



Technical information on animal experimentation

Announcement of constraint observed in animal lines (Form-M and data sheet)

1 Overview

To be able to recognise lines with an impaired phenotype and to take measures to reduce constraint a recording of constraint has to be done according to Article 124 TSchV.

If in a laboratory animal facility animal lines with an impaired phenotype are kept or existing lines show new constraint, the cantonal authority has to be informed regardless of whether it is a genetically modified or spontaneously mutated line (Art. 12 TSchG, Art. 126 TSchV). For this purpose, **Form-M** in combination with the **data sheet** for genetically modified lines or strained mutants is used.

2 Monitoring of constraint

According to the animal welfare legislation, monitoring of constraint must be carried out for genetically modified animal lines and for lines showing an impaired phenotype (Art. 124 TSchV, Arts. 12-16 TVV). This must be done under the responsibility of the head of the laboratory animal facility (delegation to the researchers is possible, must be documented) and is examined by the cantonal veterinary authorities during inspections.

The monitoring of constraint includes both visual inspections and examinations of the animals, particularly while changing cages¹. In order to describe a line definitively as showing no impaired phenotype, a minimum of 100 individuals from at least 3 generations must be observed and documented.

The decision that a line does not show an impaired phenotype is taken by the head of the laboratory animal facility. This decision can be substantiated by data from an internal monitoring of constraint or by such a monitoring based on other findings, if the latter is sufficient, i.e. equivalent to monitoring of constraint in accordance to the TVV² (for example, previous recording carried out by the producer of the line or by other institutes, including the decision of the authorities). The documents must show how many animals were examined, how frequently and according to which criteria.

¹ According to Article 14 para. 1 TVV, animals must be inspected for traits according to Annex 4 while changing cages and observed at least once in between cage changes.

² Exception: In the case of lines which (probably) do not show an impaired phenotype and were kept before the provisions entered into force (1 May 2010, Art. 124 TSchV), there is no need for a monitoring of constraint provided the line remains in the same facility (conversely, the same line in a new location is covered by the new provisions).

The results of the monitoring of constraint (according to Annex 3 TVV) are summarised in the **data sheet** for genetically modified lines or strained mutants, which must also contain all technical data on the animal line (according to Annex 2 TVV).

For targeted lines, one **data sheet** must be used per objective.

In the case of suspected or demonstrable constraint, this should be announced to the cantonal authorities. Monitoring of constraint should also be carried out when breeding small numbers of animals, even though it may be clear from the outset that not enough animals will be produced or kept as would be required for a definitive announcement, and there is no intention of establishing the line. Monitoring of constraint documents must be kept available to the enforcement authorities at all times.

3 Form-M – Announcement of lines with an impaired phenotype

Animal lines in which genetically related harm, suffering, pain, anxiety or other impairments occur may be kept only with a special licence and may be bred only under limited circumstances (Art. 127 TSchV). If the monitoring of constraint in a line reveals that the animals affected have an impaired phenotype³, an initial provisional announcement must be submitted to the authorities within two weeks using **Form-M** (Art. 17 TVV). This must describe the constraint (e.g. harm and suffering) as well as the measures that can be taken immediately to reduce the constraint⁴.

A line should be announced even if measures to reduce constraint result in the disappearance of all symptoms. Measures to reduce constraint should be listed in **Form-M** (e.g. keeping animals only up to an age at which the constraint does not yet occur).

The monitoring of constraint should be continued after the provisional announcement has been submitted (Art. 15 TVV). Once the monitoring of constraint has been completed or the available documents are sufficient to demonstrate the specific constraints⁵, the definitive announcement must be submitted (Art. 18 TVV, also using **Form-M**). This announcement must demonstrate the scope and results of the monitoring of constraint, measures taken to reduce constraint, the intended scope of use in animal experiments and the benefit of further breeding (Art. 18 para. 2 letter d. TVV).

If the initial findings of the provisional announcement are not confirmed or the breeding of a line is discontinued, this must be reported informally to the cantonal authorities in order for the procedure to be completed (Art. 17 para. 4 TVV).

If constraint is observed in several animals of a targeted line, i.e. in animals which represent merely an “intermediate product or by-product”, this must be announced to the authority (**Form-M**). A targeted line must also be announced if animals of a line showing an impaired phenotype are cross-bred. From this point, the entire targeted line is regarded as “provisionally announced”. Further observations are

³ The wording used in Article 17 para. 1 TVV “if similar signs of constraint are found in several animals...” (or, for fish, in Article 20 para. 1 letter a. TVV: “if evidence of genetically related constraint is found in several animals”) means:

- Constraint: Changes in morphology, physiology or behaviour that either suggest constraint in connection with genetic modification or constitute generally known symptoms of constraint.
- The first occurrence of genetically related constraint merely prompts a suspicion. It is only when several animals show similar constraint that a provisional announcement is justified. The aim is to inform the cantonal authorities that a line, which may have an impaired phenotype, is being investigated further.
- Number of animals: An announcement must be submitted at the latest when 5 animals are affected.

⁴ Established breeding lines in which blind or deaf individuals regularly occur (e.g. BALB/c) are by definition covered by the reporting obligation in Article 17 TVV. However, for the time being these lines or strains should not be announced until more is known about how widespread the constraint is and whether any breeding measures could be taken to counteract it.

⁵ In order to identify and describe specific constraints, it is not necessary to observe 100 animals, but only as many as are needed to substantiate the statement.

entered in the **data sheet** for genetically modified lines or strained mutants. Any radical developments must be announced to the authorities (supplement to **Form M** with updated **data sheet**).

If a known line showing an impaired phenotype is reintroduced to a laboratory animal facility, this must be reported to the cantonal authorities using **Form-M** (example: SCID mouse). The definitive announcement under Article 18 TVV can be submitted immediately, because the line is already known and relevant data is available, provided that the new husbandry environment does not lead to new constraints. In these cases, the competent committee on animal experimentation will be able to refer to existing decisions of other cantonal authorities and take its decision quickly. Because constraint can also depend on environmental factors (climate, care, etc.), the existing data of constraint must be verified.

In the case of back-crossing on a new genetic background, the effects of the mutation may change, which is why the monitoring of constraint must be carried out again.

So-called inducible lines, in which the gene in the genetically modified animals is not expressed until a substance is administered, are not regarded as showing an impaired phenotype because the animals do not show any impairment without induction. As a result, it is not necessary to submit an announcement using **Form-M** for this line. The induction of the gene which leads to an impaired phenotype is regarded as an intervention and must be applied for as part of an animal experiment (**Form-A**).

4 Decision of the admissibility of lines and strains that have an impaired phenotype

The cantonal authority sends the definitive announcement on lines or strains that have an impaired phenotype to the cantonal committee on animal experimentation, which decides whether further breeding is admissible. The committee weighs the severity of the constraint against the benefit for research, therapy or diagnostics (weighing of interests).

The more severe the constraint for the animals, the more restrictive the licence conditions are. In the case of DS3, all animals bred must be justified in the context of licensed animal experiments. In addition, the duration of breeding is limited accordingly. In the case of DS2, the breeding of the animals must be justified by licensed animal experiments as well, but without compulsory restrictions on the number of animals or duration of breeding.

The cantonal authorities lay down the conditions for further breeding and the measures to be taken (such as the scope and duration of breeding, humane endpoints, hygiene precautions, etc.). The decision is issued in the name of the head of the laboratory animal facility.

The head of the laboratory animal facility must ensure that the conditions and restrictions laid down for the breeding line are stipulated in the **data sheet**, to make sure that everyone involved and any possible recipients of the line are informed (Art. 127 para. 4 TSchV).

The FSVO may lodge a formal appeal against decisions made by cantonal authorities; to that end, the canton must quickly and fully notify the relevant decisions (Art. 25 TSchG).

Under Article 146 TSchV, the FSVO keeps a register of decisions on the lines and strains that have an impaired phenotype, including the decreed conditions and requirements. The register is listed in the electronic information system E-Tierversuche (Art. 20b TSchG).

The table below (table 1) summarises the cases in which a monitoring of constraint, **data sheet** or announcement is required for an animal line in an existing laboratory animal facility. (See also the

information published by the ZH veterinary office: [Versuchstierhaltung - Informationen zu den gesetzlichen Neuerungen](#), February 2012).

Established line vs. targeted line	Are sufficient documents available for the assessment of constraint?	Does the line show an impaired phenotype (suspected or demonstrated)?	Is a monitoring of constraint necessary (Art. 124 TSchV)?	Is a data sheet necessary?	Is an announcement necessary?
Established	Yes	No	No	Yes	No
Established	Yes	Yes	No	Yes	Yes
Established	No	No	Yes / (No) ⁶	Yes	No
Established	No	Yes	Yes	Yes	Yes
Targeted	No	No	Yes	Yes ⁷	No
Targeted	No	Yes	Yes	Yes	Yes

Table 1: Overview monitoring of constraint, report and data sheet for established lines and targeted lines.

5 Data sheet for GMA (genetically modified animals)

The **data sheet** according to Article 23 TVV contains the scientific data as stipulated in Annex 2 TVV, the summary of monitoring of constraint as stipulated in Annex 3 and the decision on lines showing an impaired phenotype. A **data sheet** must be drawn up at the latest when

- an initial, provisional announcement on a line showing an impaired phenotype is produced (**Form-M**)
- an application is submitted to use an animal line in an animal experiment (**Form-A**); if the information concerning the line is still incomplete at the time when the application is submitted, the **data sheet** should be attached nevertheless and submitted again later in updated form
- animals of the line are transferred to third parties
- the monitoring of constraint is completed and a line is definitively classed as not showing an impaired phenotype

The head of the laboratory animal facility is responsible for ensuring that data sheets are kept up-to-date and are available to the authorities during inspections⁸.

⁶ Exception: In the case of lines which (probably) do not show an impaired phenotype and were kept before the provisions entered into force (1 May 2010, Art. 124 TSchV), there is no need for a monitoring of constraint provided the line remains in the same facility (conversely, the same line in a new location is covered by the new provisions).

⁷ From the outset, targeted lines require a data sheet which indicates the purpose.

⁸ Data sheets for lines not showing an impaired phenotype can also be kept in the facility and made available to the authorities in a different form, e.g. as an Excel list, provided they are complete

6 Announcing process

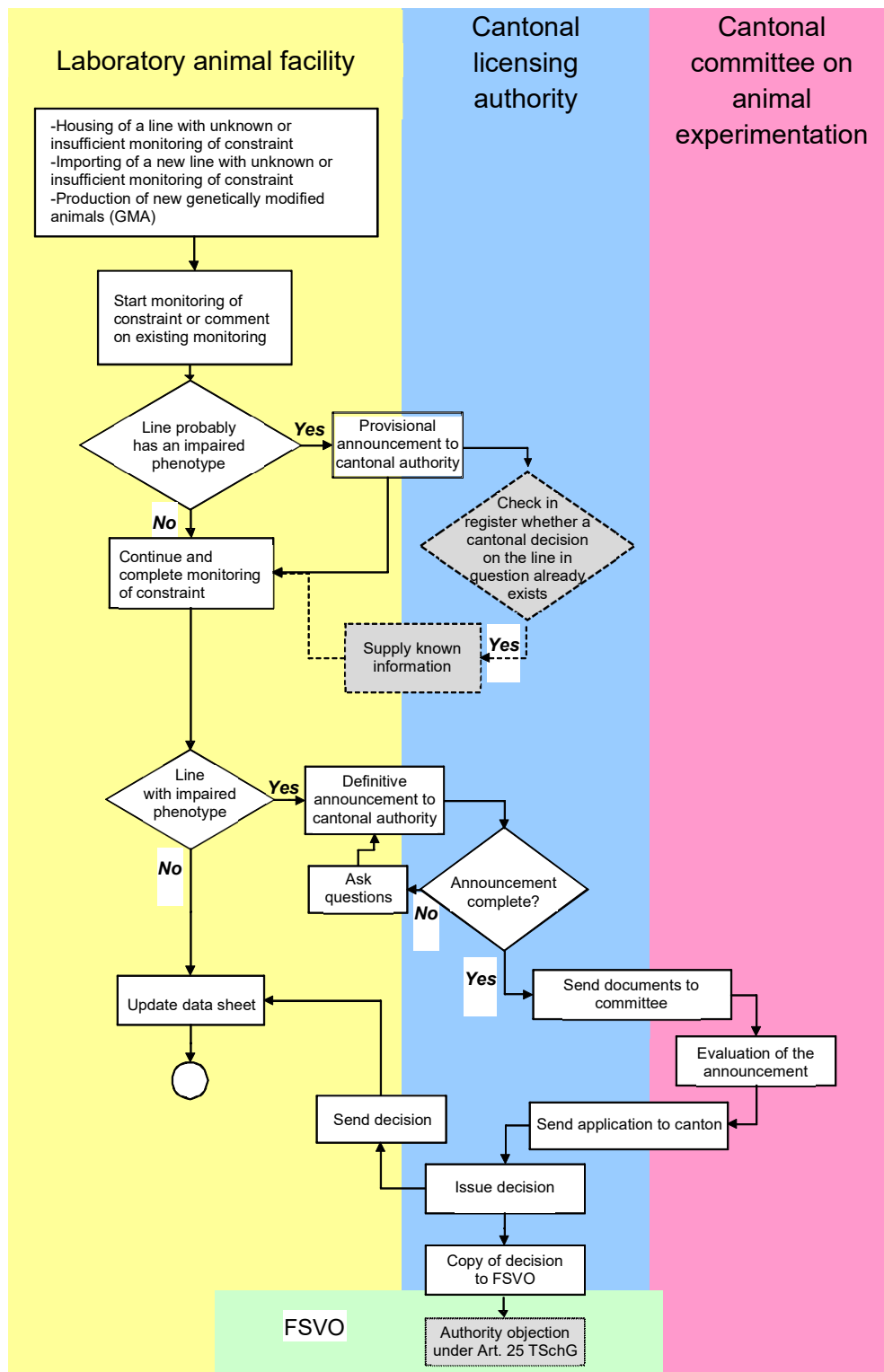


Figure 1: Flowchart: monitoring of constraint and announcement of lines that have an impaired phenotype.

7 Annex

7.1 Glossary

Term	Signification
Data sheet	Data sheet for genetically modified lines and strained mutants. Form for the summary of the monitoring of constraint and for the decision of the competent authority on lines showing an impaired phenotype.
Decision	Decision of the cantonal authorities on the admissibility of lines and strains that have an impaired phenotype (Art. 12 TSchG and Art. 127 TSchV).
DS	Degree of severity. Categorisation of constraint in 4 degrees of severity (DS 0: no impairment, DS 1: slightly impaired, DS 2: moderately impaired, DS 3: highly impaired).
Form-M	Form for the provisional and definitive announcement of a line showing an impaired phenotype.
GMA	Genetically modified animals. Offspring from lines or strains with genetically modified animals (according to Art. 3 letter d of the Containment Ordinance; SR 814.912) are deemed to be genetically modified until evidence is provided to show that they do not carry the genetic modification of the parent animal (Art. 123 TSchV).
Inducible line	A line in which, in the genetically modified animals, the administration of a substance regulates the expression of a gene. Accordingly, constraint can depend on the manifestation or modification of the transgene. Inducible lines are not regarded as having an impaired phenotype as long as the animals do not show the impairment.
Laboratory animal facility	Animal husbandry unit in which laboratory animals are kept, bred or traded.
Line or strain with an impaired phenotype	Breeding lines or strains which include mutants that have an impaired phenotype or in the breeding of which animals are excessively instrumentalised (see Art. 2 para. 3 letter l. TSchV).
Mutant with an impaired phenotype	An animal which, as a result of genetic predisposition, experiences pain or suffering, shows damage, lives in fear or suffers any other form of radical interference in its appearance or its capabilities. The stress-inducing mutation may occur spontaneously, be induced physically or chemically or also caused by genetic modification (Art. 2 para. 3 letter k. TSchV).
Targeted line	Group of animals, which are produced by crossing different lines with different genotypes to reach a specific goal. The intended genotype may be created after one or at the end of a series of crossings. During the intermediate stages a variety of unwanted or temporally needed genotypes will occur. Usually only few animals with the aimed genotype will be created.
TSchG	Tierschutzgesetz (Animal Welfare Act) of 16 December 2005 (SR 455).

Term	Signification
TSchV	Tierschutzverordnung (Animal Welfare Ordinance) of 23 April 2008 (SR 455.1).
TVV	Tierversuchsverordnung (Ordinance on laboratory animal husbandry, the production of genetically modified animals and the methods of animal experimentation; Animal Experimentation Ordinance) of 12 April 2010 (SR 455.163).

7.2 Legislation

English is not an official language of the Swiss Confederation. No official English translation of the law is available. The translation is provided on the FSVO website for information purposes only:

<https://www.blv.admin.ch/blv/en/home/tiere/tierversuche.html>.