

Recommendations on the application for approval of an animal experiment project according to § 8 para. 1 TierSchG at the Eberhard Karls University Tübingen

According to § 8 para. 1 TierSchG, **interventions and treatments on vertebrates and cephalopods for experimental purposes which are associated with pain, suffering or damage to the animals are generally subject to authorization**, provided that they fulfil the requirements in § 7 para. 2 sentence 1, nos. 1 to 3. This does not apply to animal experiments which do not actually have an experimental character and/or which are only notifiable under §8a TierSchG. The application for approval of an experimental project must be submitted in written form **in German language** to the Regierungspräsidium (R.P.) (§ 31 TierSchVersV). The same form must be used for both procedures (application for approval and notification of animal experiments). The current form can be downloaded from the homepage of the Regierungspräsidium Tübingen (<https://rp.baden-wuerttemberg.de/Themen/Landwirtschaft/Seiten/Tierschutz.aspx#TIERSCHUTZ>) or from the Einrichtung für Tierschutz, tierärztlicher Dienst und Labortierkunde (<http://www.med.uni-tuebingen.de/tierschutz/html/download.html>).

I. Required application documents for discussion, examination and consultation with the animal welfare officer

Please first submit the following documents and application forms to the Animal Welfare Officer (TSchB) in printed, single copies or electronically by e-mail. Under point II. of this recommendation "Final Application Forms - Checklist" you will find a detailed list of all required documents (with number of copies), which have to be submitted after consultation with the TSchB.

- 1) Complete animal experiment application
- 2) Personal data sheet for all contributors named under 1.2 and, if applicable, for the test designer named under 1.1.3 (not required for supervisor and deputy)

Please mark the personal data sheet if it has been updated and does not correspond to the version available at RP.
- 3) Non-technical project summary
- 4) Key publications (max. 5 publications)
- 5) Current final assessment of genetically modified breeding lines when working with genetically modified animals (even if the TSchB already has an assessment from previous projects, please always enclose a copy)
- 6) If already determined: Information on biometric planning, alternatively biometric expertise

If you have difficulties filling in specific sections, please mark them in colour. We will be happy to help during a joint discussion of an initial draft of the application.

General Considerations:

The purpose of an animal experiment application is to estimate the burden on the animals in relation to the benefit for the scientific question. Therefore, it must be clearly stated which burdens the animals will experience within the framework of the project and which interventions will be carried out. It must also be explained what will be done to minimize pain, suffering and harm and when animals will be prematurely withdrawn from the experiment.

The scientific purpose of the project should be described in as precise a manner as possible, without requiring your specific expertise, but that of a normal bio-medical academic education. It must be clear from the text that alternative methods (e.g. in vitro experiments) are out of the question or have already been exhausted and that it must be explained why this question can only be answered in an intact organism.

It is helpful to have the completed application read by someone who is not familiar with the specific question, but who corrects spelling and translation mistakes and recognizes passages of text that are difficult to understand.

First the general problem is to be described and then explained, how the planned attempts can contribute to the clarifying. Specific details, as they are usual in scientific papers or in proposals for research funds, can possibly lead to comprehension problems for readers not familiar with the subject. The use of finished text blocks from DFG or comparable proposals is generally not advisable.

Please pay attention to the exact question and always answer all questions completely, especially if several things and aspects are asked in one point at the same time. Please regard this information sheet as a recommendation. It does not deal with every single point in the application form.

1) Application for animal experiments

Please tick that the application is subject to approval. The applicant does not have to be the same as the project supervisor. However, he/she will become the approval holder and the authority will issue the official approval to the applicant (not the project leader). Please note that correspondence (including queries from the authority) will be addressed to the applicant and not to the project leader. The applicant does not formally need to have the technical knowledge and skills required of supervisor, deputy, planner and staff.

1.1.1 Project leader/supervisor

1.1.1.1 Professional education

Please check the appropriate profession (veterinarian, physician, scientist (which branch?), other) and check if the certificate is attached to this application or if it was already sent with the application for project nr.

to point 1.1.1.2 and 1.1.2.2 respectively (knowledge and skills):

Please list the activities of the project leader and the deputy leader with regard to the animal experimental interventions and treatments to be carried out in the project and indicate where they have the knowledge from (e.g. approvals, notifications or § 4 notices can be listed in which these animal experimental interventions or killing methods have already been carried out).

(See also the recommendations for the qualification of experimenters).

Certificate is attached / was sent with application nr....

to point 1.1.1.3 and 1.1.2.3 respectively (participation in a course on laboratory animal science):

Among other things, it must be stated whether a course on laboratory animal science with teaching content in accordance with Annex 1, Section 3 TierSchVersV was attended. If no, this can only be accepted by the authority if the same knowledge and skills have been demonstrably acquired elsewhere. If yes, indicate the course name and scope (in hours) and attach a certificate. All details for the supervisor and deputy must be noted on the application form and no separate personal data sheet must be enclosed.

to point 1.1.1.4 (special permit if applicable):

Please describe for which procedures, a special permit was issued.

to point 1.1.1.5 (expertise for the killing of laboratory animals):

Yes or No. This expertise is usually imparted during a course on laboratory animal science or may be acknowledged through a small exam in front of an animal welfare officer.

1.1.2 Deputy supervisor / leader

For an explanation of the following points regarding the deputy supervisor see the equivalent points for the supervisor above.

to point 1.1.3:

Usually the supervisor or deputy is also the test planner at the same time. In this case, no personal data sheet should be enclosed. Please note that the test planner must also have the laboratory animal knowledge and skills in accordance with Annex 1, Section 3 TierSchVersV. For further details, please refer to our recommendation on the qualification of experimenters.

to point 1.2:

Please indicate here other persons who carry out operations and treatments as well as killings on animals within the framework of this project (contributors). In principle, it is also required that these persons have the knowledge in accordance with Annex 1, Section 3 TierSchVersV. A personal form must be enclosed for each person. Please describe in detail for each person the individual procedures and treatments, including anesthesia and killing, which are carried out as part of the animal experiment and are therefore subject to approval. Breeding is only subject to approval in the case of animal strains with genetic burden. Removal of organs and other interventions on already dead animals should not be indicated here. If applicable, please enter in the right column of the table the application number with which a personal data sheet was submitted to the RP Tübingen. If no application number has yet been assigned, please enclose a duplicate of this person sheet with the new project.

to point 1.3.1:

Are the mentioned persons employed by the institution? If "No" please name the appropriate person(s). The term "institution" refers to the entire university including the associated institutes and departments.

1.3.2 If No, are they allowed by the responsible head of the department to use the facility?

to point 1.4.1:

veterinary care for the animals

<u>Name:</u>	<u>Dienstliche Anschrift:</u>	<u>Qualifikation:</u>
Tierärzte der Einrichtung für Tierschutz, tierärztlicher Dienst und Labortierkunde (ggf. Name des tierärztl. Leiters der Einrichtung)	Calwerstraße 7/4, 72076 Tübingen	Tierärzte und Fachtierärzte für Versuchstierkunde und für Tierschutz

to point 1.4.2:

Name and address of the expert or veterinarian to assess the surviving animals after the experiment. This is only applicable if there are surviving animals. If the animals are killed at the end of the experiment, nothing should be entered here.

In the case of primates, ungulates (even-toed and equids), dogs, hamsters, cats, rabbits and guinea pigs, a veterinarian has to see the animal immediately after the experiment.

In the end of part 1 you will find the following

Declaration of commitment:

With the signature the project leader and his deputy commit themselves to assume the responsibility for the compliance with the regulations according to § 9 Abs. 6 TierSchG in connection with §§ 15-31 (resp. with notifications § 36) TierSchVersV as well as if applicable for obligations according to § 8 TierSchG and explanations or changes concerning this

application/this notification, which were transmitted by the project leader/deputy in writing to the RP Tübingen after further inquiries and to consider the recording obligation according to § 9 Abs. 5 TierSchG in connection with § 29 Abs. 1 und 2 TierSchVersV.

At the same time the knowledge of the TierSchG and the TierSchVersV is confirmed.

With the signatures it is confirmed that the licensing requirements according to §§ 7, 7a and 8 TierSchG, which are set out in the application including all annexes, are met.

to point 2.1:

Please remember to re-enter the title here (identical to title on page 1), as this is mandatory for administrative reasons.

to point 2.2:

This is for notifications only and asks about the legal basis of the notification.

2.3 Scientific background

to point 2.3.1:

The purpose to which the experimental project is to be assigned according to § 7a para. 1 TierSchG must be ticked here (several crosses are also possible).

to point 2.3.2:

After the purpose of the experimental project was marked with a cross under point 2.3.1, the purpose must now be described in detail in the field "Erläuterungen". It should be explained how the planned project can contribute to clarifying the question.

to point 2.3.3:

Points 2.3.1 and 2.3.2 explained the purpose of the experimental project. Here, the indispensability shall be described, i.e. why the results cannot be dispensed with or otherwise obtained. Particular attention should also be paid to individual interventions and treatments, whether they are burdensome and whether they can be dispensed with. Furthermore, it should be checked whether all partial experiments or control groups are indispensable. If necessary, reference should also be made here to own preliminary investigations and those of other working groups.

to point 2.3.4:

Here it should be explained how certain results obtained with the experimental setup support or disprove the hypothesis. In the case of several hypotheses, this must be done in each case.

to point 2.3.5:

Here it should be explained why it is not possible to use other methods to meet the purpose of this project (e.g. cell culture, isolated organs, meta-analysis of clinical data, etc.).

to point 2.3.6:

Here the previous scientific work of the working group shall be outlined in relation to the proposed project and, if possible, one or more publications with a key function shall be named and attached.

to point 2.3.7.1:

Please explain which databases and resources you have used for literature research, the keywords used, last date of research and number and relevance of the publications found.

to point 2.3.7.2:

Here the "scientific gap" is to be described by explaining what was found under point 2.3.7.1 as knowledge from the literature in the marginal area of the knowledge gap.

to point 2.3.7.3:

Here should be specified, if the intended experiments are a repetition (retry) or double test. If yes, a scientific justification has to be given, that the planned experiments are indispensable.

2.3.8 Specie(s) and number of animals to be used**to point 2.3.8.1:**

Please state and justify your choice here:

- (a) the intended species of animal
- (b) age or weight
- (c) sex

to point 2.3.8.2:

Please enter the name of the strain in the official form (scientific nomenclature). This is particularly important for genetically modified animal strains and sublines.

Please attach the form „Abschlussbeurteilung genetisch veränderter Zuchtlinien“(Final assessment of genetically modified breeding lines) for each genetically modified animal strain in order to prove whether or not there is any genetical burden. Please always use the exact strain and line name. You can find help on the Jackson Laboratories page.

<http://www.informatics.jax.org/mgihome/nomen/strains.shtml>

to point 2.3.8.3 and 2.3.8.4

The planning of the number of animals on the basis of the case number estimate for each group and all groups in total of laboratory animals shall be presented. Normally the group size is calculable by scattering, relevant differences of mean values, etc. If this is not possible due to the scientific question (e.g. feasibility study without statistical data evaluation), this must be explained particularly thoroughly. Please note that in most cases only very few animals can be applied for in the context of feasibility studies and pilot experiments. "Feasibility studies" are about whether something is "feasible" in principle. Here it would be sufficient to prove the "feasibility" on one animal. However, if it does not work on one single animal, the maximum number of animals one would like to use must be considered and well justified in order to be able to prove the basic "feasibility" at least once.

For better clarity, it is advisable to use tables.

It must be clarified whether any "reserve animals" applied for lead directly to an increase in the group size in order to compensate for probable failures and ensure a certain number of cases, or whether these are real reserves which are only used when animals have actually failed. The indispensability of reserve animals shall be scientifically justified.

For biometric planning, members of the Medical Faculty can take advantage of advice from the Institute of Clinical Epidemiology and Applied Biometry (<http://www.medizin.uni-tuebingen.de/Mitarbeiter/Institute/Klinische+Epidemiologie+und+angewandte+Biometrie/Beratung.html>). If you would like to calculate the size of your groups yourself, you can also make use of freely available programs such as SISA

(<http://www.quantitativeskills.com/sisa/calculations/sampshlp.htm>) or G*Power

(<http://www.gpower.hhu.de/>). With WinEpi (<http://www.winepi.net/>) a calculation can be carried out directly online.

to point 2.3.8.5

Here the origin of the ancestors of the animals used in the experiments is not asked, but the origin of the individuals used in the experiments. If these were born inside the institution, please write "Eigenzucht".

to point 2.3.8.6:

Here it is asked, if the intended animals have already been used for other projects according to §18 TierSchVersV and if so, please specify type, duration and burden of the procedures and interventions, reference number and responsible authority.

2.4 Practical realization**to point 2.4.1:**

Address of animal facility and place (address), start date and planned duration of the experiments should be entered here.

The application can be approved in its present form for a maximum of 5 years.

A maximum of two extensions for a maximum of one year each are possible if the project was originally applied for and approved for only 3 years or less.

to point 2.4.2:

Here it should be described, how the animals are kept. Number of animals per cage, single housing, cage size, equipment and possible deviations from the husbandry standard are asked here.

Equipment refers to environmental enrichments, such as tunnels, houses, etc. Please note that male mice should only receive enrichment (tunnels, houses) in single housing, but not in group housing, due to territorial fights.

to point 2.4.3.1:

Depending on how the animals are kept, specify how they are to be monitored for hygiene. As a rule, "random samples" of mice and rats in open housing and "litter sentinels" in IVC cages are tested serologically, bacteriologically, mycologically and parasitologically twice a year by the veterinary service. In addition, samples are usually taken from sick animals and tested for the pathogens mentioned in point 2.4.3.2. Please also comment on the following points:

Barrier status, protective clothing and controlled access.

to point 2.4.3.2:

Please enter here a list of pathogens for which these animals have been tested and from which these animals should be free (SPF). These can be found in the user and hygiene regulations of the respective animal husbandry. Please note that the pathogens listed in the health certificates only contain the laboratory diagnostic findings and are therefore not complete. The complete list can be obtained from the respective person responsible (according to §11 TschG) for animal husbandry, but can also be obtained from the veterinary service if necessary.

to point 2.4.3.3:

Please tick "yes", "no" or "not evaluated" (explanation why?) to the question if there were found organisms in the animal facility room which should not be there according to the defined hygiene standard.

If the answer was "yes", which organisms? Are they able to influence the outcome of the experiments? Which measures were taken in order to prevent the infection of the animals, planned for this project.

2.4.4 Interventions

to point 2.4.4.1:

Here the practical realization of the experiments are to be described. Also the duration of the experiments considering the chosen anesthesia protocol. It may be useful to outline in a time axis which measures are to be carried out over time. Depending on the experiment, this can possibly begin with the birth or stabling of the animals. All interventions should be described here precisely and completely, i.e. operations, applications including indication of quantity, type and localisation of the application on the animal, etc. The active substances used should be described in terms of dosage, volume and route of administration. It should also be described when and how often the animals are checked after the procedure and which parameters are collected. The duration of the observation period and the method of killing the animals at the end of the test should be stated. The reader must be able to form a picture of what happens to each individual animal. In the case of unusual procedures with increased stress, the indispensability for this unusual procedure should be explained here again.

to point 2.4.4.2:

All parts of the experimental setup described under 2.4.4.1 that are performed under anesthesia should be listed here. It should be described how and with which active substances and dosages the anesthesia is performed (induction, maintenance, duration, depth of anesthesia) and how long the procedure lasts overall. Possible after-treatment of the animals with analgesics or other substances should be discussed. Since the anesthesia is described here in great detail, it can only be mentioned in point 2.4.4.1.

to point 2.4.4.3:

Are there painful interventions carried out without anesthesia?

Here it must be taken into account that not only very severe painful interventions are meant, but also less severe pain (e.g. through injections, etc.). One possible reason for not using anesthesia would be, for example, that the burden caused by the injection pain is less than the burden on the animal caused by the anesthesia.

to point 2.4.4.4:

Description and explanation of actions for pain relief and, if applicable, explanation of why no such actions are to be taken.

to point 2.4.5:

Describe and evaluate the stress on the animals (intensity and duration of pain, suffering or harm) during the experiment. Assign these to the categories (a-d) of the classification of severity levels according to Annex VIII of Directive 2010/63/EU.

a) No restoration of vital function:

Procedures carried out entirely under general anesthesia from which the animal no longer awakens shall be classified as 'no restoration of vital function'.

(b) Minor:

Procedures which are expected to cause animals mild pain, suffering or distress for a short period of time and procedures which do not significantly impair the welfare or general condition of the animals shall be classified as "Minor".

(c) Moderate:

Procedures which are likely to cause animals short-term moderate pain, moderate suffering or distress or prolonged mild pain and procedures which are likely to cause animals to suffer moderate impairment of welfare or general condition are classified as "moderate".

(d) Severe:

Procedures which are expected to cause severe pain, suffering or distress, or prolonged moderate pain, suffering or distress in animals, and procedures which are expected to cause severe impairment of the welfare or general condition of animals, are classified as "severe".

The burden due to genetic deficiencies in the animals must also be indicated here. The sum of individual exposures must be taken into account. In this case it is advisable to draw up a score sheet (see point 2.4.7).

If a weight loss is given as a criterion, the reference weight must be given. In case of a longer test period, we recommend that the initial weight be used as reference value corrected for the expected increase in weight of same-age, same-sex, unburdened animals of the same strain in the observation period.

to point 2.4.6:

Please describe here the health control protocol (time, frequency, collected parameters and executing persons). Only the measures which are carried out by the experimenters are asked here. The daily inspections by animal keepers or health checks by veterinarians are not required here.

to point 2.4.7:

If necessary, specify specific endpoints, i.e. circumstances in which an animal is no longer used or at which threshold experimental animals are killed without pain (= definition of so-called humane endpoints). With the help of a score sheet and regular inspection of the animals and/or measurements (e.g. laboratory parameters, tumor size, blood pressure, body weight, etc.) it can be ensured that the necessary time of termination is recognized in time for all animals. Among other things, the reduction of body weight, as described under point 2.4.5, can also serve as an endpoint criterion.

You will find assistance for the creation of a score sheet and endpoint criteria under the following link: <http://www.charite.de/tierschutz/download/2013Empfehlungen-der-Berliner-TschB-zu-Score-Sheets+Abbruchkriterien.pdf>

An example of a score sheet can be found in Appendix I. It may have to be modified and supplemented for specific experiments.

Please note that the Score Sheet and the termination criteria must relate to the parameters collected under 2.4.4.1 and 2.4.6.

to point 2.5.1:

Here an ethical consideration of the two goods is expected: "well-being of the animals" versus " Knowledge gain for patients, environment, consumer protection and basic knowledge".

Describe your assessment of this relationship and explain why you consider this to be ethically justifiable.

2.6 Procedures at the end of the experiments

to point 2.6.1:

- In a final experiment (no restoration of vital function – “Terminalversuch”), no animal may have undergone surgery or treatment prior to anesthesia (other than the induction of anesthesia) and the animal may not awaken from this first anesthesia. In the case of burdened strains, an experiment may begin with the transport from the breeder to the scientist, with the mating, or with the birth of the animals. Experiments with such

genetically burdened animals can therefore only be carried out as final experiments if the animals have previously been produced for this purpose in another independently approved experimental project.

- Killing after an observation period of...: Here, the total period from the first intervention, which leads to a stress, plus adaptation time if necessary, to the death of the animal is relevant.
- Continuation of life without any impairment of well-being.
- Continuation of life with justifiable impairment of well-being (to be described further)
- Alternative accommodation according to §10 TierSchVersV (with explanations/annotations)

to point 2.6.2:

Description of the intended killing procedures

3. Anonymization of the application

It has to be stated if the applicant wishes to pass on the anonymization of his/her application. Usually this should be answered with “yes”, if there is no reason not to do so.

4. Bibliography

5. List of abbreviations

2) Personal data sheet

For each person involved in the test (test planner - point 1.1.3 and other persons - point 1.2) a personal data sheet must be enclosed. This is not necessary for the project supervisor and deputy, as the information for these two persons must be entered directly in the application form (items 1.1.1 - 1.1.2.2). A personal data sheet must be resubmitted as long as it has not yet been accepted by the authority as part of an application for approval or notification. It must also be updated, if necessary, if new interventions and qualifications are to be notified for the person.

3) Non-technical project summary (NTP)

With the entry into force of the Third Act amending the Animal Welfare Act on 12 July 2013 and the Animal Welfare Experimental Animal Ordinance on 13 August 2013, a non-technical project summary must be attached to every application for approval of an animal experiment project.

The web application "AnimalTestInfo-Antragsteller" is available online on the BfR website (Federal Institute for Risk Assessment) for the preparation of the non-technical project summary: www.animaltestinfo.de/antragsteller

Please submit a draft to the TSchB together with the first draft of the application. To create a draft, you can enter and save your data directly on the platform. After saving, the version gets an NTP-ID and a PDF can be created. You can then attach this to the application. If the NTP is only cached, the NTP ID including version number remains the same saving it another time.

The Regierungspräsidium Tübingen asks you to use the web application for all newly submitted applications for animal experiments.

The ten-digit identification number (NTP-ID) obtained during the preparation of the NTP should be noted on the first page of the application form and a printout of the NTP should be attached to the application documents.

For non-technical project summaries, a revised version of the NTP must also be deposited in the web application for subsequent applications for changes requiring approval (in the sense of § 34 para. 3 TierSchVersV) and the corresponding number must be submitted to the Regierungspräsidium together with the application for amendment.

After approval of the project, the NTP will be activated for publication and published by the BfR on the homepage within 12 months. Thus, the information on animal testing projects is made publicly accessible and the information of citizens on animal testing is guaranteed. Please make sure that the public does not misunderstand the sense of the experiment and that there is no suspicion of unnecessary animal experiments. The content and form of the NTP should also not allow any conclusions to be drawn about the author. The author and all persons involved in the experiment, as well as the facilities, must remain anonymous. The BfR has drawn up a guideline for the preparation of the NTP. It informs about purpose, form and content, which is explained in detail and with an example (in German):

<http://www.bfr.bund.de/cm/343/leitfaden-zur-erstellung-der-nichttechnischen-projektzusammenfassung-ntp-fuer-tierversuchsvorhaben.pdf>

4) Key publications

At two places in the form you will be asked for key publications (item 2.3.3 and 2.3.6). Please do not enclose more than 5 publications. As a rule, it is sufficient to enclose one basic publication and one publication of your own.

5) Biometric Expertise

It is recommended to include a biometric expert opinion to justify the number of animals. Experience has shown that in the absence of a biometric report, the Commission often has to ask questions about biometric planning. We recommend that the biometric expertise only be prepared after the initial meeting with the Animal Welfare Officer, as experience has shown that there may still be changes in the number of animals.

6) Final assessment of genetically modified breeding lines

Please add this form for each genetically modified animal strain. This form must be used to clarify whether there is any burden and the level of burden caused by the genetic modification. Assistance with the final assessment can be found on the homepage of the Animal Welfare Officer.

II. Final Application Forms - Checklist

As soon as the Animal Welfare Commissioner has agreed the draft application with you, the completed application will be submitted to the Regierungspräsidium via the TSchB. Please note the following checklist:

- 1 complete animal experiment application**
1x in printed form with original signature
 - 2 copies of the complete application**
 - 6 application copies from point 2**
 - 1 Confirmation of objective means**
1x in printed form with original signature
 - 3 Personal data sheets for all contributors named under 1.2 and, if applicable, for the test planner named under 1.1.3, if these are not already available to the RP in the current version.**
1x in printed form with original signature for every contributor
 - 2 non-technical project summary**
2x in printed form (the ten-digit identification number (NTP-ID) obtained during the creation of the NTP should be noted on the first page of the application form)
 - 1 copy of key publication(s)**
1x in printed form und 1x via e-mail to the animal welfare officer in order to forward them to the Regierungspräsidium (max. amount 5 MB) or 9x in printed form
 - 9 copies of the biometric expertise / forms "Angaben zur biometrischen Planung" (1x original and 8 copies)**
- In case of genetically modified lines additionally:**
- 9 copies of the final assessment of genetically modified breeding lines**
in case of a genetic burden
9x in printed form or 1x in printed form and 1x via e-mail to the animal welfare officer in order to forward it to the Regierungspräsidium
- or**
- 1 final assessment of genetically modified breeding lines without genetic burden**
1x in printed form

III. Procedure of the approval proceeding

As soon as the TSchB has received a complete final version of the application, then the TSchB forwards the application, including its opinion, in parallel to the R.P. and the Veterinary Office responsible for the monitoring of animal husbandry. Each application for approval of animal experiments will be submitted by the R.P. to the advisory commission according to § 15 para. 1 TierSchG / § 42 TierSchVersV. If this is to be done in anonymous form, personal data must be avoided starting from point 2 as well as in all annexes submitted to the commission! (The whole point 1 (1.1.1-1.4.1) is not submitted to the commission.) The applications will be sent to the members of the commission approx. 12 days before the meetings after processing by the Regierungspräsidium. When submitting an application, a period of at least two weeks for the animal welfare officer to comment and at least one week for the various postal channels must be planned. Commission meetings take place approximately every 2-3 weeks. Following the meetings, authorizations are granted or questions from the Commission are forwarded to the applicants. Experience has shown that the processing time by the approval authority is on average about 6 weeks. In the case of amendments and to avoid interruption of follow-up projects, this time schedule must be taken into account. The maximum processing time on the part of the Regierungspräsidium is 40 working days, with the possibility of an extension by 15 working days (§ 33TierSchVersV). By a carefully elaborated, with the animal protection commissioner co-ordinated application, further inquiries can be avoided or minimized and the processing time can be shortened considerably. If the applicant has to answer questions, the 40 working days processing time of the Regierungspräsidium are extended. The duration of experiments requiring approval must be limited to a maximum of 5 years. If the license has been granted for a period of less than 5 years, it can be extended upon application for a maximum of two extensions of up to one year each (but no longer than 5 years in total). For an extension, a reasoned application (also informal) must be submitted (§ 33TierSchVersV).

IV. Amendment requests

Amendments must also be submitted through the Animal Welfare Officer. Please note that you must use the special, ready-made amendment form to request a substantive change. Extensions and personnel changes may still be requested/notified by means of informal letters. Depending on the type and scope, changes must be notified or an approval requested. According to § 34 TierSchVersV, changes to approved animal experiments may be notified if the purpose of the experiment is maintained, the degree of pain, suffering and damage caused to the animals used is not increased by the changes, or the number of animals used is not significantly increased. Otherwise, those amendments have to get approved. The final decision on the classification shall be taken by the Regierungspräsidium. You will therefore receive a letter from the R.P. with each amendment. (Confirmation of receipt or notification of the obligation to obtain an approval). Please also note that for non-technical project summaries prepared in accordance with the new procedure, a revised version of the NTP must

also be filed in the web application with a subsequent application for changes requiring approval (in the sense of § 34 para. 3 TierSchVersV) and the corresponding number must be submitted to the Regierungspräsidium together with the application for amendment.

All paragraph disclosures refer to the following laws:

- 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. Official Journal of the European Union L 276/33, 20.10.2010
- Third Act Amending the Animal Welfare Act of 4 July 2013, BGBl. I No. 36, p. 2182
- Regulation implementing 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. Federal Law Gazette I No. 47, p. 3125

Abbreviations:

BfR: Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment)

NTP: nichttechnische Projektzusammenfassung (Non-Technical Project Summary)

TierSchG: Tierschutzgesetz (Animal Welfare Act)

TierSchVersV: Tierschutz-Versuchstierverordnung (Animal Protection and Experimental Animal Regulation)

TSchB: Tierschutzbeauftragte (Animal welfare officer)

R.P.: Regierungspräsidium (Regional Council)

We will be very grateful for any suggestions and improvements regarding this recommendation. Please contact the office of the Institution for Animal Welfare, Veterinary Service and Laboratory Animal Science: Tel 07071-29-80125 or E-Mail

<mailto:sekretariat.tschb@med.uni-tuebingen.de>

Appendix I:

Score sheet example	Assessment	Score	Date
Care condition	smooth, glossy	0	
	no coat care, dull coat	1	
	no coat care, dirty	2	
	no coat care, dirty, erecting the body hairs (piloerection)	3	
Eyes	normal	0	
	moderately sunken in, swollen	1	
	closed eye lids	2	
	heavily sunken, lids closed, sticky (discharge)	3	
Posture	normal	0	
	moderately crooked	1	
	crooked back,	2	
	strongly humped, legs placed under the belly	3	
Mobility	normal	0	
	slow forward movement of the limbs	1	
	unsteady gait	2	
	movement hardly provokable by touch, strongly restricted or wobbly movement	3	
Nutritional condition			
Body condition score	vertebrae, pelvis palpable only with light pressure	0	
	vertebrae, pelvis palpable, lateral abdominal retraction visible	1	
	vertebrae are visible and pelvic bones can be felt	2	
	vertebrae, pelvis and ribs visible	3	
Weight in relation to the initial weight, corrected for the expected increase in the weight of same-age same-sex animals of the same line during the observation period	normal, continuous increase (variations by 5%)	0	
	Weight reduction 5-10%	1	
	Weight reduction >10 bis <20%	2	
	Weight reduction by a maximum of 20%	endpoint	
Respiration	regularly	0	
	regular, slightly increased	1	
	significantly increased	2	
	difficult breathing, pumping	3	
Behaviour/ Activity	normal	0	
	slight modification	1	
	little movement, isolated	2	
	apathetic, indifferent	3	
Experiment-related criteria e.g. tumour size/condition	no tumor growth	0	
	tumor diameter <10 mm	1	
	tumor diameter <15 mm	2	
	tumor diameter > 15 mm or ulcerated	endpoint	
Points total:			
Extraordinary measures	With 20% weight loss With tumor diameter n >15mm With allocation of 2x 3 points	endpoint	
Assessment			
0 -2 points	normal		
3 -8 points	increased monitoring, if necessary seek veterinary advice (administration of painkillers, increase in the frequency of weight control)		
9 and more points	Animal suffering reaches defined humane endpoint -> Euthanasia		