



Letter

Undervaluation of suffering of experimental animals in Germany

According to Directive 2010/63/EU on the protection of animals used for scientific purposes (EU, 2010), all procedures on animals must be classified as “non-recovery”, “mild”, “moderate”, or “severe”. The severity category “shall take into account any intervention or manipulation of an animal within a defined procedure. It shall be based on the most severe effects likely to be experienced by an individual animal after applying all appropriate refinement techniques” (Annex VIII, 2). “Severe” experiments involve severe pain, suffering or distress, or long-lasting moderate pain, suffering or distress and procedures that are likely to cause severe impairment of the well-being or general condition of the animals (Annex VIII, 1). Examples for “severe” procedures according to the Directive are listed in Table 1 (column 1). The Directive gives only two examples of when the duration of suffering is to be considered “long-lasting”, i.e., food withdrawal in adult rats exceeding 48 h or enclosure in metabolic cages with moderate restriction of movement exceeding 5 days.

The combination of severe intensity and long duration is deemed suffering exceeding the upper limit of pain. “Member States shall ensure that a procedure is not performed if it involves severe pain, suffering or distress that is likely to be long-lasting and cannot be ameliorated” (Art 15(2)). However, Art 55(3) contains a safeguard clause according to which a Member State “may adopt a *provisional* measure” (emphasis added) to allow such a procedure “for exceptional and scientifically justifiable reasons”.

The severity categories have been implemented into German law (Germany, 2017); however, here the competent authority is invested with the power to allow procedures exceeding the upper limit of pain under certain provisions but not as a provisional measure (Germany, 2015; Maisack 2016). Anonymous non-technical summaries (NTS) of approved animal experiments must be published on <https://www.animaltestinfo.de>. NTS must include information about the harm, such as pain, suffering or distress, caused to the animals and an assessment of the severity category of the procedure.

4,780 NTS published until December 30, 2015 on <https://www.animaltestinfo.de> for the years 2014 and 2015 were searched for criteria for severe procedures using phrases and their derivatives extracted from the Directive’s examples for

severe procedures (Tab. 1, column 2). NTS found more than once using different search terms were assigned to one of the search terms. No further measures were taken to ensure that all relevant entries were recorded. The resulting 893 documents were reviewed and assessed for information on the harm to animals, including its duration, and on the stated level of severity. Only few NTS contained information on the duration of the animals’ suffering. Of the 893 NTS, 235 appeared to fit the criteria in Table 1 (column 1) for severe procedures based on the available information. However, of these, the applicants had not classified 24 NTS and had classified 23 as “mild”, 58 as “mild to moderate”, 47 as “moderate” and only 83 as “severe” or “possibly severe for some animals”. According to this analysis, 65% of NTS appearing to fit the criteria in Table 1 for severe procedures based on the available information were not classified as such.

Examples of potentially misclassified procedures all classified as “moderate” by the applicants include procedures causing tumors accompanied with cachexia; enclosure in metabolic cages with restriction of movement for seven consecutive days repeated four times; a forced swim test with exhaustion as endpoint; a vaccine test in which control animals were expected to die within five to six days after infection; an acute toxicity test on fish with death as endpoint; a procedure with transgenic mice that model amyotrophic lateral sclerosis (ALS), which suffer muscle atrophy, weight loss and progress to paralysis; and breeding of transgenic mice to model Huntington’s disease. Notably, a retrospective review of an animal experiment assessing the actual level of harm experienced by the animals is only required for “severe” experiments and experiments involving primates.

Some of the 83 procedures classified as “severe” appear to exceed the classification of “severe” as the NTS indicated that severe pain, suffering and distress are of long-lasting duration and cause severe impairment of the well-being or general condition of the animals. Examples of such procedures include a vaccine test in mice in which the suffering is described as “severe” over at least four to eight days; transplantation after lethal irradiation in which the suffering occurring over two weeks was classified as “severe”; and a procedure where pigs are kept in metabolic cages for 30 days and experience



social impairment as a result. Notably, the German Ministry of Food and Agriculture communicated to Doctors Against Animal Experiments in 2016 that it had to date received no applications for procedures exceeding the category of “severe” procedures.

Taken together, the unstandardized format and information requirements of the NTS preclude them from fulfilling their purpose of transparently and objectively informing the public about experimental procedures being conducted on animals in Germany. The NTS should include a breakdown of the different treatment groups within the procedure and each group should be assessed individually for severity regarding pain, suffering and distress as well as its duration. This information should be given for every intervention within the procedure. Refinement or amelioration measures employed should also be stated. The content of the NTS should be checked for completeness by the competent authority before publication.

Despite the limited information available, this analysis has found concerning examples of apparent undervaluation of the severity of experimental procedures by the applicants as

well as of procedures probably exceeding the classification of severity class “severe”. The competent authorities should not leave the classification of experimental procedures up to the applicants but should be obliged to employ their expertise to adjust the classification of experimental procedures to ensure the law on the protection of animals is upheld and to increase the awareness of the applicants of the severity of the planned experiments.

In view of the fact that the original draft of Directive 2010/63/EU even provided for a ban on procedures of the severity class “severe” and that the final version states “this Directive represents an important step towards achieving the final goal of full replacement of procedures on live animals for scientific and educational purposes” (Rec. 10), it should at least be ensured that animal experiments that exceed the upper limit of pain are not performed. Further, considering that animal protection is a state goal enshrined in the German constitution, Germany should consistently refrain from making use of the safeguard clause (Art 55(3)) of the Directive.

Tab. 1: Derivation of search phrases and results of search of <https://www.animaltestinfo.de>

Examples of severe procedures according to the EU Directive (EU, 2010, Annex VIII)	Search phrases derived from column 1 used to search https://www.animaltestinfo.de	No. of initial hits	No. of projects categorized as severe according to column 1 criteria
(a) toxicity testing where death is the end-point, or fatalities are to be expected and severe pathophysiological states are induced. For example, single dose acute toxicity testing (see OECD testing guidelines)	toxicity test (<i>Toxizitätstest</i>)	14	10
	toxicity (<i>Toxizität</i>)	187	23
	acute toxicity (<i>akute Toxizität</i>)	4	1
(b) testing of device where failure may cause severe pain, distress or death of the animal (e.g., cardiac assist devices)	devices (<i>Geräte</i>)	58	2
	cardiac assist (<i>Herzunterstützung</i>)	7	2
	cardiac assist devices (<i>Herzunterstützungsgerät</i>)	0	0
	pacemaker (<i>Herzschrittmacher</i>)	4	3
(c) vaccine potency testing characterised by persistent impairment of the animal’s condition, progressive disease leading to death, associated with long-lasting moderate pain, distress or suffering	vaccine (<i>Impfstoff</i>)	143	41
	potency testing (<i>Wirksamkeitstest</i>)	7	0
(d) irradiation or chemotherapy with a lethal dose without reconstitution of the immune system, or reconstitution with production of graft versus host disease	graft versus host (<i>Graft-versus-Host</i>)	9	7
	graft versus host disease (<i>Graft-versus-Host-Reaktion</i>)	1	1
	lethal dose (<i>tödliche Dosis</i>)	0	0



Examples of severe procedures according to the EU Directive (EU, 2010, Annex VIII)	Search phrases derived from column 1 used to search https://www.animaltestinfo.de	No. of initial hits	No. of projects categorized as severe according to column 1 criteria
(e) models with induction of tumours, or with spontaneous tumours, that are expected to cause progressive lethal disease associated with long-lasting moderate pain, distress or suffering. For example tumours causing cachexia, invasive bone tumours, tumours resulting in metastatic spread, and tumours that are allowed to ulcerate	induction of tumors (<i>Induktion Tumor</i>)	0	0
	tumors resulting in metastatic spread (<i>metastasierende Tumore</i>)	2	2
	metastases (<i>Metastasen</i>)	109	51
	tumors that are allowed to ulcerate (<i>Geschwürbildung</i>)	0	0
	bone tumor (<i>Knochentumor</i>)	6	2
	invasive bone tumor (<i>invasiver Knochentumor</i>)	0	0
	cachexia (<i>Kachexie</i>)	58	41
(f) surgical and other interventions in animals under general anaesthesia which are expected to result in severe or persistent moderate postoperative pain, suffering or distress or severe and persistent impairment of the general condition of the animals. Production of unstable fractures, thoracotomy without adequate analgesia, or trauma to produce multiple organ failure	unstable fractures (<i>instabile Frakturen</i>)	0	0
	fracture (<i>Fraktur</i>)	52	0
	thoracotomy (<i>Thorakotomie</i>)	14	3
	multiple organ failure (<i>multiple Organversagen</i>)	0	0
(g) organ transplantation where organ rejection is likely to lead to severe distress or impairment of the general condition of the animals (e.g., xenotransplantation)	organ transplantation (<i>Organtransplantation</i>)	17	4
	xenotransplantation (<i>Xenotransplantation</i>)	15	6
(h) breeding animals with genetic disorders that are expected to experience severe and persistent impairment of general condition, for example Huntington's disease, Muscular dystrophy, chronic relapsing neuritis models	Huntington's disease (<i>Huntington-Krankheit</i>)	4	2
	Huntington (<i>Huntington</i>)	33	16
	Muscular dystrophy (<i>Muskeldystrophie</i>)	9	2
	chronic relapsing neuritis models (<i>chronische wiederkehrende Nervenentzündung</i>)	0	0
	nerve inflammation (<i>Nervenentzündung</i>)	2	1
(i) use of metabolic cages involving severe restriction of movement over a prolonged period	metabolic cage (<i>Stoffwechselkäfig</i>)	36	9
(j) inescapable electric shock (e.g., to produce learned helplessness)	electric shock (<i>Elektroschock</i>)	4	1
	helplessness (<i>Hilflosigkeit</i>)	3	0
	learned helplessness (<i>erlernte Hilflosigkeit</i>)	0	0



Examples of severe procedures according the EU Directive (EU, 2010, Annex VIII)	Search phrases derived from column 1 used to search https://www.animaltestinfo.de	No. of initial hits	No. of projects categorized as severe according to column 1 criteria
	electric foot shock (Fußschock)	4	1
(k) complete isolation for prolonged periods of social species, e.g., dogs and non-human primates	isolation (Isolierung)	33	0
(l) immobilisation stress to induce gastric ulcers or cardiac failure in rats	immobilization (Immobilisierung)	8	1
	immobilization stress (Immobilisierungsstress)	0	0
	gastric ulcer (Magengeschwür)	6	0
	cardiac failure (Herzversagen)	28	0
(m) forced swim or exercise tests with exhaustion as the end-point	swim test (Schwimmtest)	1	1
	exhaustion (Erschöpfung)	8	1
	forced (forciert)	7	1
	Total	893	235

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