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Society for Laboratory Animal Science

Specialist Information

from the Committee for Genetics and Laboratory Animal Breeding

Housing genetically engineered animals of risk group 1:

Recording strategies according to gene technology law using databases

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1. Recording procedures according to gene technology law

Records kept in the housing of genetically engineered animals, as with all genetic engineering work, must satisfy the German regulations on gene technology recordings (Gentechnik-Aufzeichnungsverordnung, GenTAufzV) in their current version.

1.1. Details of the facility and the persons responsible

An animal housing facility licensed according to gene technology law must provide details of its location, together with the name and address of the operator, the project manager and the biosafety officer. The details must also include the reference number of the facility and the notice date or starting date and safety level/risk group of the facility. If unexpected incidents occur in the animal facility that could jeopardize the objects of protection under the Gene Technology Act, these must likewise be documented.

1.2. Details concerning the animals

The point when animals are first introduced or embryos, sperm, or ovaries (germ plasm) (also cryopreserved) are imported into a facility marks the beginning of genetic engineering work in the housing facility of genetically engineered animals. The genetic engineering work is ended when breeding is no longer continued and neither genetically engineered animals nor (cryopreserved) embryos, sperm, or ovaries (germ plasm) are present in the facility.

The description of a genetically engineered animal line must in principle include all the information that is necessary for the description of genetically engineered microorganisms. In addition, a risk assessment must be carried out. The information must be suitable overall for distinguishing the genetically engineered animal from others. Details of the donor organism from which the genetic information was transferred, details of the nucleic acid transferred and its function and that of the recipient organism are therefore also a minimum requirement. If parts of the vector (e.g. an antibiotic resistance gene) remain in the organism, information about this is also necessary. With long-established lines, this information is not always complete. In this case, the competent authority should be provided with documentation confirming that, for example, no literature on the generation of the line is available, and agreement will be sought on the next steps.

1.3. Formal requirements of recordings

Recordings subject to gene technology law can be kept electronically and stored on a data storage device. All the requirements that apply to written records are also applicable to these recordings. That is to say, no cuts or deletions may be made that render unreadable what has been recorded, and any changes must be duly marked. This can be done, when using a database, by automatic logging of all changes or by documentation (when and what was changed).

When recordings are stored on a data storage device, it must be ensured that subsequent changes are no longer possible and that the data is readable at least for the duration of the retention period (ten years for work classified as Safety Level 1 / risk group 1 research).

The recordings must further be signed by the operator, project manager or an assigned person (e.g., the head of the animal facility). The use of a qualified electronic signature is possible here. However, this requires registration with an accredited certification service and availability of the appropriate hardware and software. One possible solution may be a signed cover sheet for a given data storage device, on which the signatory confirms that the recordings on this data storage device are complete and correct.

Since the regulations governing these technical solutions for keeping recordings are not standardized at federal level and there is a considerable diversity of options available for electronic documentation, clarification should always be sought beforehand with the competent authority as to whether the animal facility's own recordings satisfy the requirements of the German regulations on gene technology recordings https://www.gesetze-im-internet.de/bundesrecht/gentaufzv/gesamt.pdf. Any recording not properly kept or not kept at all may then be penalized as a violation of the regulations if this arose through negligence (i.e., not only with premeditation).

2. Suggestions for practical implementation (in consultation with the competent authority)

Electronic records are generally made using commercially available software programs which (in the case of simple applications) range from table or text programs (e.g., MS-EXCEL or WORD) to complex databases. What is important is that the content can be secured at a verifiable time, e.g., using a document creation program (pdf/A). The operator must make sure the electronic records remain accessible and readable within the given retention period. This can be achieved by saving the records on an appropriate server. In case of a data transfer to another server, the readability must be preserved. Here, more complex database programs offer the advantage that this more detailed information and also precise change dates can be saved, and parts of entries protected or placed under administrator restriction.

This documentation can be easily achieved with appropriate programming of (also commercial) database software. It is more difficult when using table or text programs, because generally any change here results in a new save date for the whole file.

Essential information can be structured as follows:

2.1. Scientific description

The objective is to provide the most precise and comprehensible description of the mutant. This description must give details of the genetic modification with generation technology, the name of the line (including designation according to International Committee on Standardized Genetic Nomenclature for Mice), the origin of the mutation (gene ID# and donor organism), the origin of the regulatory elements and their donor organisms, as well as the vectors used. Characterization/description, use as animal model, genotype, zygosity, genetic background, backcrossing generation and a possible phenotype should be listed.

A mutant must be defined as unambiguously as possible. A big help here is the availability of international nomenclature rules (see: http://www.informatics.jax.org). For many mutants, a gene ID (e.g., MGI or NCBI) is available that can likewise be tracked through corresponding

internet portals. Since mutants can increasingly be sourced from so-called consortia, it makes sense to include in a database any “Stock No.” that may be indicated. It is also important to give the correct information on the laboratory of origin (lab code) according to the National Academies in Washington DC, USA (https://www.nationalacademies.org/ilar/lab-code-database). With these details, a mutant should be unequivocally identifiable, because many a mutant has been produced in different laboratories in a similar but not identical way.

Experience shows that mutants for which there are no requirements on record keeping under gene technology law (e.g. spontaneous mutants) are often housed together with and also paired with mutants classified as safety level 1 organisms: this must be indicated accordingly.

2.2. Synonyms, possible publications, keywords

Since several differing official and published names exist for many mutants, especially those already generated some time ago, it makes sense to include a section headed “Synonyms”. It should be borne in mind here that the current nomenclature is used in the scientific description. It is accordingly useful also to give keywords and publications, especially for search functions.

A corresponding database can logically be used also for issues relating to animal welfare law. Details currently remain to be established because implementation of the Animal Welfare Act is still under way. In our experience, the availability of a database in several languages, especially also in English, is a great help. Since German authorities generally insist on information in the official language (German), it makes sense to establish print functions in which, on the one hand, only the fields of a data sheet relevant to the authority in question are printed and which, on the other, allow a printout in German. High-end commercial database systems allow such functions.

3. Conclusion

As mentioned above, details on documentation configuration should always be agreed with the competent authorities. One example of a database with an associated web application, which meets both in-house requirements and the requirements of gene technology and animal welfare legislation, is the database used by the German Cancer Research Centre in Heidelberg (Staudt et al 2012). Our experience also shows that a database/application needs constant and costly maintenance and that all new entries have to be verified by a competent administrator. To make sure that all mutants are recorded, an in-house procedure must be established which makes it mandatory to use the available database. Since requirements may change for a variety of reasons, capacity for further development of a database makes sense and can prove useful.

4. Annex

The above-mentioned publication by Staudt et al. can be found under the following link:
http://suppl.dkfz.de/Articles/Schenkel.pdf

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