kept in stable groups or as stable pairs (as a rule two females). Ideally, individual cages can be combined to form interlinked units. Group floor housing has proved successful, but care must be taken to ensure adequate hiding places are provided. The area must be large enough to allow flight and evasion opportunities for the animals and to subdivide it into functional areas (feeding, resting, and elimination place etc.). Enclosures and hiding places should not form dead ends, and lower-ranking animals must always have some areas to which they can escape. Also in the case of floor housing, raised observation and lying areas must be provided. Male animals, however, must be housed individually as a rule when they reach sexual maturity.

In regards to the floor, rabbits have minimal requirements. Plastic perforated floors have proved

suitable as have solid floors. Rough floors must be avoided. The paws should be regularly checked for lesions. It has proved useful, however, to provide bedding material in floor housing systems. For breeding, the mother animals need a separate nest box, which allows them to keep their distance from the litter, as well as nesting material for the young. When the young leave the litter box, the mother should be provided with an elevated area to which she can escape. For weaning purposes, it is better to remove the mother and leave the young together in the litter cage until they reach sexual maturity.

Table 7/6-1: Cages and enclosures for rabbits aged > 10 weeks

Final bodyweight in kg that every	Minimum floor area for one or	Minimum height
rabbit reaches in this accommoda-	two socially harmonious animals	cm
tion	cm ²	
≤ 3	3500	45
3-5	4200	45
> 5	5400	60

The table is to be used both for cages and for pens. A raised area should be provided in cages (see Table 7/6-4.). Enclosures should contain structures that subdivide the space allowing the animals to initiate or avoid social contact. The additional floor area is 3000 cm² per rabbit for the third, fourth, fifth and sixth rabbit, while 2500 cm² should be provided for each additional rabbit above a number of six

(Source: ETS 123, Appendix A 2007)

Table 7/6-2: Cages for a doe plus litter

Weight of doe	Minimum enclosure	Additional area for	Minimum height
(kg)	size	nest boxes	cm
	cm ²	cm ²	
≤ 3	3500	1000	45
3-5	4200	1200	45
> 5	5400	1400	60

At the latest, three to four days before giving birth, the does should be provided with a separate compartment or a nest box where they can build a nest. The nest box should preferably be outside the cage. Straw or other nesting material should be provided. The cage should be designed so that the doe can move to another compartment or raised area away from her pups when they leave the nest. After weaning, the pups should remain in their breeding cage as long as possible. Up to eight litter mates may be kept in the breeding cage from weaning until seven weeks of age; five litter mates may be kept on the minimum floor area from eight to ten weeks of age.

(Source: ETS 123, Appendix A 2007)

Table 7/6-3: Cages and enclosures for rabbits aged < 10 weeks

Age	Minimum enclo- sure size cm ²	Max. number of ani- mals on the mini- mum floor area	Extra area for each additional animal cm ²	Minimum height cm
Weaning to 7 weeks of age	4000	5	800	40
8-10 weeks	4000	3	1200	40

The table is to be used both for cages and for pens. Pens should contain structures that subdivide the space allowing the animals to initiate or avoid social contact. After weaning, the litter mates should stay together in their breeding cage as long as possible.

(Source: ETS 123, Appendix A 2007)

Table 7/6-4: Recommended dimensions of a raised area in rabbit cages

Age weeks	Final bodyweight kg	Approximate dimensions cm x cm	Approximate height above cage floor
			cm
< 10	-	55 x 25	-
> 10	<3	55 x 25	25
	3-5	55 x 30	25
	>5	60 x 35	30

To allow proper use of the raised area and the cage as a whole, the values given above for the raised area size and height are optimum dimensions, with very close minimum and maximum limits (\pm 5-10%). If there are scientific or veterinary justifications for not providing a raised area, then the floor area should be 33% larger for a single rabbit and 60% larger for two rabbits to facilitate the locomotor activities of the animals and to give the inferior animal the opportunity to escape from a more dominant one.

(Source: ETS 123, Appendix A 2007)

7.2.7 Cat

Domestic cats (*Felis catus*) should be kept in groups of not more than 10 animals if possible. There may be various reasons, however, for taking an individual animal from a group and housing it separately. This applies to pregnant cats, including in the first weeks of raising their kittens. This also applies to animals in the group that are incompatible but should be separated if possible together with a compatible partner.

In principle, the accommodation recommended for cats comprises enclosures with a floor area of $3 \, \text{m}^2$ in which the animal can walk around and which have a height of at least $2 \, \text{m}$ and are closed at the top. It should be possible to put the floor areas of several enclosures together by removing part of the partition walls.

ETS 123 specifies a floor area of at least 1.5 m² for a single animal with an additional area of 0.75 m². In addition, shelves measuring at least 0.5 m² per cat and 0.25 m² for every additional animal should be provided as shelfs on the walls.

The three-dimensional structuring of the animal room is especially important with cats: they need observation points and resting places protected on three sides. The number of these places must always be greater than the number of group members. If there are more than 3 cats in a group, several feeding places must also be provided at a distance of at least 50 cm from each other. Similar requirements also apply to watering places and litter trays. The possibility of withdrawal and not having to compete for the important resources in the enclosure is the basis for social harmony. The side walls should provide the cats with climbing opportunities.

Well-secured outdoor runs with pendulum flaps providing a connection with the indoor enclosures are an enrichment for cats. Here, too, the living space of the cats must be provided with three-dimensional structuring. Outside runs make it easier for the cats to escape when cleaning work are carried out in the enclosure.

Table 7/7: Cats – minimum dimensions and space allowances

	Floor* in m ²	Shelves in m ²	Height in m
Minimum dimension for one adult animal	1.5	0.5	2
Extra for each addi- tional animal	0.75	0.25	-

^{*} Floor area excluding shelves

(Source: ETS 123, Appendix A 2007)

7.2.8 Ferret

Ferrets (*Mustela putorius furo*) and their ancestor, the polecat or common ferret, are solitary living animals. Their marked instinct for play and activity, however, means they should be housed in groups, if possible.

Ferrets may be accommodated both in cages and in pens on the floor. In both cases, care must be taken to ensure the enclosure is escape-proof, because the animals are very smart and may be capable of opening locks. If there are drains in the floor of the animal room, they must be specially secured to prevent escape into the sewage system, which may result in death. Security measures are also essential for wire walls or wire doors, because ferrets are very good at jumping and climbing.

Cages and pens are provided with wood granules and plastic tubes, which are intensively used by the animals. Connecting two plastic cages by means of a tube has proved very useful: the animals use this to keep defaecation and feeding places separate. Defaecation boxes are only partially accepted in pens, whereas standing or suspended sleeping boxes are always used. Whole groups within the sleeping box especially like to retreat into large, solid bags (feeding bags), which they seek out after mealtimes and for sleep.

If pens or enclosures are appropriately equipped, very low room temperatures (above 0°C) are tolerated if they do not suddenly occur, but develop in the course of the seasons. Room temperatures above 24°C are poorly tolerated. Newborn animals need a room temperature of 20 to 22°C to maintain their body temperature.

The high-protein diet means that the feeding troughs must be cleaned and disinfected daily in order to reduce the risk of botulism. To prevent spoiling of the feed, dry feed is administered at night or the troughs have to be removed.

Table 7/8: Ferrets – cage and enclosure size and stocking density

Weight in g	Minimum housing	Minimum floor area per animal	Minimum height in cm
	area in cm²	in cm²	
up to 600	4500	1500	50
over 600	4500	3000	50
Adult males	6000	6000	50
Jill with litter	5400	5400	50

(Source: ETS 123, Appendix A 2007)

7.2.9 Dog

The housing of dogs (*Canis familiaris*) is regulated by both, the guidelines specified in ETS 123 Appendix A and Directive 2010/63/EU and in Germany additionally also by the German animal welfare ordinance on dogs in its currently valid version. For this reason, the following includes both the guidelines on minimum enclosure sizes from Appendix A of ETS 123 and also the requirements of the animal welfare ordinance on dogs, which is legally binding in Germany. Both the specifications from Appendix A of ETS 123 and the identical values of Directive 2010/63/EU are as a rule lower than those of the animal welfare ordinance on dogs. The values specified in the animal welfare ordinance on dogs are binding in Germany, because they were already applicable law at the time of the Directive. They also specify group housing of dogs, call for an adequate run, which is not otherwise legally required for any other animal species, daylight with a window area corresponding to 1/8 of the floor area and adequate handling by supervisors.

<u>Table 7/9-1: Minimum dimensions and space allowances for dogs according to ETS 123 Appendix A 2007</u>

Weight in kg		Minimum floor area for one or two ani- mals in m ²	Add for each additional ani- mal (in m²)	Minimum height in m
up to 20	4	4	2	2
over 20	8	8	4	2

(Source: ETS 123, Appendix A 2007)

<u>Table 7/9-2: Minimum dimensions and space allowances for weaned dogs according to ETS 123 Appendix A 2007</u>

Weight in kg	Minimum enclosure Minimum floor area per anisize in m ² mal in m ²		Minimum height in m
	0120 111 111	marini	
up to 5	4	0.5	2
over 5 to 10	4	1.0	2
over 10 to 15	4	1.5	2
over 15 to 20	4	2.0	2
over 20	8	4.0	2

(Source: ETS 123, Appendix A 2007)

According to the animal welfare ordinance for dogs, the minimum enclosure size in Germany is measured on the basis of withers height. Kennels or pens must have the following minimum sizes:

Table 7/9-3: Minimum floor area for dogs depending on withers height as specified in the animal welfare ordinance for dogs 2001:

Withers height in cm	Minimum floor area in m ²	
up to 50	6	
over 50-65	8	
over 65	10	

(Source: German animal welfare ordinance for dogs 2001)

It must be borne in mind here that the floor area specified in Table 7/9-3 must be available without restriction to the dog in a kennel based on its withers height, where the length of each side must be at least twice as long as the length of the dog's body and no side may be shorter than two metres. In addition, half the floor area defined in Table 7/9-3 must be provided for each additional dog and for each bitch with pups. The height of the enclosure must be such that the dog cannot reach the upper edge of the enclosure with its front paws when standing upright.

It has also proved useful in dogs if the areas can be adapted to group size by taking out dividing walls.

Dog enclosures should have a floor covering that is easy to clean. Like in pigs and cats, <u>daily</u> cleaning is necessary, because otherwise dogs spread their excrement throughout the enclosure with their intense need for activity. Dogs require thermally insulated lying areas that are easy to clean and difficult to destroy or mobile installations such as dog baskets or mats for lying on. The required runs may also be at a distance from the dog enclosures. The walk to and from the runs is an important part of the activity programme for the animals. Soundproofing measures should be taken in the area of the dog housing facility.

7.2.10 Pig

Pigs (*Sus scrofa domesticus*) should be housed in groups as a rule, even in laboratory animal facilities, with the exception of sows with piglets and sexually mature boars. They are housed in pens, which as a rule must be at least 1.20 m in height. It should be possible to partition the enclosures so that animals can be placed separately for experimental reasons, without them losing contact with the group. The partitions must have closed surfaces in the lying area, whereas they should have a lattice structure in the area where the animals defecate and urinate. Pigs tend to mark their territory, also from pen to pen, by defecating around the boundary. Particular attention must be paid to the floor. For all biungulates, the floor must be rough enough to ensure that the animals do not slip even when it is wet. At the same time, it must be easy to clean. For the housing of pigs, it is a considerable advantage if the lying areas can be warmed by means of a heating system. The lying area must at least be thermally well insulated. As a result, it dries quickly after cleaning, and the animals identify it as a comfortable place to lie and keep it clean. Straw bedding in the lying area provides the animals with comfort and the opportunity for occupational activity.

The minimum areas required for housing domestic pigs and mini-pigs according to ETS 123 (2007) are shown in the following table.

Table 7/10: Minimum areas for housing domestic pigs and mini-pigs

Bodyweight (kg)	Minimum permitted pen size (m²)	Minimum area per animal (m²/animal)	Minimum lying area per animal (m²/animal)
up to 5	2.0	0.20	0.10
over 5 to 10	2.0	0.25	0.11
over 10 to 20	2.0	0.35	0.18
over 20 to 30	2.0	0.50	0.24
over 30 to 50	2.0	0.70	0.33
over 50 to 70	3.0	0.80	0.41
over 70 to 100	3.0	1.00	0.53
over 100 to 150	4.0	1.35	0.70
over 150	5.0	2.50	0.95
full-grown and (conventional) wild pigs	7.5		1.3

(Source: ETS 123, Appendix A 2007)

As a rule, restricted feeding is provided several times a day. To ensure that all animals up to a weight of 70 kg can get to the feed at the same time, a trough length of 24 cm per animal must be provided. For animals with a higher bodyweight, the trough should be longer. The animals are usually watered from nipple drinkers. With a pen system that can be partitioned, each subunit must be provided with a trough and nipple drinker. The nipple drinkers should always be fitted at the lowest point in the pen, so that the dripping water can drain off directly and do not damp the lying area. In room units where pigs are housed, particular care must be taken to ensure that soundproofing measures are taken and that all parts of the pens are non-slip.

7.2.11 Small ruminants - sheep and goat

While sheep (*Ovis gmelini aries*) can be housed very well in groups, whereas group housing of goats (*Capra aegagrus hircus*) frequently leads to disputes with the locking of horns, which must be prevented either by means of very large, strongly structured enclosures or by partitioning the enclosures with wire mesh walls. Even when individual animals are fenced off, visual contact must be preserved. The enclosures for small ruminants do not need any specified structuring in lying and defecation areas.

They should have solid floors and, whenever possible, straw as bedding material. For watering purposes, sheep and goats need automatic drinkers with drinking bowls. Hay and straw are generally provided ad libitum in racks, the upper edge of which should be at a height of about 1.10 m and the lower edge at 60 cm.

The following table shows the areas needed for housing sheep and goats according to ETS 123 (2007).

Wherever possible, outdoor runs should be provided for sheep and goats, with or without the opportunity for grazing. Fencing must be provided using special sheep fences together with a support in the form of electric wire.

Table 7/11: Minimum areas for housing sheep and goats

Bodyweight (kg)	Minimum permitted pen size (in m²)	Minimum area per animal (m²/ani- mal)	Minimum partition height* (m)	Trough length for ad libitum feeding (m/ani- mal)	Trough length for restricted feeding (m/ani- mal)
up to 20	1.0	0.7	1.0	0.10	0.25
over 20 to 35	1.5	1.0	1.2	0.10	0.30
over 35 to 60	2.0	1.5	1.2	0.12	0.40
over 60	3.0	1.8	1.5	0.12	0.50

^{*} In the case of full-grown goats, the partitions might need to be higher to prevent the animals escaping.

(Source: ETS 123, Appendix A 2007)

7.2.12 Poultry

Poultry, which includes chickens, ducks, geese, turkeys and pigeons, lend themselves well to housing in enclosures with a floor area of 3 m² and a height of 2 m. Chickens need perches, which should ideally be installed at a height of 1.20 m to 1.50 m; in this case, a chicken ladder should be provided up to the perches. Chickens need nest boxes, for which e.g. so-called "cat toilets" with straw bedding are very suitable. Chicken boxes should contain at least enough bedding for the animals to scratch around in. A type IV cage with a mixture of sand and peat dust enables the animals to have a sand bath, but needs regular cleaning.

Ducks and geese should be housed in small groups with only one male animal. A lying area with straw bedding is a useful addition. If the animals do not have a run with a bathing area, a flat trough, (30 cm water depth, 1 m length, 60 cm width) must be provided in the box for feather care. Boxes in which pigeons are kept require several landing perch as far from each other as possible and an entry airlock. If the pigeons are breeding, protected shelves with very rough surfaces should be installed as high up as possible.

ETS 123 (2007) contains more nuanced specifications for the housing of various poultry species. Here only the table for chickens is presented (table 7/12).

Table 7/12: Chickens – minimum dimensions and space allowances

Weight in kg			Minimum height in cm	Minimum length of feeding trough per
	in m ²	area per animal in m²		animal in cm
≤ 200	1.00	0.025	30	3
> 200 to 300	1.00	0.03	30	3
> 300 to 600	1.00	0.05	40	7
> 600 to 1200	2.00	0.09	50	15
> 1200 to 1800	2.00	0.11	75	15
> 1800 to 2400	2.00	0.13	75	15
> 2400	2.00	0.21	75	15

(Source: ETS 123, Appendix A 2007)

If compliance with these minimum dimensions is not possible for scientific reasons, the duration of the confined accommodation must be justified by the study director and defined in consultation with the head of the facility and the animal welfare officer. In this case, the birds can be accommodated in smaller housing areas, but these should provide suitable enrichment elements and a minimum floor area of 0.75 m². Then either 2 laying hens or a small group of chickens can be kept in these areas if they comply with the above dimensions.

7.2.13 African clawed frog

African clawed frogs (*Xenopus laevis*) used as laboratory animals should be kept either in aquariums, basins or equivalent containers with a dark underground. The animals also live exclusively in water after metamorphosis. Since African clawed frogs breathe through their lungs, the water surface must be freely accessible to the animals and well aerated. The preferred water temperature lies between 20 and 22°C. Upward deviations (above 25°C) have a detrimental effect in terms of susceptibility to infection and oocyte quality. Since downward deviations (down to 16°C) pose fewer problems to the animals, somewhat lower temperatures of 18 to 20°C are aimed at in the case of oocyte harvesting, for example. A relatively sharp increase in temperature can lead to considerable problems; latent disease pathogens, for example, can result in outbreaks of red leg disease.

With regard to water quality, care should be taken to ensure water stands for about 2 to 3 days before it is used for a change of water, so that it reaches ambient temperature and any gases in the water, such as chlorine, can escape. It is recommended to clean the water by a permanent circulating filter system (aquarium filter). In the absence of filter cleaning and with a stocking density (adult animals) as shown in the table below, at least a weekly partial change of water (up to 50% of the water volume) may be necessary.

Table 7/13: Space allowance (*) for Xenopus laevis

Body length(**) (in cm)	Minimum water sur- face area (in cm²)	Minimum water surface area for each additional animal in group holding (in cm²)	Minimum water depth (in cm)
< 6	160	40	6
6 to 9	300	75	8
> 9 to 12	600	150	10
> 12	920	230	12,5

^{*} These recommendations apply to holding tanks but not to tanks for breeding purposes (natural mating and super-ovulation), especially since smaller individual tanks are more suitable for this purpose. Space requirements are determined for adults in the relevant size categories; juveniles and tadpoles are either kept separately or dimensions are altered according to the scaling principle.

(Source: ETS 123, Appendix A 2007)

^{**} Measured from snout to cloaca.

In several publications, much higher values have been specified with regard to minimum space requirements, which certainly provide much better conditions for species-appropriate behaviour. For example, Hilken et al. (1997) recommend 2400 cm² per frog in single holding and 600 cm² per frog in group holding. Values of this order of magnitude are also given by Scharmann et al. (1994) and Iglauer et al. (1997). The values shown in Table 7/13 are thus to be seen as absolute minimum dimensions.

7.2.14 Fish

Fish are adapted to their element, water, in different ways and very much more dependent on this surrounding medium than other vertebrates. Thus, a distinction is drawn between freshwater and marine fish according to the salt content (salinity) of the water and between warm water and cold water fish according to temperature. There are both ecological demanding (stenoecious) and tolerant (euryoecious) species.

The holding conditions must be adapted to the natural demands of the species in question to ensure that the optimal water parameters are provided. In principle, when a fish housing system (holding facility) is set up, particular attention must be paid to ensuring a specific water quality that is characterized by stress parameters (ammonia, nitrite, nitrate, phosphate), temperature, pH value, salinity and hardness.

Fish facilities

Fish may be accommodated in individual aquariums, in large group facilities or in outdoor enclosures (artificial ponds etc.), depending on the species and the research project. Separate facilities for housing individual groups or single fish are of advantage in terms of reduced spread of diseases and parasites, while relatively large interconnected facilities are easier in terms of care and maintenance and better suited to offspring and strains (also mutants or transgenic fish). The containers are usually made of glass or transparent plastic, but in the case of outdoor enclosures they may also be made of other materials (concrete, plastic film). Individual tanks can be obtained through the aquarium trade, while larger facilities are obtainable from specialist companies, which also provide planning and construction services. Fish facilities in the laboratory should be set up in quiet, air-conditioned rooms which are connected to drinking water supplies and which also guarantee constant access to fully desalinated water or reverse osmosis water, as far as possible, in order to provide water with a suitable salt content for tropical fish species (corresponding water treatment systems or mixture of drinking water and completely desalinated water in a certain ratio). Appropriate storage tanks are necessary for regular water changes and to compensate water loss caused by evaporation. Mixed and storage tanks for the preparation of artificial seawater must be provided for marine fish. Artificial seawater can also be obtained from specialists in the trade. The tanks should as far as possible possess movable covers to prevent fish from jumping out and minimize the loss of water due to evaporation, because evaporation leads to a hardening of the water. Water lost can also be substituted by adding fully desalinated water. Fish tanks or individual aquariums are usually operated with a water circulation system, i.e. the medium is conveyed from the tanks to the filter systems and back for cleaning by means of electric pumps. The constant flow-through holding facility with fresh water demands greater technical complexity. At all events, the water flow through the aquaria should be controllable.

For rheophilic fish species, which prefer to live in fast-moving water, suitable flow conditions should be generated by flow pumps; for rheophobic species, the water flow should be reduced.

In clean fish-holding facilities (without plants) the lighting should not be too bright, but rather subdued.

The facilities and important components, such as filters, pumps, lights, water inlets and outlets, must be regularly checked to ensure they are functional and there are no leaks, and vital water parameters must be permanently controlled with automatic alarm systems.

Water quality

Stress parameters:

Water quality is primarily determined by the nitrogen and phosphorus in fish excretions. Nitrogen excretions are converted in a process of nitrification by various bacterial species: Ammonia as the primary excretion product becomes increasingly toxic at pH values above 7; the conversion product nitrite (NO₂) is also toxic. The toxic concentration depends on the fish species and the chloride concentration of the water (guideline NO₂ concentration lees than 0.1 mg/l).

In most cases, the end product, nitrate, is non-critical even in relatively high concentrations (recommended 20 mg/l). Under anaerobic conditions, gaseous nitrogen may also be formed. If phosphate concentrations are too high, they usually have a negative impact on the water conditions in the form of increased growth of algae.

To eliminate waste products, biological mechanical filter systems are required, in which the bacterial nitrification takes place. The filters must be designed according to the overall size of the holding facilities and the size of the expected fish stock. Individual aquaria may be equipped with external or internal filters, which are obtainable in the specialist trade. The use of electric air pumps that improve oxygen supply via outflow stones and outflow pipes is also recommended. In the case of seawater systems, so-called protein skimmers should additionally be used to remove proteins and thus reduce the production of ammonia.

A regular change of water, i.e. <u>partial</u> replacement of aquarium water with freshwater, is also necessary. Depending on the facility and the fish stock, the change of water may be carried out daily on a minor scale or at longer intervals with larger volumes of water. Automatic regulation of the water exchange is possible in large facilities.

Cold-water fish usually need more frequent water changes or can be kept e.g. in a constant flow of freshwater. However, this involves increase water consumption and greater technical complexity to maintain a constant flow.

Problems with water quality often manifest themselves in a change of fish behaviour and appearance, which is why daily monitoring by appropriately trained personnel is necessary. Nitrite and nitrate concentrations should be checked at regular intervals, especially after work on the filter system or cleaning procedures.

Temperature, salinity, pH value, and hardness:
 These parameters must be adjusted according to the needs of the fish species concerned and monitored accordingly. Major fluctuations, e.g. with the water change, must be avoided.

Stocking density

Defined values for stocking density are contentious and sometimes vary considerably in the literature, because they depend on many factors. Very important factors are the water quality, the efficiency of water treatment, and the volume/frequency of the water change. In addition, the spatial requirement of fishes varies depending on the species, age, way of life, social behaviour and other specific behaviours (territorial, courtship, reproduction and brood care behaviour). Gender ratio, socialization of different species, and the equipment and dimensions of enclosures (surface, height and length) also play an important role in determining the maximum stocking density.

If there is an increase in stocking density or the stocking density is too small (e.g. in the case of schooling fish), problems can occur such as slower growth, lack of fertility or more rapid spread of diseases.

Quarantine, hygiene and care

For the medical treatment or isolation of sick fish and for temporary monitoring of fish that should be newly introduced to the facilities, it is recommended that a sufficiently large quarantine facility be installed whose water circulation is kept separate from that of the main facility. The most suitable systems for this are individual aquariums or smaller units operated independently of each other with several tanks.

Diseases such as white spot disease, fish tuberculosis or ascites frequently occur in facilities with excessive stocking density, poor feeding and housing conditions and inadequate hygiene. Direct restocking with fish from other facilities without a period in quarantine can also result in diseases being brought in. The fish stock must be constantly checked by trained personnel. If diseases occur, appropriate action must be taken (medical treatment, isolation or euthanasia). Catching devices and other utensils that come into direct contact with fish or containers should be regularly sterilized or replaced with new material. Excessive accumulations of detritus in the tanks must be regularly removed. Dirty aquariums colonized with algae along pipes, tubes and filter systems must be regularly cleaned. Areas where diseases occur should be isolated and disinfected with appropriate drugs and disinfectants.

One of the fish species most often used in research is the zebrafish (*Danio rerio*). The facility used to house zebrafish for research includes certain peculiar features, which deviate in some cases from the more general specifications indicated above. For this reason, reference is made here to recommendations for housing zebrafish from the European Society for Fish Models in Biology and Medicine (EuFishBioMed) – which grew out of the European Network on Fish Biomedical Models of the European Cooperation in Science and Technology (COST). These recommendations can be downloaded at http://www.eufishbiomed.kit.edu/59.php.

7.2.15 Monodelphis domestica (Grays-short-tailed opossum

The Grays-short-tailed opossum (*Monodelphis domestica*) is a territorial solitary living animal. However for beeding purposes it can be kept in pairs. Suitable enclosures are type IV cages with flat or raised covers without a feeding rack, because the animals have to be fed in the cage with soft feed from feeding dishes. The cages should be equipped with several nest boxes/retreats, a litter pan and an exercise wheel. The animals like to be supplied with nesting material. The animals are able to evade adequately in a cage enriched in this way. It is sufficient to clean the cages every few weeks, provided the litter pans are emptied at least once a week. Exercise wheels were accepted very well and are suitable for satisfying the need of this barely domesticated animal species for exercise.

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8. Building and technology

The processes and content of the various planning steps have already been described in detail in chapter 3 "Planning". The implicitly determined structural and technical aspects are now presented here in depth.

8.1 Flexibility

Animal experiment facilities are an essential part of the infrastructure for biomedical research. Nothing is more constant in research than change. Also the requirements of animal laboratories that come from the different scientific disciplines and research institutions demand a high degree of flexibility (e.g. for "new" species, special genetically modified animals etc.).

For this reason, the possibility of later changes in the use of the building should always be borne in mind when considering the structure and technical equipment of a facility. An essential ingredient of good basic planning is therefore the thorough determination and documentation of potential and also consciously excluded possibilities for change and modification. With timely consideration, the price of flexibility can prove lower than initially expected. (see Planning, chapter 3).

8.2 Room sizes and equipment

To avoid repetitions, the technical aspects concerning the size and equipment of rooms are described exclusively under chapter 4 "Functional areas and types of room".

8.3 Cages and accessories

In this booklet, the cages are already described in detail in chapter 5 "Housing systems" and chapter 6 "Housing units".

Chapter 8 "Building and technology", therefore, only refers to the following aspects:

- Logistics:
 - The fewer different cage types that are used in a laboratory animal facility, the easier it is to optimize logistical processes (procurement, provisioning, storage and handling).
- Cleaning and sterilization equipment must be matched to the cage types or housing systems used.
- <u>Ergonomic aspects</u> (e.g. sizes and weights) must on no account be underestimated during planning, because many activities, such as cage change procedures, are repetitive; i.e. they may have to be carried out hundreds of times a day in the same way.
- Also of considerable importance is the selection of the correct <u>cage material</u>, because this
 determines many aspects of operations, especially when it comes to cage preparation (e.g.
 possible autoclaving temperatures and thus cycle times, stability of the material, compatibility with process chemicals of cage preparation etc.). Extensive information on this broad
 field can be found in the brochure "Cage Processing in Animal Facilities properly done".

8.4 Building materials

The following aspects should be considered when selecting the building materials:

- The wall, floor and ceiling constructions must be water- and airtight, void-free and made of inorganic materials (e.g. no wood or wood-based materials).
 The surfaces must be smooth, largely without joints, easy to clean and resistant to the cleaning agents and disinfectants to be used according to the user's list of products for these purposes. Mechanical stress, e.g. caused by trolleys, high-pressure cleaning or falling materials, must be absorbed without damage. With the installation of floor surfaces, there is a conflict of objectives between ease of cleaning and the requirements for non-slip surfaces: to ensure that surfaces are sufficiently non-slip, for example, quartz sand or glass beads can be mixed into the synthetic resin coatings, but this has the disadvantage that the floors are then more difficult to clean; alternatively appropriate footwear can be worn.
- Monolithic constructions, such as concrete with synthetic resin or polyurethane coatings, and special construction systems, such as pharma partition walls, have proved successful. Especially when different materials are used in combination, particular care is required to avoid incompatibilities that could lead to damage (e.g. formation of cracks, separation etc.). Wall coatings are sensitive to shock. They must be regularly checked and, if necessary, repaired. The installation of ram protection bars in rooms and corridors is recommended. Tiling is not recommended in barriers for reasons of hygiene in view of the many joints between the tiles. The joints can also cause high levels of noise when transport trolley are driven over them.
- Outer windows are to be avoided in the animal rooms because of the controlled light-dark cycle and air-conditioning in the rooms. If there is a species-specific requirement for such windows (e.g. in the case of dogs), the windows must be absolutely airtight with a high thermal insulation coefficient and, if necessary, suitable protection against the sun.
- The door elements should be capable of meeting the following requirements:
 - sufficiently large doors (internal height at least 200 cm and width at least 100 cm),
 - resistance to inclusion of air pressure differences and humidity levels (avoidance of material deformations),
 - void-free or self-contained airtight door panel and frame construction,
 - mechanical resistance,
 - resistance to cleaning agents and disinfectants to be used (wet-room door elements),
 - ease of operation in conjunction with electric door opening and closing devices or mechanical one-handed operating elements,
 - tightness of door element matched to the design of the ventilation system (pressure control or air overflow) and room gassing (see section 8.8),
 - equipment with access control installations,
 - eventually equipped with darkened, airtight inspection windows for monitoring of animal rooms.

8.5 Installations

The following general principles should be considered in the planning and execution of media, electricity and ventilation installations:

- As few installations as possible in the animal area and in the hygiene barrier area.
- Building parts to be serviced as far as possible outside the animal area and the hygiene barrier area to ensure ease of access for maintenance staff.
- Few wall ducts (to be made gas-tight) at the barrier boundaries.
- Simple and straightforward installation for easy cleaning and disinfection.
- When selecting materials, attention must be paid to their resistance to the cleaning agents and disinfectants to be used.
- Horizontal surfaces (e.g. rectangular duct cross-sections) must be avoided to reduce deposits of dust and dirt.
- In case of a failure of systems that are required for supplying the animal rooms, provision
 must be made for adequate redundancy (in the case of ventilation about 60% of maximum
 necessary capacity).

The following media may be necessary in the animal rooms depending on the animal species and their use:

- cold and hot water,
- sterilized water for barrier areas,
- soft and completely demineralised water,
- centrally prepared disinfectant solution,
- · water for automatic watering system,
- electricity (230/400 V, if necessary with substitute power supply system),
- low voltage (for computer systems, telephone, alarms),
- room supply air and exhaust air (if necessary with direct exhaust air connection for individual devices).
- data network connections for PCs.

8.6 Room air-conditioning

The room temperature in each animal room should be capable of being regulated separately because of different stocking densities in each room. If different species are being housed, further climate zones may have to be established, which may be differentiated with regard to other parameters (humidity etc.). In some cases, several rooms may also be combined into climate zones. The room climate (temperature, humidity, air change rate) is set according to the species and stocking density of the animal room by means of an individual room control system. The room ventilation systems must be such that compliance with specified values for room air conditions (fixed

values with permitted tolerance limits or circadian fluctuations) can be self-regulated. If part of the system fails, it must be possible to maintain emergency operation with at least 60% maximum efficiency until a repair has been completed.

The installation of the air-conditioning system with respect to air change rate is dependent on the stocking density of the room and the laboratory animal technology used: for housing laboratory animals in open cages, Appendix A of ETS 123 stipulates a rate of 15 to 20 air changes per hour. If small laboratory rodents are housed in climate chambers or individually ventilated cages with a direct connection of the exhaust air to the exhaust air ducts (pressure uncoupling) the air change rate in the room (!) can be reduced to 10 to 12 air changes per hour. This substantially reduces energy costs for the room climate and lessens the exposure of the animal rooms to allergens and infectious dusts.

The room ventilation equipment of a barrier system should on no account be connected to that of a neighbouring system or to other areas. The ventilation efficiency of a room should be aligned to its maximum possible stocking density. The basis for calculation is the amount of sensible and latent heat released by the animals (see annex to chapter 8 "Release of heat and water vapour by different vertebrates") and the factors of the room relevant to air-conditioning technology (position, size, construction), its installations and personnel. The outside air intake should be located at a height of 3 m above the ground.

The values indicated in the following sub-chapter are standard values for the animal housing unit in the experiment based on customary international standards. They also serve in particular to allow the results of animal experiments to be compared. The values indicated are not absolute threshold values that have to be observed 365 days of the year. They are rather intended as values for the planning and installation of air-conditioning systems that should be observed for most of the year. Fluctuations resulting from extreme weather conditions are permitted within certain limits, similar to the regulations for workplaces in non-residential buildings as set forth in DIN 1946-2/ EN 13779 and DIN 4108-2.

For the purpose of cleaning and disinfection, it should be possible to separate each room completely from the air-conditioning so that the room can be individually gassed with disinfectants.

There are various technical solutions for installing and controlling the air-conditioning system within the animal rooms. This concerns the form of airflow (induction ventilation or source ventilation), humidification and temperature control. The airflow design is crucially important for occupational safety and for protecting the animals against cross-contamination.

Induction ventilation results in good and rapid mixing of supply air and room air, but at the same time it can lead to the distribution of contaminants and odours. Aside from different types of air inlets and outlets in/on the ceiling, exhaust air ducts on the walls close to floors or ceilings have become established. The disadvantage of induction ventilation is that the supply air flows into the room at relatively high velocity, which can result in draughts and turbulence. This can be reduced by adjusting the number and design of air inlets.

By contrast, source ventilation uses the fact that air rises when it warms up. The air reaches the room via long source outlets parallel with the wall and close to the floor at relatively low velocity, then rises and is led off to the ceiling via the exhaust air ducts. The disadvantages of this solution lie in the need for more space and also higher investment costs.

8.6.1 Room temperature

<u>Table 8/1: Recommended room temperature for different animal species</u> (see Appendix A of ETS 123)

Species	°C
African clawed frog (water temperature)	.18-22
Chickens	15-25
Mice	.20-24
Rats	20-24
Guinea pigs	20-24
Rabbits	15-21
Cats*	15-21
Dogs*	15-21
Pigs* (here: 30-100kg)	.18-22
Non-human primates**	.20-28

- * Cats and dogs can be kept in a wide range of temperatures, provided their wellbeing is not compromised. A temperature range between 15°C and 21°C should be observed if close monitoring is required during the experiment.
- ** Species-specific differences must be borne in mind.

To ensure compliance with the above room temperatures, the cooling load must basically be calculated taking into account the thermal load both of the animals (see Appendix "Release of heat and water vapour by different vertebrates" at the end of chapter 8) and of the equipment and personnel deployed.

8.6.2 Humidity

Plans should be based on a relative humidity of $50\% \pm 10\%$. This planning basis allows for relative humidity values of 30% to 70% that can occur in practice as a result of extreme weather conditions. Values must not be allowed to fall outside this range, because no negative effects are known to occur on most mammalian species within these limits. The limits are therefore also specified in the Guide for Care and Use of Laboratory Animals and GLP guidelines.

8.6.3 Air change rates

To maintain the above-mentioned room temperatures, a cooling load calculation must be drawn up, taking into account the thermal load of the animals and the equipment and personnel deployed, which gives the required minimum air change rate. If no other, more specific data are available (for example from the laboratory's own measurements), the heat release values can be taken from the appendix to chapter 8. On the basis of many years' experience, it is recommended that the air in the animal rooms is changed 15 to 20 times per hour for the most commonly used animal species. This is in keeping with the current EU guidelines for the accommodation of animals (ETS 123, 2006). The change of air in animal housing units should not on any account fall below 10 times per hour. With an air change of 10 times per hour, the rate of 25 m³/m² floor space also required for

laboratories (DIN EN 1946-T7) is realized (room with 3 m height and 20% air reserve). In intensively occupied animal rooms and open housing systems, a higher rate of air changes may be necessary to ensure sufficiently rapid removal of noxious gases, such as CO₂ and ammonia. This then corresponds to the "work rooms with odour annoyance" of the above-mentioned DIN standards, for which air changes 15 to 20 times per hour are required.

For example, if IVC systems are used in rodent rooms and the cage exhaust air is fed directly into the room exhaust air ducts, a reduced air change may be sufficient, provided the thermal loads that occur (from equipment, animals and users) are also reliably extracted. The exhaust air from the IVC systems must be connected to the room exhaust air system in such a way as to ensure that, in the event of pressure fluctuations in the exhaust air system of the building, the entire room air is available as a buffer and thus avoids any direct impact on pressure conditions in the cage. The velocity of room air should not exceed 0.3 m/s, measured at 22°C and at height of 1.6 m, in the aisle between the shelves. The room air supply must ensure an optimum mixing of room air and an adequately constant microclimate in the individual cages.

8.6.4 Air pressure

There are two commonly applied principles of air distribution to ensure the hygienic protection of the animal rooms:

- Controlled overflow:
 - In this variant, a controlled air flow in the desired direction is generated by a defined difference in air volume between supply air and exhaust air.
- Pressure control (required by law in BSL-3 areas according to GenTSV [German ordinance on safety levels and safety measures during gene technology work in gene technology facilities]):
 - In this variant, a given pressure difference is set between two hygiene areas. A pressure difference between animal room and outer area should not fall below about 50 Pa. If airlock systems are used, the pressure difference can be achieved by a cascading arrangement.
- In the case of pressure control, stricter control requirements must be set. The control system must ensure that the pressure does not collapse when the door is opened and that no pressure peaks occur in the room when the door is closed.

8.6.5 Air filters

Suitable air filters must be built into the supply and exhaust-air ducts in animal laboratories. For the sterilization of supply air in animal rooms with a hygienic barrier or in so-called cleanrooms, three-stage filter systems have proved suitable: pre-filter or outside-air filters, fine filters and high-efficiency particulate air filter. The latter, also commonly known as HEPA filters, have a separation efficiency of 99.95% in respect of all particles bigger than 0.2 μ m (filter class: H 13, DIN EN 1822-1). These HEPA filters for the sterile-filtration of supply air must be installed in suitable casings, which allow a hygienic replacement of filter elements, close to the animal rooms. The outside-air filters, built into the air-supply or air-treatment system, and the fine filters serve mainly to protect the HEPA filters. The filters are classified according to European or international standards.

Since large quantities of dust are generated in the housing of small laboratory animals, the exhaust-air outlets in animal laboratories should be fitted with coarse dust filters. This serves to reduce any deposits of dust in the exhaust-air ducts (microbial growth, fire risk!) or on the sensors installed there. The filters and the connecting ducts must be cleaned and disinfected, and filters (after replacement) also on their own (see section 8.7 "Room gassing"). In the housing of infected animals, agents must not be allowed to escape from the animal rooms to the outside air. Additional fine and HEPA filters must therefore be built into the exhaust-air system.

8.6.6 Air supply of IVC systems

When it comes to the air supply of IVC racks for housing rodents, the following aspects must be taken into account: one of the great advantages of (decentralized) air handling units over centralized ventilation units regarding room climate, is that they take the air from the room and the room thus acts as a "buffer" for conditioned air. This means that any sudden changes in supply air conditions are buffered by the room, so the animals are not immediately exposed to these changes and the staff therefore have time to intervene. With centralized systems, a sudden change in temperature is immediately felt by the animals in the cages, thus exposing them to the risk of a hypothermic or hyperthermic shock. The idea of using centralized systems to achieve differing temperatures in the cage and the room, respectively (for example 24°C for the animals and 18°C for personnel) has proved impracticable as a result of the heat exchange between cage and room.

The following figure shows some of the possible technical variants for the air supply of IVC systems – from centralized, through semi-centralized to decentralized air supply.

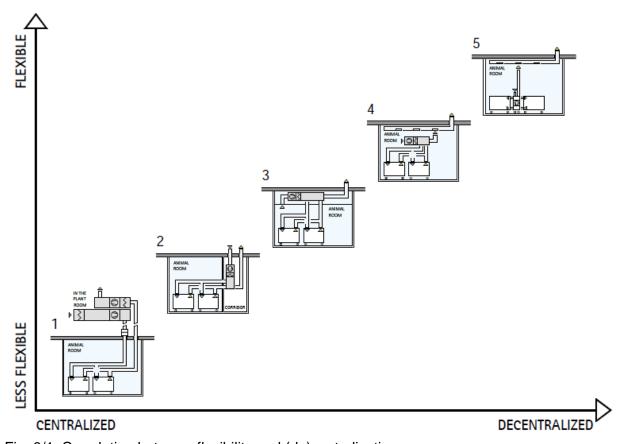
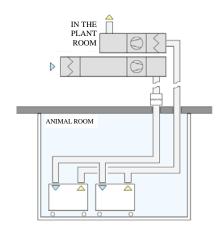


Fig. 8/1: Correlation between flexibility and (de)centralization

Brief description of variants:

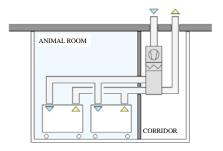
Variant 1 – Centralized ventilation system

Air supply and air exhaust for all IVC racks in the building are provided by a central unit in the control room. The fresh air is conditioned here and fed directly to the racks in the animal rooms via a separate clean-air duct system. The supply air may be filtered either directly in the plant room or via filter boxes upstream of the animal rooms concerned. Exhaust air from the racks is likewise fed back to the plant room via a separate air duct system and then optionally filtered through the exhaust air system and blown out over the roof.



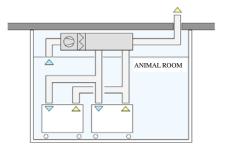
Variant 2 – External ventilation system centralized on a room-by-room basis

The functions are identical to those of Variant 1, but the functional elements such as ventilator, control and filtration are combined in each cases for a given room or group and housed in a modular arrangement outside at the boundary of the animal room (for example in the corridor or at an adjoining installation level).



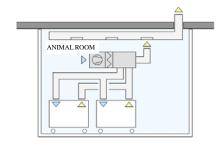
Variant 3 – Internal ventilation system centralized on a room-by-room basis

The ventilation system is installed in the room or within the hygienic barrier at the room boundary (i.e. usually just beneath the ceiling or on the wall) and takes the supply air directly from the animal room. This is filtered and fed directly to the racks. The cage exhaust air from the racks is connected via draught diverters either to the room exhaust air system or to a separate cage exhaust air duct (similar to the arrangement with Variants 1 and 2).



Variant 4 – Decentralized wall or ceiling-mounted air handling unit

Air handling units are mounted on the wall or suspended from the ceiling in the animal room for supplying up to 2 double-sided or 4 one-sided racks. All other functions are essentially as described in Variant 3. But since several air handling units are fitted instead of just one, it is easier to achieve differing conditions in different racks.



Variant 5 – Decentralized floor standing air handling unit

The ventilation system is identical to that of Variant 4, except that the air handling unit is a stand-alone, mobile module between the racks. (With some brands, the air handling units are also fitted to the racks.)

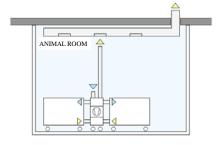


Fig. 8/2: Presentation of different technical variants for the air supply of IVC systems

Notes on the illustration and the description of the variants:

Flexibility:

The more flexible the system is, the easier it is to adapt to changing or specific housing conditions.

Interfaces:

The more centralized the system is, the more complicated it is to explain and adjust the interfaces and also to adjust the system.

Operational safety:

The more centralized the system is, the more racks will be affected if any outages occur in the system. In the case of systems that takes in air from the animal room, these will be buffered by the room volume in the event of sudden changes in the conditioning of supply air.

• Space requirements:

Only in Variant 5 with decentralized, floor-standing air handling units additional animal room space is needed. In the case of the centralized solutions of Variants 1 and 2, corresponding areas in the technical plant area or in technical plant corridors must be documented.

8.7 Room gassing/disinfection

As a rule, the gassing of an individual animal room or an entire animal housing area is always necessary when a defined level of hygiene is required, e.g. before the stocking of animal rooms or for decontamination after a hygiene break-in. Usually, procedures are used that involve working with formaldehyde, hydrogen peroxide, chlorine dioxide or other special, nebulized chemical disinfectants.

The following technical conditions must be met for all procedures:

- Absolute tightness of the rooms (walls, ceilings, ducts, technical installations). Doors that are not gastight in design must be capable of being made gastight with adhesive tape.
- Airtightness of the air ducts, including appropriate shut-off devices (DIN EN 12237; minimum tightness category C or, better still, D).
- The necessary gas ports must be arranged so that the supply-air and exhaust-air ducts belonging to the hygiene area are also treated (see sketch at the end of this section).
- Material compatibility with the disinfectants used.
- The disinfectant must also reach hollow spaces (e.g. cable ducts) connected to the hygiene area in sufficient quantity and concentration.
- Filters must be capable of being gassed individually (provide for ports and shut-off devices).

The following further aspects must be taken into account:

- The effectiveness of all procedures should be documented through a validation.
- Room gassing with formaldehyde requires official approval. Moreover, the operators concerned must be in possession of a relevant certificate (e.g. TRGS 522 "Room disinfection with formaldehyde").
- It must also be considered that gassing with formaldehyde is usually followed by a neutralization phase with ammonia, so the compatibility of materials with ammonia must also be taken into account. As an alternative, the rooms may be ventilated and left to stand empty for a sufficient length of time (several days). It is absolutely essential that they are subsequently cleaned using cold water.
- Room gassing with hydrogen peroxide places high demands on the surface (coatings) and components such as electrical switches, lights etc., standard versions of which cannot withstand H₂O₂ gassing. It must also be taken into account that plastic materials absorb H₂O₂ and can release it back into the room air over a prolonged period.
- Rooms and goods for which decontamination with formalin or peracetic acid had to be selected in the past can be decontaminated with using VHP (vaporized hydrogen peroxide) without toxic residues. The gassing of plastic cages with H₂O₂ should only be considered in exceptional cases, because the material absorbs the gas and releases it again only very slowly, over the course of several days.
- Test gassing of coatings (epoxy resin etc.) and materials (power sockets, network sockets
 etc.) has proved a successful way of testing material compatibility beforehand.

ROOM GASSING FILTER GASSING

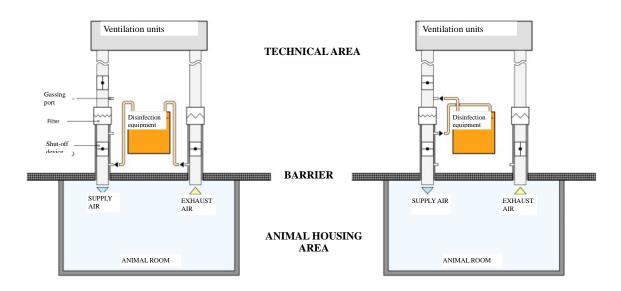


Fig. 8/3 Schematic diagrams for room and filter gassing

8.8 Treatment of drinking water

With regard to the treatment of drinking water, reference is made in particular to the GV-SOLAS brochure on drinking water treatment. Many procedures and solutions for the treatment of drinking water are described here.

In terms of technical construction, the following should also be noted:

- Compliance with the drinking water ordinance and relevant standards (in particular DIN EN 8006 und DIN 1988).
- Consideration of the impact that pipe materials have on water quality.
- Possibility of disinfecting the water pipes (depending on their intended purpose).
- If a centralized drinking water supply is planned, it is necessary to provide the animals with a separate piping system.

8.9 Water/wastewater

For reasons of hygiene, water connections and drains in the barrier area should be kept to the absolute minimum necessary. If wash basins are required, they should be provided in a hygienic design and with a hygienically safe connection to the wastewater system. Floor drains are often dispensed with in rodent rooms, which is associated with marked effects on the cleaning concept. This also has the disadvantage that it can limit the use of these rooms for other animal species. If a floor drain is necessary in the animal room, it must be capable of being sealed and made airtight to

exclude the possibility of any contamination from the wastewater system and the escape of animals from the animal room. If drains are dispensed with in the animal rooms, they may be positioned in the corridors - provided the hygiene concept allows this - so that the cleaning solutions used can be removed from the animal rooms using squeegees. Wet vacuum cleaners are also often used here.

8.10 Electrical installation (including data cables)

Open cable routing and freestanding equipment should be avoided in the animal room or reduced to a minimum. Power sockets and data connection points must be splash-proof and easy to decontaminate. In order that writing utensils are not constantly carried into the rooms for documentation purposes and the exchange of information during breeding work remains effective, the computer networking of the animal and laboratory rooms and the option of working with the computer (animal management program) are an essential prerequisite.

8.11 Energy supply

The demand for a high level of energy supply security for all systems, especially for air-conditioning systems and air handling units, can only be met with separate and redundant connections, i.e. reserve capacity and emergency power supply. Networking with other consumers does not make sense. Especially when it comes to the use of IVC systems, it must be established whether a redundant power supply is required, depending on the ventilation concept (centralized/decentralized) and the cage system (e.g. with/without "rescue filter").

For the energy supply to autoclaves and also cleaning and air-conditioning systems, centralized steam supply is advantageous because of the high levels of energy required. Decentralized electrical steam production involves very high operating costs.

8.12 Lighting

Daylight in the animal room is undesirable with some laboratory animal species, especially rodents, because uncontrollable fluctuations in light intensity and duration can affect both breeding and the experiment. The room climate can also be negatively affected by sunlight. Therefore luminaire emitting daylight spectrum are recommended, which are fixed to the ceiling so as to ensure that the illumination of the room is as uniform as possible. The luminaires selected must be such that the lighting tubes can be easily changed by the animal attendants or technical staff. The luminaires must be the same as for wet rooms, i.e. casings and wet-room power sockets and switches that are splash-proof and easy to decontaminate must be installed.

For birds, the illuminance during the dark phase should be 15 lux. When working in the dark room, illumination with a red light is suitable with many rodent species, because this allows for observation and work in the room without the animals being disturbed by light stimuli. However, other species (e.g. birds, dogs or guinea pigs) are well able to detect red light. For animal laboratories, dual-circuit systems are to be provided for the lighting, where one circuit controlled by a time switch determines the light period, while the other allows the activation of additional lamps (workplace lighting). According to workplace guidelines, a light intensity of 300 to 500 lux, measured 1 m above the floor beneath the lighting fixture, is the standard for workplace lighting. In the common area shared by the animals, the light intensity should lie within the range of 130 to 325 lux (see Guide for the Care and Use of Laboratory Animals, 8th ed. 2011). Particular attention must be paid here to the

uppermost cage level (if necessary cover the uppermost level). If the light intensity is higher, pathological changes in the retina and also increased activity of the endocrine organs can be expected. When assessing the lighting intensity for rodents housed in cages, it is crucial to know the light intensity at cage level in the common area shared by the animals and also whether the animals in the cage have a choice between lighter and darker areas. Relatively dark, sheltered areas are especially important for albino animals.

The following factors play a role here:

- Arrangement of luminaires in the room in relation to the position of the cage racks.
- Position of the rack in the room and of the cage in the rack.
- Dimensions and design of the cage (including covers, filter top, bottle, feeding rack and accessories).
- Selection of cage material and its light transmission.

The following must also be considered:

- Monitoring systems for checking the day-night rhythm.
- No influx of light from adjacent rooms or corridors.
- Caution is required in the use of dimmers and electronic ballast devices (owing to ultrasound emissions).

Note:

The above statements relate to the common laboratory animal species, especially rodents. In special cases, other special conditions may be necessary. Appendix A (ETS 123) can be a useful reference with respect to lighting, not only for general recommendations but also for animal-specific peculiarities.

8.13 Noise

Noise is a major disruptive factor in the animal laboratory. Recent findings indicate that frequencies above the human hearing threshold up to 60,000 Hz can be detected by various laboratory animal species. To avoid negative influences on the animals, the noise level in the animal rooms must be kept as low as possible. Of particular importance here are air-conditioning systems, because they constitute a constant stress factor for the animals 24 hours a day and 365 days a year. They also serve as the base noise exposure to which the animals are subject and to which further noise emissions may be added through additional equipment in the animal room and from general operations. With the air-conditioning system in operation, a sound pressure level that is both technically possible and to be aimed at is 40 dB(A), measured in the empty animal room with its sound-reflecting surfaces and no mobile equipment.

During operations, the noise emissions are substantially higher as a result of routine work, but the animals usually adapt to this. To achieve this value, it is basically necessary to make sure that all equipment and systems are acoustically decoupled from the building. It is therefore recommended in particular to locate the processing centre ("wash-up area") at a sufficient distance from the animal rooms and to move the vacuum pumps for autoclaves to a building services floor. Soft background music, on the other hand, shows no adverse effect on laboratory animal behaviour.

The following points must also be taken into account:

- Avoidance of floor joints and bumps where possible to keep transport noises as low as possible.
- Sound-absorbing materials and design of animal room equipment, especially of transport facilities and mobile components (e.g. cage-changing stations).
- No acoustic alarms in the animal rooms (also no acoustic fire alarms or sirens, alternative: red flashing lights).
- · No ultrasound emissions.

Note:

The above statements relate to the common laboratory animal species, especially rodents. In special cases, other special conditions may be necessary. Appendix A (ETS 123) can be a useful reference with respect to noise, not only for general recommendations but also for animal-specific peculiarities.

Further details on the subject of laboratory mice are contained in the publication *Tiergerechte Haltung von Labormäusen* (Humane housing of laboratory mice) from the GV-SOLAS committee for humane laboratory animal housing, an extract of which is cited below:

Rodents are sensitive to ultrasound. They perceive sounds between 500 Hz and 120 kHz. Their auditory range is thus higher than the human range (20 Hz to 20 kHz). Maximum sensitivity values lie at 15-20 kHz and 50 kHz, so likewise well over that of humans (3-4 and 12 kHz) (Ehret 1983, 1989). Mice also communicate in an ultrasound range inaudible to humans, e.g. during sexual interactions and in acute fear (Gourbal et al. 2004, Holy & Guo 2005). High noise levels, ultrasound and sudden high-pitched noises must be avoided. During work time, considerable sound pressure can occur in animal rooms (Sales et al. 1988a, Milligan et al. 1993, Voipio et al. 2006). In general, therefore, care should be taken to avoid making a noise. Technical installations such as motors, washing machines etc. in the animal housing area should be checked for ultrasound emissions (Sales et al. 1988b, Voipio et al. 2010). Ultrasonic cleaning equipment must not be used in animal rooms. However, deep humming sounds below 500 Hz, such as those caused by some ventilation motors, are inaudible to mice. Moderate background music is not known to have any negative effects.

8.14 Lock installations

Sterilizers:

<u>Sterilization</u> means the killing or irreversible inactivation of microbes. A correctly performed sterilization therefore offers reliable protection against viruses, bacteria and other infectious pathogens. Sterilization is always the procedure of choice when thermostable goods (i.e. goods that tolerate treatment at min. 121°C) are to be treated and a high level of hygiene is required.

A distinction is made between two basic principles: sterilizers in an immission barrier guarantee protection against the entry of unwanted agents (immission control); sterilizers in an emission barrier serve to protect the environment against pathogenic agents (emission control) from the animal laboratory.

The types of sterilization can be differentiated according to the methods used, i.e. physical

(e.g. wet or dry heat) or chemical (formaldehyde or H₂O₂). The most widespread type of sterilizers is the steam sterilizer (= autoclave), which operates with steam as the carrier of wet heat.

Aside from other aspects, <u>autoclaves</u> also have the crucial advantage that they allow the vacuum and steam to be repeatedly changed by means of special programming so that, in the case of porous goods, not only can the material be treated on the surface, but the steam can penetrate the material, where it can also exert its microbicidal action.

To <u>check the efficacy</u>, either direct test methods (such as spore tests) must be carried out or – as is customary today – validated programmes must be used to show evidence that the required result can be reproducibly achieved.

The <u>sterilization of feed</u> placed particularly high demands on the autoclave and the sterilization programme, because it is a question here of generating as much heat as necessary (to kill the agents), while at the same time not generating so much heat that the ingredients of the feed suffer unnecessary thermal damage.

For the design of the programme, careful <u>capacity planning</u> is absolutely essential, in which precise consideration must basically be given to the nature and scope of the sterile material, the programme run times, the work time of the staff and the equipment.

There are special <u>structural requirements</u> as a result of:

- the weight (especially in the case of autoclaves) (→ statics of building),
- the need for a "pit" in the floor in the case of autoclaves used on floor level,
- the size of the (usually indivisible) autoclave chamber (→ routes in and out!).

It must also be taken into account that maintenance work should be performed as far as possible from the unclean side.

Disinfection locks/disinfection chambers:

<u>Disinfection</u> is understood to mean processes in which agents are reduced to the extent that infection or transmission can be excluded. It is used when sterilization is either unnecessary or impossible.

<u>Disinfectants</u> can have a broad spectrum of action. When sprayed in disinfection chambers, they are very suitable for the superficial disinfection of temperature-sensitive materials, although it is crucially important that the entire surface of the materials is in contact with the disinfectant in the right concentration for a sufficiently long period of time. Unlike with autoclaving, the disinfectant does not reach the substance within the containers (e.g. bags, cartons etc.) or the inside of porous goods.

<u>Disinfection chambers</u> are suitable for bringing in goods that are either manufactured and packed (often in two bags/containers) under sterile conditions or have been sterilized in their microbe-resistant packaging, e.g. by gamma radiation.

In all <u>two-door disinfection locks</u>, technical precautions should be provided to ensure that the door to the clean area can only be opened after the sterilization or disinfection programme has run its proper course and then only when the opposite door is locked.

The <u>chemical substances</u> that come into question are either in gaseous or vaporized form that can be used as aerosols or as sprays. All these active substances are hazardous chemicals. To protect the health of staff, the handling of these substances must conform strictly to the technical directives, laws and manufacturer-specific safety regulations (see safety data sheets).

The following must be noted with regard to the various substances:

- <u>Formaldehyde</u> shows an excellent microbicidal and sporicidal effect. Special safety regulations must be observed because of its potentially carcinogenic effect and toxicity.
- Peracetic acid (PAA) is only stable to a limited degree in its non-stabilized form. Highly concentrated PAA is flammable and extremely corrosive. Concentrated PAA causes severe chemical burns upon skin contact and a potentially carcinogenic substance. The microbicidal effect is excellent. PAA is not recommended for combating persistent forms of parasites.
- Hydrogen peroxide: Gassing with hydrogen peroxide is an environmentally friendly, residue-free (active substance disintegrates in water and oxygen), rapid and reproducible method of biodecontamination that is capable of validation. Concentrated hydrogen peroxide solution causes chemical burns; on contact with combustible substances there is a risk of fire. Certain materials such as natural rubber, cellulose, PVC, polyethylene and nylon are not resistant.

IVC shelves, electrical equipment (computers etc.), safety workbenches, production plants and isolators, including the materials contained therein, can be disinfected with vaporized hydrogen peroxide on surfaces with which the gas comes into contact. This method is not suitable for disinfecting porous goods.

8.15 Special technical questions

- Adequate storage capacity (also and especially in barrier areas) for about 30% of the material needed for routine care of the animals (cage shells, covers, bottles etc.).
- Sufficiently wide corridors, corresponding to the relevant items of equipment used, but at least 2 m in width.
- Loading docks for delivery of materials.
- Adequate dimensions (cabin dimensions/loads) of lifts.
- Separation of transport pathways for clean and unclean materials wherever possible.
- Recommended locks:
 - Autoclave (floor level, HxWxD ideally about 2000x1300x1600 mm).
 - Material lock for heat-sensitive goods (floor level, HxWxD ideally about 2000x1300x1600 mm), gassable if necessary.
 - Material lock for small heat-sensitive goods (loading height to about 800 mm, HxWxD ideally about 600x600x900 mm).
 - Personnel airlock, designed as air shower and/or water shower (ideally as triple-chamber airlock).

- Sprinkler systems, especially behind the barrier, are to be avoided and, if necessary, replaced with other installations offering a similar protective function for reasons of hygiene and operational safety / false alarms.
- If fire alarm systems are required, they should be insensitive to dust (e.g. photo-optical smoke detectors in the exhaust air duct behind the filter or thermal fire detector) and designed in such a way that no maintenance needs to be carried out in the animal rooms. Fire alarm systems are to be designed primarily so as to guarantee personnel protection. The sensitivity of the laboratory animals to noise should also be considered in the design of the alarms as far as possible and permissible.
- Animal treatment rooms and the desirable functionalities in these rooms must already be agreed upon with the user during the planning phase. Their size, number and position depend on individual circumstances.

8.16 Guidance on planning of capacity and investment costs

Animal housing facilities are special buildings, the design of which is determined by very individual factors. For instance, the location, the focus of research, the species used, the infrastructure and local provisions and requirements will vary widely from case to case. And the cost of investment in such facilities will thus differ very considerably. For this reason, it is impossible to provide specific details on capacity and investment costs with any generalized validity. For operational costs, see chapter 12.

Literature

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Safety data sheets of the producers of disinfectants.

Annex to chapter 8: Release of heat and water vapour by different vertebrates

	Bodyweight	Individual release	of heat/hour	Release of water vapour	
	(kg)	sensible heat ¹	latent heat ²	(glh)	
		(Watt)	(Watt)		
Human	75	112.49	60.57	86.6	
Mouse	0.018	0.22	0.12	0.17	
Rat	0.200	1.32	0.71	1.02	
Golden hamster	0.080	0.66	0.36	0.51	
Guinea pig	0.300	1.79	0.97	1.39	
Rabbit	2	7.42	4.00	5.72	
Cat	2	7.42	4.00	5.72	
Non-human pri-	5	14.76	7.95	11.37	
mates					
	4	12.48	6.72	9.61	
	8	21.00	11.31	16.17	
	12	28.46	15.32	21.9	
Dog	16	35.31	19.01	27.9	
	20	41.74	22.48	32.2	
	24	47.86	25.77	36.8	
	28	53.73	28.93	41.3	
	32	59.39	31.98	45.7	
Mini-pig	30	56.58	30.47	43.6	
Pig	125	165.01	88.85	127.1	
Sheep	40	70.21	37.80	54.0	
Goat	36	64.87	34.93	49.9	
Horse	400	394.80	212.58	303.99	
Cow	300	318.18	171.33	245.0	
Chicken	1.8	6.86	3.69	5.3	
Pigeon	0.280	1.70	0.91	1.3	
Quail	0.140	1.01	0.54	0.77	

Basis of calculation:

¹ Sensible heat: heat release by radiation and convection = 2.92 x kg/b.w. ^{0.71}

⁽⁼ kcal/h basal metabolic rate³) x 2 (activity factor) x 65 % (proportion of sensible heat), on the basis of: Kleiber, M. *The fire of life, an introduction to animal energetics*. Robert E. Krieger Publishing Company, Huntingdon und New York, 1975, und Besch, E.L., Woods, J.E. "Heat dissipation biorhythms of laboratory animals" in: Lab. Anim. Sc. 27: 54-59, 1977.

²Latent heat: heat release by evaporation (release of water vapour).

³ 1 kcal/h= 1.162791 W.

9. Documentation systems

Breeders, keepers and experimental users of laboratory animals are required by animal welfare and gene technology laws to keep comprehensive documentation.

This includes:

- Applications for approval and registrations of animal housing units and the operation of gene technology facilities,
- Specification of rooms and housing systems,
- · Records on genetically modified animal lines and assessments of constraints,
- Animals received and allocated to projects,
- Applications for approval of animal experiments,
- Procedures and treatments in laboratory animals,
- Report on number and species of laboratory animals used.

In addition, documentation of the technical processes in the operation of animal housing facilities is also required. This involves documentation not only of the technical installations, e.g. autoclaves, disinfection airlocks and cleaning systems, but also of the technical parameters, e.g. temperature and relative humidity in the animal housing and functional rooms.

Electronic documentation systems are increasingly used to ensure that all requirements in the various installations and numerous available animal strains and animal models can be comprehensively and correctly met.

In the planning and selection of individual software solutions, the various basic and priority requirements for animal welfare and research as well as for technical operations must be carefully evaluated. Normally, this will lead to the establishment of two systems (animal welfare / research and building control system).

From a given size of facility upwards, the use of corresponding software is not only useful from a logistical perspective, but also advisable in terms of cost-effectiveness. The possibility of (partial) automation and the associated continuity of monitoring and documentation will lead in most cases to a reduction of personnel-intensive processes and a marked improvement in the quality of procedures and animal welfare.

The explicit mention of any individual software solutions or producers is consciously avoided here and reference is made to a separate statement by GV-SOLAS.

10. Staff requirement

10.1 Staffing plan

It is recommended that the following job groups be provided for relatively large laboratory animal facilities used by several institutes:

- 1. Responsible manager
- 2. Animal welfare officer (AWO)
- 3. Scientific associates
- 4. Technical laboratory staff
- 5. Administrative staff
- 6. Animal caretaker staff
 - Supervisor
 - Certified animal caretaker (specialised in research and clinical care)
 - Trained animal attendants
 - Unskilled workers
- 7. Training positions
- 8. Cleaning staff
- 9. In-house technicians

In smaller facilities, one or more job groups may be dispensed with. In all cases, a high level of staff training is required. This also involves regular re-training and continuing professional education (CPD) as required by EU law. For this reason, establishment positions for laboratory animal scientists must be created at universities where laboratory animals are housed.

10.2 Animal caretaker staff

The need for animal caretaker staff depends on a large number of variables such as:

- local conditions (e.g. available buildings, distances),
- · nature of animal housing and "penning",
- cage types,
- hygienic conditions,
- level of technical equipment and rationalization,
- · inclusion of staff for maintenance of technical systems,
- breed and strain-specific differences in care needs of laboratory animals,
- Quality Management Systems,
- · level of caretaker's training,
- degree of support from the caretakers for experimental work.

In view of the differing location-specific requirements of animal housing facilities, no staff to animal ratio is specified here. The number of animals housed per animal caretaker depends, as above, on very many factors and cannot therefore be reliably represented here. Mice are the exception, because a survey has been conducted on this subject in the various housing facilities (see section 10.3).

When calculating the number of animal caretaker positions, experience shows that absences for continuous professional education, holidays and sick leave must be accounted for every animal caretaker position. To ensure that care of the animals can be guaranteed throughout the year, a certain number of animal attendants must be available for all 365 days of the year. In view of the above-mentioned absences, 1.3 Full time equivalent (FTE) position must be provided for every animal caretaker present. The daily check of laboratory animals by a competent animal caretaker, taking into account the hygienic conditions, must also be factored in when calculation animal caretaker positions.

10.3 Personnel needs for the supervision of genetically modified mice (1)

The following text is taken from the identically titled GV-SOLAS booklet of 2003, which is based on a survey conducted throughout Germany.

To determine whether the staff requirement data published at the time are also valid for the housing and breeding of genetically modified mice, the Education Committee of the Society for Laboratory Animal Science (GV-SOLAS) conducted a survey on this subject from 2003 to 2006. Responses to the survey were received from 12 universities, 12 Max-Planck Institutes or major research institutions and 4 pharmaceutical companies based in Germany. The results of the survey are presented and evaluated below.

Design of survey

The aim of the survey was to gather data on the general conditions of the animal housing facilities in Germany, on the animal rooms, the housing units and the job groups involved in animal care. A particular focus, however, was the question of how much time is required for the various animal care activities.

Since the time invested in animal care varies widely in the five different housing categories, it was recorded separately, depending on the housing category. Conventional housing has no complicated technical and hygienic safety precautions to prevent the entry of infections and is also open for users. In the barrier system, the animals are housed in strict isolation from their surrounding environment. The barrier system may only be entered and exited via personnel airlocks with a shower and gowning area for changing clothes. For housing in IVC systems, the cage is closed with a special hood and is supplied with HEPA-filtered, conditioned air via a blower unit. A quarantine area is a room or group of rooms with a hygienic barrier for the isolated housing of animals that are potentially infected or suspected of being sick (infected). An isolator is a bacteria/virus-proof, sealed environment for breeding and housing of e.g. specific pathogen-free animals or animals associated with certain microbes. Mixed forms are possible in the housing categories, such as the operation of IVC systems within a barrier system.

The various activities of an animal caretaker involved in the supervision of genetically modified

mice were summarized in three groups, namely basic care, breeding supervision and care support measures.

Basic care involves all activities directly related to animal care, such as transfer activities, feeding and watering, inventory control, daily monitoring and sampling for health surveillance, receipt of animal deliveries, unpacking, transfer of cage and so on.

Breeding supervision covers the mating, weaning and marking of animals, performing biopsies, euthanizing animals taken from breeding, documentation (database if applicable), transfer of animals and communication with users.

Care support measures include activities such as transporting cages within the facility, emptying the bedding, washing and filling of cages with bedding, autoclaving of materials, and the cleaning and disinfection of material and rooms.

This differentiation makes it possible to establish the personnel needs determined by the survey for the applicable range of services of one's own facility. The results of the survey are shown in the following tables.

Time required for various activities

Table 1 provides an overview time required for the supervision of 1000 mice using five different housing categories: conventional, barrier, IVC, quarantine and isolator. Taking into account to the complexity of the survey elements, a statistical analysis of the results was not performed. Instead, the data are presented in the form of the median and the minimum and maximum values.

Housing category	Basic care (h)	Breeding support (h)	Care support measures (h)	Total (h)
Conventional	16.2 (4.2 – 54.5)	10.8 (1.5 – 23.3)	6.3 (2.2 -16.7)	33.3
Barrier system	16.5 (8.6 – 106.3)	10 (3.4 – 83.3)	7.8 (0.5 – 166)	34.3
IVC system	23.3 (7.5 – 36.8)	13.3 (3 – 23)	15.5 (5 -45.5)	52.1
Quarantine	40 (21 – 157)	13.3 (7 -24.5)	38.6 (11.5 – 185.7)	91.9
Isolator	68.7 (16.4 – 73.1)	15 (10 -15.4)	100.2 (2.1 -151.2)	183.9

<u>Table 1:</u> Time required for the supervision of 1000 genetically modified mice in 5 different housing categories in h per week. Data given as median values (with minimum and maximum values in brackets). Basic care: transfer, feeding and watering, inventory control, daily monitoring and sampling for health surveillance, receipt of animal deliveries, unpacking, Transfer cage etc.. Breeding supervision: mating, weaning and marking of animals, performing biopsies, euthanizing animals taken from breeding, documentation (database if applicable), transfer of animals and communication with users. Care support measures: transport of materials within the facility, emptying of bedding, washing and filling of cages with bedding, autoclaving of materials, and the cleaning and disinfection of material and rooms.

In the three activity groups, the result basically shows a positive correlation between the complexity

of the housing category on the one hand and the time required for the care of the animals on the other: The more complex the housing system is, the more time has to be devoted to it. The time required for the basic care of 1000 mice is highest in isolator housing with 68.7 h (median) and lowest in conventional housing at 16.2 h. The time required for the breeding supervision of 1000 mice ranges from 10 to 15 h a week depending on the housing category.

Care support measures are the most time-consuming in isolator housing with 100.2 h, whereas in conventional housing they are the least time-consuming with 6.3 h.

Personnel requirements

Table 1 shows the time required for the various activity groups in the supervision of genetically modified mice. On the basis of these times, it is possible to calculate the number of mice that can be estimated for supervision by each animal caretaker present (see Table 2). The calculations were made on the basis of a 38.5 h per working week. In those German states (Länder) or institutions that have different working weeks on the basis of the collective agreement (TV-L, TVöD, LeistungsTV-Bund), the values in the tables must be adjusted accordingly.

Housing category	Basic care	Basic care + breeding supervision	Basic care + care support measures	Basic care + breeding supervision + care support measures
Conventional	2337	1426	1711	1156
Barrier system	2333	1453	1584	1122
IVC system	1652	1052	992	739
Quarantine	963	722	490	419
Isolator	560	460	228	209

<u>Table 2:</u> Number of genetically modified mice that can be considered in the various housing categories per animal caretaker present. The values derive from the absolute time required for the activities (see Table 1) on the basis of the 38.5-hour week that is generally applicable in the public sector at present in Germany. For a definition of the different activity groups see legend to Table 1.

It is not possible, however, to determine the staff requirements directly from the mouse data shown in Table 2. To do this, it has to be taken into account that the animal attendant staff are not available for 38.5 h in every 52 weeks of the year. From the 260 working days of the year, it is necessary to deduct absences amounting to 11 days of national holidays, 29.5 days of annual leave (vacation) and 10 days of sick leave (average values), which corresponds to a total absence of slightly more than 19% in Germany.

Barrier housing requires the animals to be strict shielded from the environment. As a rule, the staff accesses the area via an airlock system with a compulsory (air) shower. Entering and exiting through this system is a time-consuming procedure, which is usually necessary three times in the course of a working day if there is no accommodation is provided within the barrier area for breakfast and midday breaks. On average, 60 minutes (13%) per working day must be reckoned on for this procedure.

Depending on the SOP, this time may be reduced by using air showers if available.

Deducting these absences from the times shown in Table 2 gives the number of genetically modified mice that can be calculated on in total for each animal caretaker position (Table 3). The actual number of staff and positions needed for a facility can be directly determined from these values. For instance, one animal attendant position can be used to supervise a total of 1893 mice e.g. providing basic care in conventional housing, but only 1586 animals in barrier housing. By contrast, one animal attendant position is only sufficient to supervise 1338 mice in IVC systems, 780 in quarantine and no more than 457 in isolators.

Housing category	Absence time in %	Basic care	Basic care + breeding supervision	Basic care + care support measures	Basic care + breeding supervision + care support measures
Conventional	19	1893	1155	1386	936
Barrier	19 + 13*	1586	988		763
system				1077	
IVC system	19	1338	852	803	599
Quarantine	19	780	585	397	340
Isolator	19	457	373	185	169

<u>Table 3:</u> Number of genetically modified mice that can be considered per animal caretaker position in total (38.5 h week). The values in the table are calculated from the figures shown in Table 2 by taking into account the average absences due to national holidays, annual leave (vacation) and sick leave (19%). *In the case of barrier housing, an additional "absence" of 13% was included in the calculation for entering and exiting the area three times in the course of each working day. The same applies to IVC systems behind a barrier. Depending on the SOP, this time may be reduced by using air showers if available.

One fundamental problem when determining the staff numbers needed is the fact that the basic conditions of laboratory animal housing units usually differ more or less markedly from one another, depending on the facility. In individual cases, therefore, the number of mice to be supervised by one animal attendant position may be higher or lower than indicated in Table 3. Additional services, technical equipment features and spatial conditions will thus impact the capacity for supervision to varying degrees. The required staff numbers presented here can therefore serve only as a reference framework. At all events, when determining the actual staff numbers needed, it is necessary to make a careful assessment of the relevant facility's specific framework conditions. To ensure that this is done with the necessary expertise, it is absolutely essential to consult an experienced laboratory animal scientist.

(1) from: Weiss, J., Dietrich, H., Kunz, E., Nebendahl, K., Treiber, A. *Personalbedarf für die Betreuung genetisch veränderter Mäuse*, GV-SOLAS, 2003, http://www.gv-solas.de/fileadmin/user_upload/pdf_publikation/aus_personalbedarf.pdf.

11. Training and continuing education

The quality of an animal housing unit and the quality of the data obtained from animal experiments depends very much on the training and qualifications of the persons engaged in these activities. The requirements for personnel groups involved in working with animals and the expertise needed for this work are set forth in Directive 2010/63/EU (Articles 23 and 24 and Annex V).

The following personnel groups are defined:

- · staff who carry out procedures on animals,
- staff who design procedures and projects,
- · staff who take care of animals and
- staff who kill animals.

The groups are required to undertake regular continuing professional education according to Directive 2010/63/EU.

At the time when this requirement was made (2014), discussions concerning the formulation of the regulations to be set forth in the EU Directive had not be completed either at EU level or at national level in Germany. For this reason, no further statements are provided here on training and continuing education. When consultations at EU level have been completed and the relevant regulations have been passed into law in Germany, GV-SOLAS will compile its own information on this important issue, which will then be published on the GV-SOLAS website (www.gv-solas.de).

12. Costs and services

In the planning of an animal laboratory, an estimation of the expected investment costs and subsequent running costs is crucially important so that the building and the work processes can be well designed not only from a technical perspective, but also in terms of cost-effectiveness. In the subsequent operation, an analysis of the given (actual) costs can provide valuable insights for potential savings.

The appropriate scale of any costing exercise may differ widely in each phase, i.e. both in the planning and in subsequent operations. It should always be determined on the basis of the objectives to be achieved with the information obtained from the costing procedure. The potential accuracy of the costing will also be influenced by the question as to how nuanced the cost data obtained – for example, from the administration of a large institution such as a university – can actually be. The spectrum between direct costing, in which e.g. only the variable costs are considered, and full costing, which theoretically considers all costs, including fixed costs, is very wide. The level of detail that allows the best cost-benefit relationship must be decided on a case-by-case basis.

With the aid of cost accounting – and assumed, that the calculation and interpretation of the data are correct – it is possible to pursue the following objectives, for example:

- Establish transparency of costs and services.
- Raise awareness of cost factors among all those involved.
- Determine appropriate transfer prices for invoicing of services.
- Provide decision-making aids for investments.
- Determine cost-effectiveness of sub-sections and seek alternatives where necessary.

As an aid to costing for animal experiment facilities, a GV-SOLAS working group has translated the "Cost Analysis and Rate Setting Manual" of the US National Institutes of Health and adapted it for Central European conditions and also developed a software on the basis of the manual. The German version can be found on the website (www.gv-solas.de).

12.1 Cost categories

A generally valid (cost) structure which defines the costs that have to be considered and how they are to be allocated is not possible; the basic conditions and objectives of the facilities are too varied. The organizational form (see section 2.2) and range of services (see section 12.2) of the animal laboratories may also be very different, which has a major influence on the cost categories. And the models for costing and invoicing of services used are correspondingly heterogeneous.

To arrive at practical data in an animal laboratory, it is advisable to depart from the classical cost categories taught in business administration (fixed and variable) and draw a distinction between <u>direct costs</u> and <u>distributed costs</u>, where the latter (in relation to the animal laboratory) may occur internally and externally.

<u>Direct costs</u> are understood to mean those costs incurred in a certain (sub)-area of the animal laboratory, such as the mouse housing unit. They are usually easy to determine (e.g. feed) and "directly" attributable to this area.

For the <u>costs distributed within the animal laboratory</u>, e.g. cost of detergents and staff for cleaning the cages, initially service cost centres should be defined, where the costs are recorded before being allocated to the individual (sub)-areas with the aid of an allocation formula.

There are also <u>external distributed costs</u>, which are incurred in the institution, such as a university or clinic, and ought to be charged or allocated accordingly. These are, for example, the costs of central administration, including personnel and material costs. In many cases, the floor areas (m²) of the departments serve as the allocation formula for these costs.

Depending in the starting position and the objectives, the costs in individual cases may also be differentiated in other ways, but they must then be inherently conclusive, complete and consistent. A comparison of cost data between different animal housing facilities is all the more difficult the more heterogeneously the structures are defined.

The following table with different (categories of) costs does not break the costs down into direct costs and costs to be distributed, because this is not generally possible, as explained above. This presentation makes no claim to be exhaustive, but it does show the most important costs and provides notes and examples.

Table 12/1: Cost categories with notes

Costs (categories)	Notes/examples
Personnel costs	are as a rule the biggest cost factor in a laboratory animal facility. They include - in the animal housing area: animal caretakers (also supervisory staff such as animal caretakers supervisors, foremen) and assistants; - in the experiment service: laboratory staff, veterinarians etc.; - the management of the facility as well as animal welfare officers and office staff. Note: occasionally personnel costs "change" (e.g. through procurement of external services, such as outsourcing of cage cleaning) into material costs. When drawing comparisons, therefore, great care is necessary and an analysis of the differences is required!
Consumables in the animal housing unit	Feed Bedding Nesting materials
Cages, water bottles etc.	Since the stability of animal cages is limited as a result of frequent autoclaving, it is advisable to record them as consumables and to budget for a certain percentage of the stock each year. This percentage can vary widely depending on the used cage material.
Cleaning agents and dis- infectants	Bottle disinfection Cage cleaning

Costs (categories)	Notes/examples
Work clothes	Cost-intensive, because staff in the animal housing area need fresh, autoclaved clothing each day, in addition to disposable articles such as face masks, caps and gloves; for the animal experiment area: surgical clothes or lab coats, work shoes. The clothes are usually cleaned by external companies, which often also rent clothing as service providers.
Hygienic quality control	Cultures, diagnostic kits Materials for ELISA, IFA and PCR assays or costs for external tests
Materials for experimental service	Medicines, anaesthetics Surgical materials (suturing material, infusion solutions etc.) Laboratory chemicals and consumables (e.g. test tubes) X-ray material
Administration	Office supplies Telephone costs
IT	Databases for administration of animal stocks
Waste disposal	Contaminated bedding Hazardous waste from laboratory / experimental area Animal cadavers Residual waste
Depreciation of large equipment	Autoclaves Hydrogen peroxide airlocks Cage cleaning machines Bottle cleaning and filling machines
Depreciation of durable animal laboratory installations	Cage racks, partition walls for pens IVC racks, clean workbenches Isolators
Depreciation of building equipment	Furniture for laboratories, offices, staff rooms
Depreciation and running costs for vehicles	Vehicles for animal transport or other services
Running costs of building	Energy in the form of electricity, heating and steam Water Gases, compressed air
Building costs	In many animal housing facilities, the invoicing of building costs is limited to renovation and maintenance costs or minor adjustments for changes in use. The correct approach would be the depreciation of buildings over 50 years (or less) or the calculation of a typical rent for the locality concerned, although there are generally no standards of comparison for high-tech laboratory animal facilities.
Indirect costs / institu- tional shared costs	 proportionate calculation for staff of building administration, facility management, accounting, management of the institution etc. proportionate calculation for maintenance of overarching technical systems (e.g. fire alarm service)

12.2 Service categories

The services of an animal laboratory are listed below. This list lays no claim to being either universally applicable or exhaustive, because many animal laboratories only offer some of the services listed, while others provide additional services.

- Animal housing services (in the relatively narrow sense)
 - Basic care:
 - Change of cages, diet and water bottles once or twice a week, daily health check, daily check on environment, operation of barrier airlocks, disinfection measures, cleaning in animal rooms and in barrier areas.
 - Cage and rack preparation.
 - Assistance with breeding and experiments:

 Mating of animals according to work assignments; weaning of young animals; identification of animals and keeping of books on animal stock and data input on computer; taking biopsies for genotyping; timed mating of animals; sampling of blood, faeces and skin for hygiene checks; preliminary work for embryo transfer; breeding of certain inbred or outbred lines or especially genetically modified lines; application of medicated feed or medicated drinking water.
 - Quarantine housing with/without check on hygiene status.
- Animal house management and administration services
 - Management function.
 - Centralized ordering and shipment of animals.
 - Cost accounting.
 - Training and teaching (laboratory animal science courses).
 - Advice and instruction on experiments including technical assistance in anaesthesia and administration of substances.
 - Project management according to gene technology legislation for breeding and housing of animals in the entire area of the laboratory animal facility.
 - Genetic and breeding advice with difficult mouse lines.
 - Application for approval and management of experiments for breeding animals with a constraining phenotype.
 - Contributions to solutions for scientific problems.
 - Radiological protection officers.
 - Safety officers (occupational health & safety).

• Services of animal welfare officer

- Advising scientists during project planning.
- Processing of applications, notices and projects dependent on post mortem organ removal.
- Processing of approvals for exemption according to § 9 Para. 1 of the Animal Welfare Act.
- Advising institutions on animal welfare issues, contacts with authorities etc.
- Recording of animal numbers for laboratory animal reporting ordinance.

Services of animal house laboratory

- Operation of diagnostic laboratory together with hygiene checks.
- Transgenic service, IVF, embryo transfers and cryopreservation.
- Pathology tests.

Services of experiment unit

- Application of test substances, immunizations with antigens or preparations.
- Blood sampling.
- Haematology, clinical chemistry.
- Pre-operative preparation and post-operative care, anaesthesia, assistance in surgical procedures.
- Measuring techniques (ECG, EEG etc.).
- Imaging.

Notes: