SmartCow

an integrated infrastructure for increased research capability and innovation in the European cattle sector

Endpoints

Véronique DEISS – veronique.deiss@inra.fr

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Grant Agreement n°730924

End-Point of a Procedure:

Endpoint can be defined as the earliest indicator in an animal experiment **of severe pain, severe distress, suffering, or impending death.**
The ultimate purpose of the application of **endpoints** is to be able to **predict** severe pain, severe distress, suffering, or impending death, **before the animal experiences these effects**

Investigators should consider choosing welfare-based end-points that allow effective prevention of more serious animal welfare problems,

Death is considered to be an unacceptable endpoint.

- If there is no information relevant to the determination of early endpoints as indicators of pain or distress, a separate pilot study may have to be performed.
- If a pilot study is performed, it should use only the minimum number of animals consistent with the objectives of the study.
- The information collected during pilot studies should also be used to prepare or alert the study team for the actions or activities related to endpoints that may be needed.

- Isolation and Crowding:

Many studies require the isolation of animals or crowded conditions.

These systems may be extremely stressful to animals. The degree of stress experienced will be markedly influenced by the species, age, sex, reproductive condition, social status, individual experience and natural behaviour of the animal.

These factors should all be considered to minimise the stress likely to be experienced by the animal

Aversive Stimuli:

Animals are sometimes deliberately exposed to aversive stimuli

If this is essential, it should be minimised in both severity and duration in accordance with achieving the aims of the experiment. The animals' perceptual and behavioural characteristics, age, experience, etc. should be considered in planning the study.

Investigators should monitor such studies frequently, or preferably, constantly in order to be able to interrupt if unacceptable levels of suffering occur, in which case the animal should be removed from the study and given appropriate treatment or euthanasia.

Barriers or escape routes should be provided for the animal to avoid the aversive stimulus where this is in accordance with achieving the aims of the experiment.
Investigators should be aware of indicators of extreme fear.

- Deprivation:

Animals are sometimes deprived of various resources for a variety of reasons, e.g. food, water.

If deprivation is essential, this should be minimised in both severity and duration in accordance with achieving the aims of the experiment.

In general, to avoid chronic hunger, it is preferable to deprive an animal of food for a pre-determined period of time before testing, rather than attempting to achieve and maintain an arbitrarily specified target bodyweight

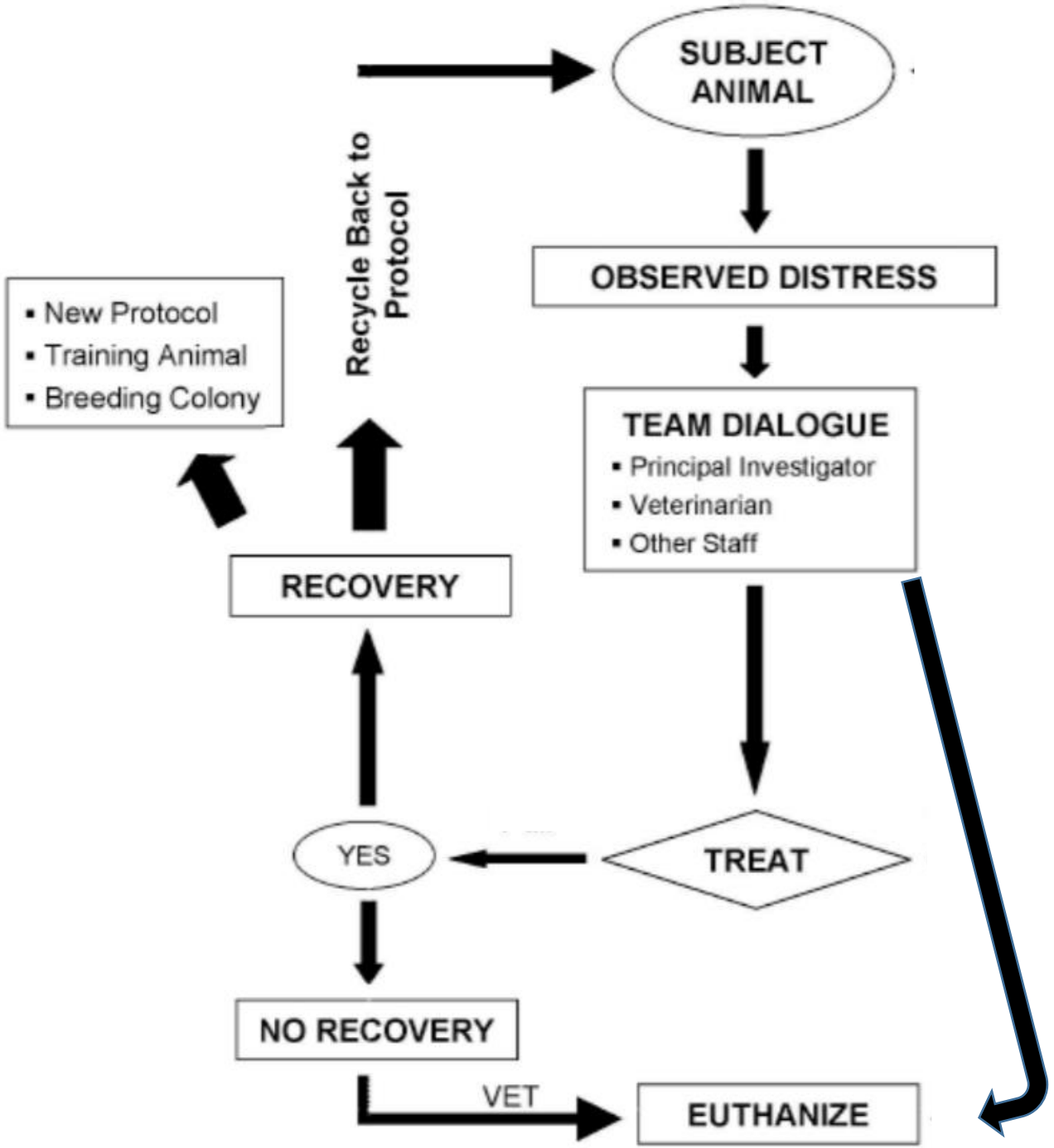
- Adverse Conditions:

Studies aimed at inducing adverse conditions in animals are sometimes conducted to gain knowledge of applied problems, e.g. parasite loads, pesticides or homeostatic challenges.

These procedures may cause suffering and again should be minimised in both severity and duration in accordance with achieving the aims of the experiment.

Investigators should plan frequent or constant monitoring of such studies, and appropriate intervention at a pre-determined end-point with appropriate care or euthanasia of the animals.

Investigators should also consider experimental designs that allow removal of the adverse condition rather than its addition


SUBJECT ANIMAL
OBSERVED DISTRESS
TEAM DIALOGUE
▪ Principal Investigator
▪ Veterinarian
▪ Other Staff
TREAT
YES
RECOVERY
Recycle Back to Protocol
▪ New Protocol
▪ Training Animal
▪ Breeding Colony
NO RECOVERY
VET
EUTHANIZE

S Picavet

There are a number of effects involved in the adequate evaluation of an animal to determine its condition and whether there might be evidence indicative of pain and or distress:

- changes in body weight, and related changes in food and water consumption
- changes in physical appearance
- changes in clinical signs
- changes in unprovoked behaviour
- behavioural changes in response to external stimuli

- In each of these categories, a rating system of 0 (normal or mild) to 3 (severe changes from normal) was proposed.

- The cumulative rating obtained by adding the score for each category indicates increasing deviation from normal in the animal, which can be interpreted as an indication of increasing pain and/or distress.

- A total score can be identified, at which point the animal's pain and/or distress will be terminated or alleviated.

EXAMPLES OF OBSERVATIONAL CHECKLISTS USED TO DETERMINE ENDPOINTS: ACUTE RESPIRATORY INFECTIOUS DISEASE IN CATTLE - A VACCINE/CHALLENGE STUDY The CCAC guidelines on: choosing an appropriate endpoint in experiments using animals for research, teaching and testing

- Clinical Evaluation
- Calves will be clinically examined each morning (8:00 a.m. - 12:00 p.m.) from day 0 to day 10 by the research veterinarian.
- In the afternoon, they will be examined in the pen by an animal health technician.

. **Rhinitis or nasal score**.

0	***Normal*** (mucosa pale pink, no visible nasal discharge).
1	***Mild Rhinitis*** (mild serous rhinitis with focal mucosal necrosis, nostrils moist, secretions transparent, mucosa mildly hyperemic, focal mucosal vesicles, small white circular necrotic plaques < 2mm diameter, mild serous nasal discharge).
2	***Moderate Rhinitis*** (moderately severe serous rhinitis with confluent areas of mucosal necrosis, mixture of focal plaques and confluent areas of necrosis, nostrils not occluded by exudates, mucosa intensely hyperemic, large confluent mucosal plaques >2mm diameter, serous nasal discharge with occasional globules or small strands of mucopurulent exudate).
3	***Severe Rhinitis*** (necrotizing rhinitis, nasal discharge partially occluding nostrils, necrotic plaques cover large portion of nasal mucosa, intense mucosal hyperemia, may have halitosis, nostrils partially occluded by exudates, nasal secretion a mixture of serous and mucopurulent exudates, large confluent mucosal plaques, necrotic tissues forming diphtheritic pseudomembranes that peel from septum).
4	***Very Severe Rhinitis*** (severe mucopurulent rhinitis with advanced mucosal necrosis, mucosal erosions bleed easily, halitosis, profuse nasal discharge, exudate hanging from nostrils, mouth breathing, head extended, thick coat of purulent of catarrhal exudate on nasal mucosa, exudates almost completely occlude nostrils).

Depression score.

0	***Normal*** (bright, alert, eyes bright, ears erect, chews cud, curious, attentive, stays with the group, stretches back muscles, hind legs when stands, licks nostrils frequently, usually within ten seconds of release from headgate).
1	***Mildly Depressed*** (ears droop slightly, rarely stands alone, licks nostrils occasionally, tries to stay with the group, difficult to corner or nearly impossible to catch in corral).
2	***Moderately Depressed*** (walks slowly, lethargic, stands alone for prolonged periods, sometimes stands with head low, easy to corner, but would be difficult to catch).
3	***Severely Depressed*** (uninterested in environment, very lethargic, apathetic, stands with head lowered most of the time, a "straggler", lies in sternal recumbency frequently, often recumbent, reluctant to stand, but can stand when encouraged, easy for one person to catch).
4	***Moribund*** (near death, no attempt to clean nostrils, recumbent almost continuously, rarely stands up, oblivious to surroundings, unable, unwilling, or very reluctant to stand, sternal or lateral recumbency).

Strength.

0	***Normal*** (healthy, strong, stands square, runs fast, well-coordinated, impossible to catch, lays with head and legs positioned normally, curled under, easily keeps up with group).
1	***Mild Weakness*** (unsteady gait, knuckles occasionally when walking, hind end wobbles, but calf does not stumble, walks slowly, but can trot and gallop when chased).
2	***Moderate Weakness*** (staggers noticeably, may fall down when struggling, but rises again without delay, can walk and trot, but cannot gallop, rests head on ground when laying down, fairly easy to push off balance, could be laid on side with moderate difficulty).
3	***Severe Weakness*** (rises with difficulty, knuckles frequently, stumbles occasionally, runs slowly, easily caught, has difficulty standing up, very easy to push off balance, often falls down when struggling).
4	***Advanced Deterioration*** (very weak, unable to stand, emaciated, dehydrated, sunken eyes, skin tenting).

SmartCow

Respiratory distress.

0	***Normal*** (normal nasal breathing, mouth closed, lips dry).
1	***Mild Respiratory Distress*** (intermittent mouth breathing, lips and jaw moist from salivation, but not observed holding mouth open, mucous membranes pink unless stressed).
2	***Moderate Respiratory Distress*** (stands with head extended, salivates profusely, muzzle dripping wet).
3	***Severe Respiratory Distress*** (mouth breathes when stressed, opens mouth frequently, occasionally extends tongue, breathes through mouth when disturbed, labored breathing, becomes cyanotic when stressed minimally).
4	***Very Severe Respiratory Distress*** (cyanotic, stands with head lowered, neck extended, mouth open and tongue extended, severe drooling, anxious expression).

Weight. The weight is recorded daily for each animal.

Temperature. Rectal temperature is taken with the animal restrained in a chute. Temperatures will be taken and recorded daily in all animals

Sickness score.

0	***Healthy Animal*** (normal healthy animal, no treatment required, no fever, no clinical symptoms).
0.5	***Suspicion of Disease*** (animal would not be treated, slight clinical signs and no fever, fever 39.5°C-39.9°C and no clinical signs, single chronic unresolved clinical sign and no fever, animal not depressed and still eating well).
1	***Mildly Sick Animal*** (animal would be treated, febrile (40.0°C) and/or clinical signs, disease progressed to where it would be selected to initiate therapy on the farm or feedlot, recovery would be expected with appropriate therapy).
2	***Obviously Sick Animal*** (animal would be treated, obvious clinical signs usually febrile, disease is now serious - animal should have been treated before disease progressed to this point, recovery even
	with appropriate therapy would not be certain). These animals are watched to see if they progress to the next sickness score.
3	***Very Sick Animal*** (animal would be treated in a clinical setting, severe clinical signs, including depression - fever may be present or temperature dropping, disease is very serious, recovery unlikely even with appropriate therapy). These animals are euthanized.
4	***Moribund*** (near death, treatment would be futile; animal would be euthanized in a clinical or experimental setting).

SmartCow