

## **Annex O** (informative)

### **Pain management and humane endpoints**

#### **O.1 General**

**O.1.1** When conducting experiments that could involve a great deal of animal distress, one should consider the option of implementing humane endpoints.

**O.1.2** The implementation of a humane endpoint should be a predicted well founded assessment of the welfare of the animal that is based on predetermined indicators such as tumour size or weightloss. Certain clinical signs can be evident of an irreversible process that will most probably lead to severely reduced welfare and, as such, these signs are an indication for a humane endpoint.

**O.1.3** When preparing a project application for all but the most minor manipulations, the researcher or teacher should develop humane study endpoints. For animal welfare reasons, these can be used to judge when an animal requires to be put to death by recognized euthanasia methods. Death as an endpoint is generally ethically unacceptable and should be fully justified.

#### **O.2 Why humane endpoints**

The following are instances that render humane endpoints as acceptable:

a) **Moral consideration**

When the laboratory animal experiences more pain, suffering or chronic distress than was originally anticipated or is justified.

b) **Scientific consideration**

1) When the scientific objective of the experiment has been accomplished and keeping the animal does not contribute to the results of the investigation or even interferes with the results, or it is clear that the objective of the experiment cannot be achieved.

2) When keeping the animals can lead to loss of data (for instance, if it dies in the cage and the animal is subsequently cannibalized by cage mates, or the animal or organs or tissue are autolysed).

#### **O.3 Types of criteria for humane endpoints**

Humane endpoints can be based on different types of parameters (see table O.1). Globally speaking, these parameters can be grouped into the following categories:

- a) clinical behaviour (tumour formation);
- b) pathophysiological indicators (drop in body temperature);
- c) serious behaviour indicators (stereotypic behaviour) ;
- d) biomedical indicators (ketonuria); and
- e) hormonal indicators.

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**Table O.1 — Some indicators used to justify humane endpoints**

1	2	3
Clinical behaviour	Pathophysiological indicators	Biomedical or hormonal indicators
Activity Aggression Posture Response to handling Vocalization	Respiration rate Complete blood count Weightloss Heart rate Dehydration Anuria	Acute phase proteins Catecholamines Corticosteroids Glucagon Insulin Prolactin

**O.4 The use of humane endpoints in research projects**

**O.4.1** In the design of a research protocol, thought should be given to the implementation of humane endpoints. Information pertaining to this issue should be laid down in the protocol and should include the following points:

- a) the clinical course, including any critical times and signs, and any anticipated discomfort or pain;
- b) observation frequency and the recording of the findings;
- c) the humane endpoint and the parameters underlying the establishment of the humane endpoint;
- d) the responsibilities of the person(s) involved in the observation, treatment or euthanasia;
- e) the type of alleviative treatment or euthanasia; and
- f) the postmortem procedure.

**O.4.2** Should there be any doubt as to the (clinical) progression of the illness or about the parameters for determining the humane endpoint, then conducting a pilot study with a limited number of animals is recommended.

**O.5 Humane endpoints and actions to be taken**

**O.5.1** Humane endpoints (see 3.10) are study-specific criteria that indicate or predict pain, distress or death and are used as signals to end a study early to avoid or terminate pain or distress (or both).

**O.5.2** Once an animal reaches the specified humane endpoint, the veterinarian and the principal researcher should be informed, without delay, to make the decision to put the animal to death by recognized euthanasia methods, as well as any other decisions that could become necessary.

**O.5.3** Specific actions should be taken, using recognized euthanasia methods, when

- a) an animal shows signs of a coma within 24 h to 48 h of the start of the experiment,
- b) an animal weighs less than its initial weight after 7 d or loses more than 20% of its initial weight at any time, or
- c) an animal shows tiptoe or slow ponderous gait.

If more than one clinical sign occurs, then the veterinarian and principal researcher should be informed.

## **0.6 Responsibility**

**0.6.1** Before the start of an animal experiment, all staff directly involved in the experiment need to be accurately informed about the critical period in the experiment by the principal researcher. All personnel should be knowledgeable about the following aspects:

- a) normal behaviour and physiology of the animal;
- b) anticipated deviations from the normal in the proposed procedure;
- c) awareness of their role and responsibility;
- d) the consultant in the event of unanticipated clinical effects;
- e) the moment at which a humane endpoint will be implemented;
- f) facilities and options for postmortem examination to establish the cause of death; and
- g) a scoring system to facilitate decision making (when to report deviations from the normal and to whom).

**0.6.2** In a case of uncertainty, expert advice should be obtained, normally from a laboratory animal scientist, veterinarian, or a pathologist.

**0.6.3** It is important that all responsible personnel be reachable at all times for consultation should questions arise concerning the implementation of a humane endpoint for an animal.

## **0.7 Pilot study**

Pilot studies should be carried out before the main experiment to allow for the definition of various elements and parameters in the study. Pilot studies for setting humane endpoints in an experiment are needed when

- a) the effects of the treatment are unknown, so that morbidity, time course of effects, and specific clinical signs still have to be more narrowly defined,
- b) the identification of humane endpoints on the basis of specific parameters (for example, telemetrically obtained data) is possible, and
- c) the pathological changes observed can be used later to set humane endpoints.

## **0.8 Recognition**

Adverse effects experienced by animals during experimentation include more than pain since they include conscious emotions such as fear, discomfort, distress (stress with which an animal fails to thrive or cope) (see Morton, 1998b) and mental distress (for example, frustration and boredom). However, before any of these states can be alleviated or assessed, or experiments refined in any way so as to cause less pain and suffering, there should be recognition of when the animal's wellbeing is being affected, both positively and negatively. Recognition can be considered as a fourth R, following on after the three As (Avoidance, Assessment and Alleviation) of animal suffering in research.

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It is important to eliminate any animal suffering in order to achieve scientific research of a high quality, specifically in relation to the scientific research questions being asked, as well as to practise humane scientific research economically (see Claasen, 1994 and Balls *et al*, 1995). Problems can be approached by using clinical signs as a way of determining the degree to which an animal's physiology and mental state have deviated from the normal. This is applicable not only to mammals, but to vertebrates and even non-vertebrates, provided there is suitable knowledge regarding their normal ethology and physiology.

## **O.9 Development and validation of humane endpoints**

### **O.9.1 Planning considerations**

**O.9.1.1** Careful planning and implementation of humane endpoints requires a certain measure of expertise. Before the start of the experiment, its course should be anticipated and a decision about when to implement a humane endpoint should be reached.

**O.9.1.2** The exact time of the endpoint is dependent on the objective of the experiment, but it should be chosen before the outset of any pain, distress or as soon as possible thereafter.

**O.9.1.3** The endpoint should preferably be chosen on the basis of objective criteria. The moral and scientific considerations relating to humane endpoints (see O.2.(a) and O.2.(b)) should be kept in mind.

**O.9.1.4** Before arriving at a suitable endpoint, the following preliminary stages should be undertaken:

- a) setting of priorities;
- b) a test analysis;
- c) identification and evaluation of potential endpoints;
- d) validation of selected endpoints; and
- e) approval by the AEC.

### **O.9.2 Criteria for endpoints**

Ideally the endpoint should:

- a) be easy to monitor;
- b) be reproducible;
- c) not be labour intensive;
- d) in some cases, show valid prediction of the lethal progression of the illness;
- e) be relevant (equivalent) and reliable (with little variation);
- f) take intermediary steps towards an ultimate *in vitro* alternative; and
- g) show maximal reduction of pain and discomfort.

### **O.9.3 Validation**

In practical terms, the following three steps should be taken to arrive at suitable humane endpoints:

- a) objective definition and recording of signs of pain and distress in the experiment;
- b) selection based on the significance of the signs in O.9.3 (a); and
- c) assurance of the scientific validation (i.e. it satisfies to a large degree the criteria in O.9.2).

## **O.10 Score sheet system**

### **O.10.1 General**

**O.10.1.1** Score sheets should be drawn up specifically for each scientific procedure, and for each species undergoing that procedure. They can rarely be generalised.

**NOTE** The score sheet lists the clinical signs that are observable and measurable and are developed through the experience of a team of observers.

**O.10.1.2** The team of observers are usually:

- a) animal caretakers since they are most likely to know when an animal is "not right" which will often indicate a change in behaviour, posture, appearance or even the feel or smell of an animal;
- b) veterinarians since they are skilled in identifying objective clinical signs and should have knowledge of the biology of the species, including the range of its relevant behavioural and physiological responses; and
- c) scientists since they should be conversant with the perturbations that might be expected during an experiment due to the scientific paradigm.

**O.10.1.3** All the factors in O.10.1.2 will be important guides in the assessment of the effects of a scientific procedure on an animal. By detailing the cardinal signs of any particular protocol and regularly observing animals at critical periods during the experiment, an objective assessment of animal wellbeing can be made throughout the experimental period.

### **O.10.2 Method used to draw up and interpret a score sheet system**

**O.10.2.1** A list of signs is developed by closely observing the first few animals undergoing a novel scientific procedure. The list is then modified with experience until a set of cardinal signs that most animals will show during that experiment, which are relevant to the assessment of suffering, is obtained.

**O.10.2.2** These clinical signs (see O.10.2.1) are set out against time in the score sheet.

**O.10.2.3** Crucially, any clinical sign has to be reduced to a level which reduces the scope for observer interpretation and can only be recorded as being present or absent. This is indicated by a plus (+) or a minus (-) sign (sometimes a  $\pm$  sign if the observer is unsure). The convention is that negative signs indicate normality, i.e. within the normal range, and positive signs indicate that the animal is outside the normal range. In this way, it is possible to scan a score sheet to gain an overall impression of animal's wellbeing in that the more plusses, the more an animal has deviated from normality with the inference that it is suffering more than before.

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**O.10.2.4** Animals should be scored during critical periods when they predictably could give rise to concern (for example, in the immediate post-operative period or in a study on infection after the incubation period).

### **O.10.3 Completion of the score sheet system**

**O.10.3.1** Practically, it is important to develop a disciplined strategy for the recognition of adverse effects in animals.

**O.10.3.2** At the beginning of an assessment, the animal should be viewed from a distance, and its natural undisturbed behaviour and appearance noted.

**O.10.3.3** Next, as the observer approaches the pen or removes the cage lid, the animal will inevitably start to interact with the observer and its response can be used to determine whether it is normal or abnormal.

**O.10.3.4** Finally, a detailed clinical examination can be carried out by handling and restraining the animal and observing its appearance carefully as well as making any relevant clinical measurement (for example, bodyweight and temperature).

**O.10.3.5** At the end of the score sheet there should be guidance notes for animal caretakers, veterinarians or laboratory animal technologists about:

- a) what should be provided in terms of husbandry and care for animals undergoing that scientific procedure;
- b) how to record qualitative clinical signs (such as diarrhoea and respiration); and
- c) criteria by which to implement humane endpoints.

**O.10.3.6** If an animal has to be killed, there should be instructions about any other actions that should be taken, such as tissue to be retrieved or placed in 10 % formaldehyde in saline (see O.10.4.3). This helps ensure that the maximum information is obtained from any animal in a study.

**NOTE** Although these score sheets take time to fill in, it is not difficult for an experienced person to see if any animal is unwell so the NAD (Nothing Abnormal Detected) box is simply checked.

### **O.10.4 Score sheet**

#### **O.10.4.1 Special husbandry requirements**

Special husbandry requirements should be stipulated before the start of the observation, for example:

- a) animals shall be fed an irradiated diet and adapted to it 2 d to 3 d before diabetes induction;
- b) animal cages shall be cleaned out twice daily;
- c) two bottles of UV water shall be provided for each cage and filled twice daily; and
- d) animals shall be deprived of water overnight.

**NOTE** Deprivation of water should not be sufficient to cause death by dehydration.

#### **O.10.4.2 Interpretation**

A sample score sheet developed to record clinical signs for rats with streptozotocin-induced diabetes is given in table O.2. It can be seen from this sample score sheet that there are more plus signs on the right hand side (see O.10.2.3). Several other points should be noted as follows:

- a) When the animal started to show clinical signs, it was scored more frequently.
- b) During day 0 (the day of the injection of streptozotocin to induce diabetes), the animal lost body weight due to the restricted food intake the previous night.
- c) Over the next 2 d, the animal lost body weight although it was normal in all other respects.
- d) By day four, the coat became starey (ruffled), the body temperature had dropped significantly, and the breathing had become more rapid and laboured.
- e) Furthermore, there was a significant body weightloss (22 %) which is a strong indication that the animal had not eaten or drunk much or that it was not maintaining its fluid balance, and tiptoe walking indicated some degree of abdominal pain. The rapid weightloss and dehydration, laboured breathing, abnormal posture, among other signs, all confirmed that the animal was becoming severely physiologically compromised and was not going to yield valid results in relation to the scientific objective.
- f) Even more significantly, the animal's temperature dropped, which is a very poor sign.
- g) The animal was given fluids, placed in a warm environment, and observed 3 h later.
- h) The animal was not responding adequately and, from experience from following such animals through to death in earlier studies, it would have died that night if not sooner.
- i) It was consequently decided that the animal be put to death by recognized euthanasia methods on humane and scientific grounds before the end of the experiment. Where an ethical balance is struck between the anticipated benefits of a research project and the degree of animal distress (as indicated by the humane endpoints), the severity limit had been exceeded. Even if the animal might not have died, the level of pain and distress was agreed to be a sufficient reason to put the animal to death by recognized euthanasia methods on humane grounds alone.

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**Table O.2 — Sample score sheet to record clinical signs for rats with streptozotocin-induced diabetes**

Date of study: 2007-08-09		Animal No.: Rat 3				
Weight (g):						
Date	9 Aug	10 Aug	11 Aug	12 Aug	13 Aug	14 Aug
Day	0	1	2	3	4	4
Time	8:40	9:00	8:50	8:55	8:05	11:00
<b>FROM A DISTANCE</b>						
Fed	Y	Y	Y	Y	Y	Y
Inactive		-	-	-	+	+
Isolated		-	-	-	-	-
Walking tiptoe		-	-	-	+	+
Hunched posture		-	-	-	+	+
Pinched face		-	-	-	+	+
Ruffled coat		-	-	-	+	±
Type of breathing <sup>a</sup>		N	N	N	120 L	70 L
<b>ON HANDLING</b>						
Not inquisitive and alert		-	-	-	+	+
Not eating		-	-	-	±	+
Not drinking		-	-	-	?	+
Vocalization on gentle palpation		-	-	-	-	-
Volume water drunk by average of rats in cage (ml)		50	113	133	140 av	0
Body weight (g)	204	209	203	192	170	168
Percentage change from pre-starved weight	7	5	7	12	22	
Body temperature (°C)		37,5	37,4	37,6	32,4	34,7
Pale or sunken eyes		-	-	-	+	+
Dehydration		-	-	-	+	+
Distended abdomen/swollen		-	-	-	±	±
Diarrhoea <sup>b</sup> 0 to 3 (+m or +b)		-	-	-	-	-
Cage wet		-	±	+	-	-
Condition grading 4 to 1 <sup>c</sup>		4	4	3	2+	2
Saline given s/c – volume/site?		-	-	-	2 ml× 2	-
Blood sugar level		nd	nd	nd	nd	nd
Nothing Abnormal Detected (NAD)		-	-	-	-	-
<b>OTHER</b>						
<b>SIGNATURE:</b>						
Scoring details:						
<sup>a</sup> Breathing: R = rapid; S = shallow; L = laboured; N = normal.						
<sup>b</sup> 0 = normal; 1 = loose faeces on the floor; 2 = pools of faeces on the floor; 3 = running out on handling. (+m = mucus and +b = blood).						
<sup>c</sup> Condition: 4 = normal; 1 = emaciated.						
nd = not determined.						



#### O.10.4.3 Scientific measures

Instructions for scientific measures should be followed, for example, a kidney should be placed into a mixture of 10 % formaldehyde in saline.

#### O.10.5 Some advantages of the score sheet system

The score sheet system used to record clinical signs for the recognition and assessment of adverse effect on animals during scientific procedures has been shown to have the following advantages:

- a) closer observation of animals can now be carried out by all staff at critical times in the experiment as the score sheets indicate the times when animals find their circumstances most aversive;
- b) subjective assessments of suffering by staff and researchers are avoided, thereby promoting more fruitful dialogue, as evidence based on opinion becomes possible supported by the clinical proof;
- c) consistency of scoring is increased as the guidance is clear and the scoring options are limited;
- d) single signs or combination of signs can be used to indicate overall severity of the procedure, as well as alleviative therapies or scientific procedures as set points in an experiment (for example, blood sampling); and
- e) the score sheet system:
  - helps determine the effectiveness of any therapy intended to relieve adverse effects;
  - can be used to determine which experimental models cause the least pain and distress (for example, by comparing alternative animal models), thus helping to refine scientific procedures;
  - can be used to analyze retrospectively the adverse effects of any scientific procedure and its severity level;
  - has been found to add to the scientific study as a more careful observation of animals is carried out;
  - provides a visual aid, opens up discussion between interested parties, and helps focus attention on an animal's condition throughout the procedures. Any analysis of the score sheet can reveal patterns of recovery or deterioration and so gives a better picture of the effect of a procedure on animals from start to finish. The sheet encourages all involved to observe the behaviour of animals and to recognize normal and abnormal behaviour, thus helping in determining animal responses to various procedures which will help to devise ways of refining experimental techniques by highlighting the type and timing of any adverse effects. The score sheets are constantly being developed and updated with further experience. Staff also start to perceive patterns of adverse effects that, when taken as a whole, indicate early death or early deterioration sufficient to warrant the animal being killed on scientific grounds alone. Such information leads to better animal care as well as provides useful scientific information such as the recognition of neurological deficit, times of epilepsy or weightloss, as well as unexpected findings. Furthermore, by picking up signs of poor animal wellbeing early, humane endpoints can be implemented sooner rather than later and so avoids animals being inadvertently lost from an experiment through unexpected death (see Redgate *et al*, 1991; Olfert, 1995; Soothill *et al*, 1993; Townsend & Morton, 1994; Mellor & Morton, 1997; Cussler *et al*, 1998; U1KCCCR, 1998); and

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- has proved to be especially useful with new procedures or when users are not always sure of what effects a procedure will have. Literature rarely records adverse effects on animals or how to avoid or measure them. Only researchers have a moral obligation to do so (see Morton, 1998b).

### **O.11 Score sheets**

#### **O.11.1 Score sheets for specific research**

Further examples of score sheets for specific research are as follows:

- a) cancer research (see table O.3);
- b) toxicity studies (see table O.4);
- c) vaccine quality control (see table O.5); and
- d) infectious disease research (see table O.6).

#### **O.11.2 Cancer research**

##### **O.11.2.1 Special husbandry requirements**

Special husbandry requirements should be stipulated before the start of the observation, for example:

- a) after the tumour becomes visible, the frequency of observation and sizing of the tumour shall be increased; and
- b) particular attention shall be paid to the growth rate of the tumour.

Table O.3 — Score sheet for cancer research

<b>Date of study</b>							<b>Animal No.:</b>
<b>Weight (g)</b>							
<b>Date</b>							
<b>Day</b>							
<b>Time</b>							
<b>UNDISTURBED OBSERVATION</b>							
Inactive							
Mobility							
Hunched posture							
Grooming							
Alertness							
Presence of a growth							
Ruffled coat							
<b>ON HANDLING</b>							
Not inquisitive and alert							
Not eating							
Not drinking							
Vocalization on gentle palpation							
Body weight (g)							
Percentage of baseline weight							
Dehydration							
Type of breathing <sup>a</sup>							
Condition grading 4 to 1 <sup>b</sup>							
<b>SPECIFIC CLINICAL SIGNS</b>							
Size of tumour							
Necrosis of tumour							
Bleeding of tumour							
Ulceration							
Nothing Abnormal Detected (NAD)							
<b>OTHER</b>							
<b>SIGNATURE</b>							
Scoring details:							
<sup>a</sup> Breathing: R = rapid; S = shallow; L = laboured; N = normal.							
<sup>b</sup> Condition: 4 = normal; 1 = emaciated.							
nd = not determined.							

### O.11.2.2 Humane endpoints or actions

O.11.2.2.1 If more than one (negative) clinical sign occurs then the veterinarian and the principal scientist should be informed.

O.11.2.2.2 Humane endpoints or actions should be taken, using recognized euthanasia methods, when

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- a) an animal weighs less than its initial weight after 7 d or loses more than 10 % of its initial body weight at any time,
- b) before a tumour reaches a predetermined size,

NOTE In general, the tumour should not exceed 10 % of the body weight. For a mouse, the appropriate maximal diameter is 2 cm.

- c) an animal is in a poor condition (condition grading of 1 = emaciated), and
- d) there is necrosis or bleeding of the tumour.

### **O.11.2.3 Scientific measures**

Instructions for scientific measures should be followed.

### **O.11.3 Toxicity studies**

#### **O.11.3.1 Special husbandry requirements**

Special husbandry requirements should be stipulated before the start of the observation, for example:

- a) the animals shall be observed several times a day;
- b) husbandry and nutritional needs shall be met and be compatible with scientific requirements; and
- c) the responses of animals to housing and husbandry regimes during their active period shall be monitored.

Table O.4 — Score sheet for toxicity studies

Date of study							Animal No.:
Weight (g)							
Date							
Day							
Time							
<b>UNDISTURBED OBSERVATION</b>							
Inactive							
Mobility							
Hunched posture							
Grooming							
Alertness							
Presence of a discharge							
Ruffled coat							
<b>ON HANDLING</b>							
Not inquisitive and alert							
Not eating							
Not drinking							
Vocalization on gentle palpation							
Body weight (g)							
Percentage of baseline weight							
Dehydration							
Type of breathing <sup>a</sup>							
Condition grading 4 to 1 <sup>b</sup>							
<b>SPECIFIC CLINICAL SIGNS</b>							
Behavioural changes							
Tremors							
Circling							
Convulsions							
Comatosed							
Nothing Abnormal Detected (NAD)							
<b>OTHER</b>							
<b>SIGNATURE</b>							
Scoring details:							
<sup>a</sup> Breathing: R = rapid; S = shallow; L = laboured; N = normal.							
<sup>b</sup> Condition: 4 = normal; 1 = emaciated.							
nd = not determined.							

### O.11.3.2 Humane endpoints or actions

O.11.3.2.1 If more than one (negative) clinical sign occurs then the veterinarian and the principal scientist should be informed.

O.11.3.2.2 Humane endpoints or actions should be taken, using recognized euthanasia methods, when

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- a) there is a case of convulsions, or
- b) there is severe weightloss (>20 %) and dehydration.

**O.11.3.2.3** The time of euthanasia shall be decided by the responsible laboratory animal or veterinary technologist.

### **O.11.3.3 Scientific measures**

Instructions for scientific measures should be followed.

## **O.11.4 Vaccine quality control**

### **O.11.4.1 Special husbandry requirements**

Special husbandry requirements should be stipulated before the start of the observation, for example, animals shall be assessed twice per day until the end of the experiment.

Table O.5 — Score sheet for vaccine quality control

Date of study							Animal No.:
Weight (g)							
Date							
Day							
Time							
<b>UNDISTURBED OBSERVATION</b>							
Inactive							
Mobility							
Hunched posture							
Grooming							
Alertness							
Presence of a discharge							
Ruffled coat							
<b>ON HANDLING</b>							
Not inquisitive and alert							
Not eating							
Not drinking							
Vocalization on gentle palpation							
Body weight (g)							
Percentage of baseline weight							
Dehydration							
Type of breathing <sup>a</sup>							
Condition grading 4 to 1 <sup>b</sup>							
<b>SPECIFIC CLINICAL SIGNS</b>							
Central nervous signs and specifications							
Body temperature (°C)							
Nothing Abnormal Detected (NAD)							
Number of animals put to death by recognized euthanasia methods or that died							
<b>OTHER</b>							
<b>SIGNATURE</b>							
Scoring details:							
<sup>a</sup> Breathing: R = rapid; S = shallow; L = laboured; N = normal.							
<sup>b</sup> Condition: 4 = normal; 1 = emaciated.							
nd = not determined.							

#### O.11.4.2 Humane endpoints or actions

O.11.4.2.1 If more than one (negative) clinical sign occurs then the veterinarian and the principal scientist should be informed.

O.11.4.2.2 Humane endpoints or actions should be taken, using recognized euthanasia methods, when

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- a) there are central nervous signs such as ataxia or convulsions,
- b) a low body temperature ( $<34,5\text{ }^{\circ}\text{C}$ ) is observed, or

NOTE Validation studies have shown that a drop in body weight is not always predictive of a lethal outcome.

- c) a decision by the responsible laboratory animal veterinary technologist to terminate is taken.

**O.11.4.2.3** For each animal group, the number of animals that die per day should be recorded.

### **O.11.4.3 Scientific measures**

Instructions for scientific measures should be followed.

## **O.11.5 Infectious disease research**

### **O.11.5.1 Special husbandry requirements**

Special husbandry requirements should be stipulated before the start of the observation, for example:

- a) cage sanitation schedules should be altered to accommodate special research needs;
- b) cages and waste pans or trays should be sanitized weekly or more often, if required; and
- c) animal food supply should comprise all required nutrients unless the requirements of the study precludes it.



Table O.6 — Score sheet for infectious disease research

Experiment No.:		Animal No.:					
Weight (g)							
	Date/time						
<b>APPEARANCE</b>	<b>Score</b>						
Normal							
Diminished grooming							
Piloerection, discharge nose/eyes							
Soiled, poorly groomed coat							
<b>BODY WEIGHT</b>							
Normal < 5 %							
Body weight 5 % to 10 %							
Body weight 11 % to 15 %							
Body weight 16 % to 20 %							
<b>CLINICAL SIGNS</b>							
Food and water intake							
Stool normal – slightly soft							
Diarrhoea <sup>a</sup>							
Increased abdominal dimension, soft on palpation, no stool							
<b>RESPONSE TO HANDLING</b>							
Normal							
Slightly decreased or increased response							
Strongly decreased or increased response/vocalization on abdominal palpation							
Decreased or increased response							
<b>TOTAL</b>							
<b>SIGNATURE</b>							
<sup>a</sup> 0= normal; 1 = loose faeces on the floor; 2 = pools of faeces on the floor; 3 = running out on handling. nd = not determined.							

### O.11.5.2 Assessment and humane endpoints and actions

#### O.11.5.2.1 The following assessment ratings apply:

- a) 0 to 4: Normal.
- b) 5 to 9: Increase frequency of assessment and observe the animal more closely.
- c) 10 to 15: Clear distress present. Treat the animal if possible. Increase the frequency of observation. Consult with principal researcher or veterinarian or head animal technologist. Consider putting the animal to death by recognized euthanasia methods.