



FishEnds/FISHEnds-DIG

Presented by

Aurora Brønstad

University of Bergen

Objectives

- Improve and refine studies in fish by focus on Score sheets and Humane endpoints
 - True predictors of animal going into a severe clinical stage
 - Appropriate actions to mitigate pain, suffering and distress
- 1. Refinement of welfare indicator scores
 - Morphological (fishwell, gill score++)
 - Behavioral
- 2. Digital solution for recording, storing, reporting and learning

Available by daily, non-intrusive/invasive observations



Refinement of Humane endpoints and Score sheets for studies in fish

Objective 1

Welfare Indicators for farmed Atlantic salmon: tools for assessing fish welfare

FISHWELL Morphological Operational Welfare Indicators (OWI's) for farmed Atlantic salmon v1.1

Level 0: Little or no evidence of this OWI, i.e. normal (not illustrated).
Level 1, minor to Level 3, clear evidence of the OWI.

	Eye haemorrhaging	Exophthalmia	Opercular damage	Snout damage	Upper jaw deformity	Lower jaw deformity	Emaciation
1							
2							
3							

	Vertebral deformity	Skin haemorrhages	Lesions / wounds **	Scales loss	Sea lice infection	Healed fin damage †	Active fin damage †
1							
2							
3							

<https://www.fishfarmingexpert.com/article/talking-our-language-welfare-indicators-handbook-now-available-in-english>



06.05.2021

2019

UIB > KI > MED > The Laboratory Animal Facility > Calendar >

SEVERITY AND HUMANE ENDPOINTS IN FISH RESEARCH

Severity and humane endpoints in fish research

Experiment i fish has to be classified as Terminal, Mild, Moderate or Severe

Opening registration 08:00

WORKSHOP

Topics

- 0830-0850 Aurora Brønstad, UoB, Norway. Introduction and Humane endpoints.
- 0850-0935 Anne D. Degryse, FELASA (WG Severity Assessment, Severity classification).
- 09:35-10:15 Trygve Poppe, Norway's Environmental and Life Sciences University, Norway. Why ethics also should apply to fish

🕒 04.10.2019 - 08.30-16.00

📍 VilVite

👤 [Aurora Margrethe Brønstad](#)

📅 Registration deadline
23.09.2019 - 12.00

2020

UIB > KI > MED > The Laboratory Animal Facility > Calendar >

SCORE SHEETS AND ENDPOINTS IN FISH RESEARCH

Establishing score sheets and defining endpoints in fish experiments

Program

- | | |
|-----------|---|
| 8:00-9:00 | Opening registration and coffee |
| 9:00-9:45 | Aurora Brønstad, University of Bergen (UoB): Introduction to humane endpoints in fish experiments |
| | Linda Andersen, ILAB & Anita Ronneseth, UoB: Outline for the workshop |

WORKSHOP

🕒 28.01.2020 - 08.00-16.00

📍 Universitetet i Bergen - Aulaen

👤 [Aurora Margrethe Brønstad](#)

📅 Registration deadline

Coffee r

10:00



Lab As
n't go



Score sheets

Standardized health and welfare
assessment sheets for animal studies

TIME, DATE AND SIGNATURE

- Documentation of actual severity and mitigating factors
- Traceability
- Transparency

ENDPOINTS AND ACTION POINTS

- Endpoints based on
 - General welfare indicators
 - Study-Specific welfare indicators
- Actions to avoid unnecessary pain, suffering or distress

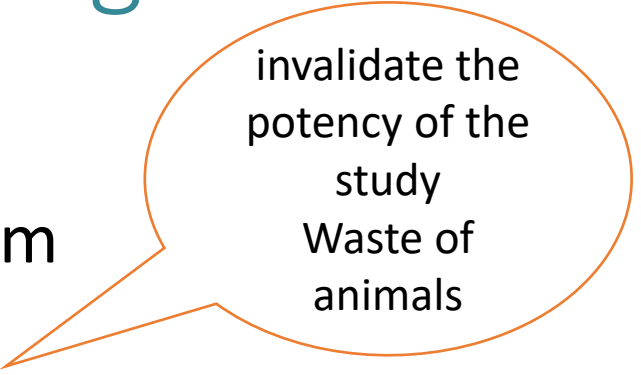
How humane is your endpoint?

- “Alternative to death” reflects a very narrow definition of humane endpoints ([Ashall and Millar, 2014](#))
- It has been questioned if all earlier endpoints can be really considered “humane” ([Franco et al., 2012](#))
- Other authors propose a broader definition of Humane Endpoint as a concept for continuous refinement of animal studies ([Hendriksen et al., 2010](#)).




Do not want False positive or False negative EP

- False positive endpoints means aborting an animal from a study while the animal would have recovered and survived the observation period of the study.
- False negative endpoints means that the animal already died before it reached the predefined endpoint



invalidate the
potency of the
study
Waste of
animals



compromise
animal welfare

(Hendriksen, 2011)

Few or many parameters?

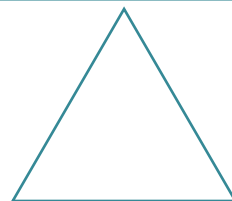
- Avoid irrelevant endpoint parameters
 - General welfare assessment information
 - Information from study-specific procedures
- Don't add additional burden to the animals

Information from study-specific procedures

Don't add additional burden to animals

- General welfare assessment information

- Weighing
- Blood samples



Aim 1:
IMPROVE ENDPOINTS
based on
DAILY WELFARE ASSESSMENTS
FROM HOME TANK OBSERVATIONS

FISHEnds-DIG

an app for tank-side registration of
clinical scores in fish
- an aid to the use of
humane endpoints for fish studies

Recording, storing, reporting and learning

Objective 2

eMar – App

<http://www.emar.no/>

FISHWELL Morphological Operational Welfare Indicators (OWI's) for farmed Atlantic salmon v1.1

Level 0: Little or no evidence of this OWI
Level 1, minor to Level 3, clear


Category	Level 1	Level 2	Level 3
Eye haemorrhaging	Minor haemorrhages	Larger haemorrhages, or traumatic injury	Large haemorrhages / traumatic injury. Eyes may be ruptured
Exophthalmia	Eye protruding a little	Moderate eye protrusion	Major eye protrusion
Opercular damage	Operculum only partly covering gills	Operculum absent on one of the gills (gill exposed)	Both opercula absent (both gills exposed)
Snout damage	Minor wound on snout (either jaw)	Moderate wound on broken skin on snout	Large deep and extensive. Can cover the whole snout
Vertebral deformity	Signs of deformed spine	Clearly visible spinal deformity (e.g. short tail)	Extreme deformity
Skin haemorrhages	Minor haemorrhaging, often on the belly of the fish	Large area of haemorrhaging, often coupled with scale loss	Significant bleeding, often with severe scale loss, wounds and skin edema
Lesions / wounds	One small wound (< 10 pence piece)*, subcutaneous tissue intact (no muscle visible)	Several small wounds	Large, severe wounds, muscle often exposed (x 10 pence piece)
Scale loss	Loss of individual scales	Small areas of scale loss (< 10% of the fish)	Large areas of scale loss (x 10% of the fish)

eMar
an AMC-Technology app


Welfare Indicators v 1.1

06.05.2024

eMar



Fish Welfare Report



Project
 Project Number: INMN-2020.06.29-22.40:17-test
 [Rep:OrderNumber] INMN-2020.06.29-22.40:17-test
 Report No.: 58
 Customer: Mowi
 Location:
 Inspection Type:
 Welfare indicators v 1.1
 Offshore Standard:
 DNV-RP-E304
 Procedure No: DSM-MR-006
 Inspection Start Dt:
 Inspection End Dt:
 MODU Name:
 AHV:

Accessory Laks-01-14
 Certificate ID:
 Dim.[mm]
 Length(org.):
 Manufacturer:
 Manufactured:

Marine Operation Project No.:
 Personnel:

Executive Summary			
Parameter	Findings and Memo	Date	Inspector
Inspection Findings and Details			
Parameter	Findings and Memo	Date	Inspector
Upper jaw deformity	Distinct malformation	29.06.2020	Test User
Sea lice infection	= 0.08 pre-adult or adult lice cm2 of fish skin	29.06.2020	Test User

Inspection Findings and Picture Documentation		
Parameter Name	Inspection Time	Inspection Findings and Data
Upper jaw deformity	2020.06.29	Distinct malformation



Parameter Name	Inspection Time	Inspection Findings and Data
Sea lice infection	2020.06.29	= 0.08 pre-adult or adult lice cm2 of fish skin



Dashboard

- Intuitive, graphic interphase
- Share key data between project partners

AWESOME CHART ELEMENTS DASHBOARD



60%

This is a sample Text

AWESOME CHART ELEMENTS DASHBOARD



35%

This is a sample Text



Title Title Title Title

AWESOME CHART ELEMENTS DASHBOARD



This is a sample text. This is a sample text.

AWESOME CHART ELEMENTS DASHBOARD



Text 90%

Text 85%

Text 65%

Text 40%

BRUK AV DYR I FORSØK I 2020

Antallet forsøksdyr er innrapporterte tall fra forskere og forsøksdyrvirksomheter.

Art	Antall
[A1] Mice (<i>Mus musculus</i>)	50 222
[A2] Rats (<i>Rattus norvegicus</i>)	3 355
[A3] Guinea-Pigs (<i>Cavia porcellus</i>)	296
[A7] Other Rodents (other Rodentia)	568
[A8] Rabbits (<i>Oryctolagus cuniculus</i>)	8
[A10] Dogs (<i>Canis familiaris</i>)	201
[A12] Other carnivores (other Carnivora)	125
[A13] Horses, donkeys & cross-breeds (Equidae)	59
[A14] Pigs (<i>Sus scrofa domesticus</i>)	696
[A16] Sheep (<i>Ovis aries</i>)	736
[A17] Cattle (<i>Bos primigenius</i>)	14
[A27] Other Mammals (other Mammalia)	541
[A28] Domestic fowl (<i>Gallus gallus domesticus</i>)	1 298
[A29] Other birds (other Aves)	11 435
[A30] Reptiles (Reptilia)	27
[A32] Xenopus (<i>Xenopus laevis</i> and <i>Xenopus tropicalis</i>)	13
[A34] Zebra fish (<i>Danio rerio</i>)	38 867
[A35] Other Fish (other Pisces)	2 174 234
SUM	2 282 710

2020 report

Zebrafish	38 867
Other fish	2 174 234
All other animals	69 609

2020 Fish numbers correspond to >97% of animals used in research

Research Article

Refining Humane Endpoints in Mouse Models of Disease by Systematic Review and Machine Learning-Based Endpoint Definition

Jie Mei¹, Stefanie Banneke², Janet Lips^{1,3,4}, Melanie T. C. Kuffner^{1,4,5}, Christian J. Hoffmann^{1,4,6}, Ulrich Dirnagl^{1,3,4,7,8}, Matthias Endres^{1,4,6,7,8}, Christoph Harms^{1,3,4,6} and Julius V. Emmrich^{1,2,6}

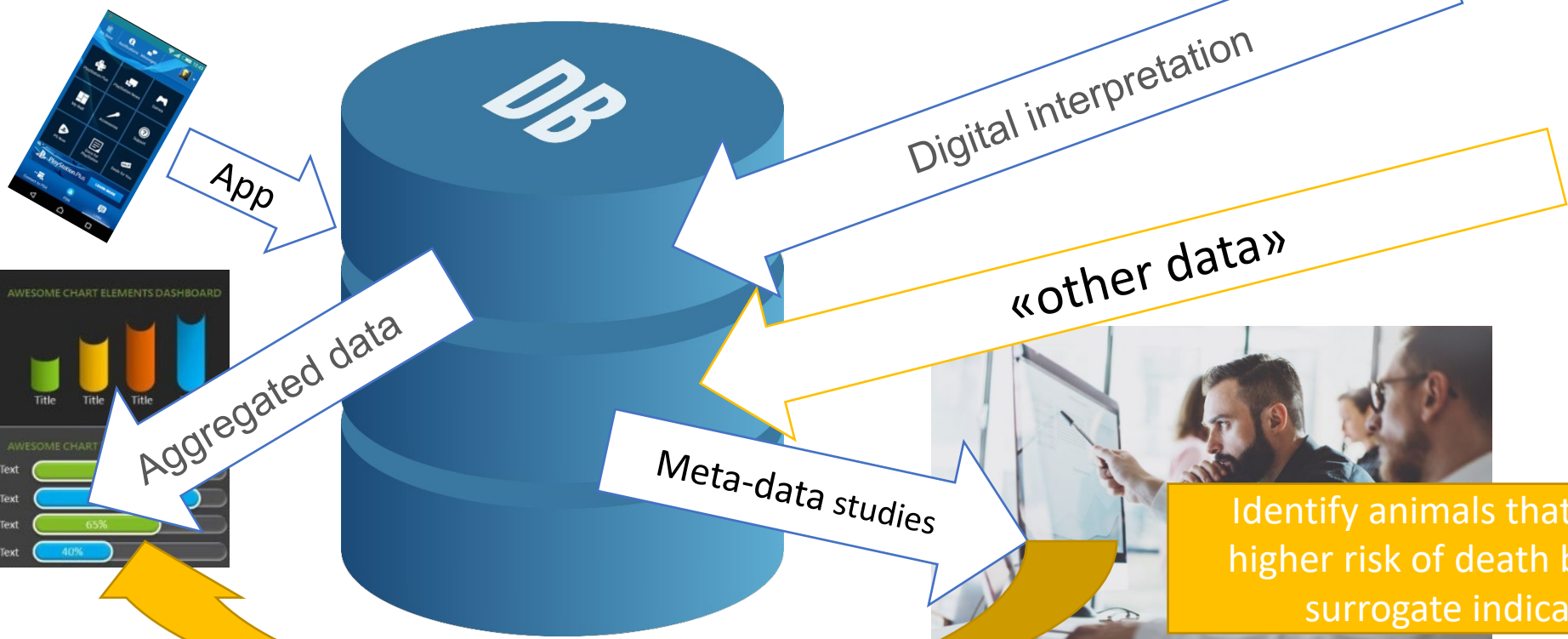
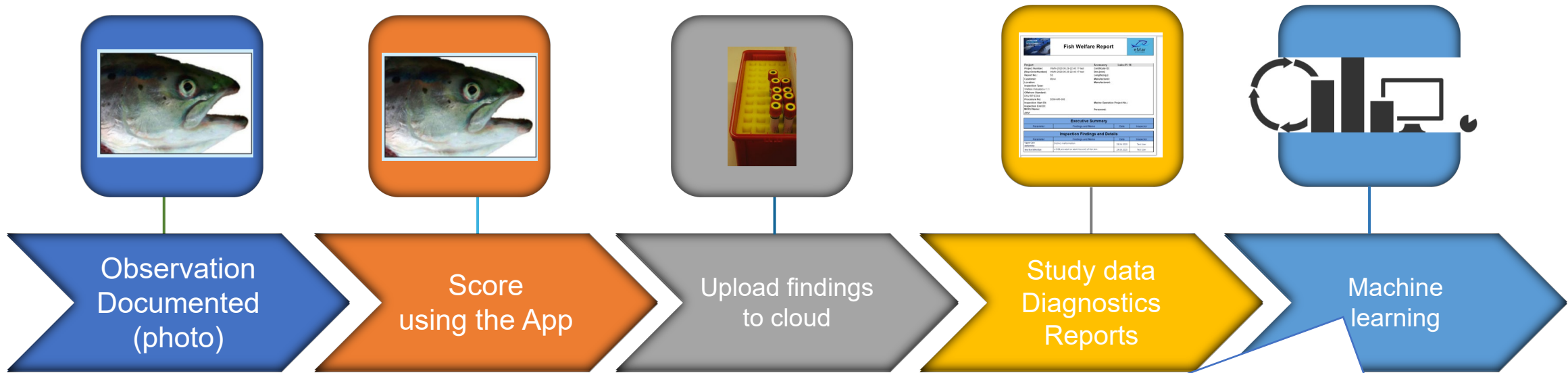
¹Department of Neurology and Department of Experimental Neurology, NeuroCure Cluster of Excellence, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany; ²German Federal Institute for Risk Assessment, German Center for the Protection of Laboratory Animals (Bf3R), Berlin, Germany; ³QUEST – Center for Transforming Biomedical Research, Berlin Institute of Health (BIH); ⁴Center for Stroke Research, Charité – Universitätsmedizin Berlin, Berlin, Germany; ⁵Berlin-Brandenburg School for Regenerative Therapies (BSRT), Berlin, Germany; ⁶Berlin Institute of Health (BIH), Berlin, Germany; ⁷German Center for Neurodegenerative Diseases (DZNE), Berlin, Germany; ⁸German Center for Cardiovascular Research (DZHK), Berlin, Germany

Abstract

Ideally, humane endpoints allow early termination of experiments by minimizing an animal's discomfort, distress and pain while ensuring that scientific objectives are reached. Yet, lack of commonly agreed methodology and heterogeneity of cut-off values published in the literature remain a challenge to the accurate determination and application of humane endpoints.

With the aim to synthesize and appraise existing humane endpoint definitions for commonly used physiological parameters, we conducted a systematic review of mouse studies of acute and chronic disease models that used body weight, temperature and/or sickness scores for endpoint definition. We searched for studies in two electronic databases (MEDLINE/Pubmed and Embase). Out of 110 retrieved full-text manuscripts, 34 studies were included. We found large intra- and inter-model variance in humane endpoint determination and application due to varying animal models, lack of standardized experimental protocols, and heterogeneity of performance metrics (part 1).

We then used previously published and unpublished data on weight, temperature, and sickness scores from mouse models of sepsis and stroke and applied machine learning models to assess the usefulness of this method for parameter selection and endpoint definition across models. Machine learning models trained with physiological data and sickness



Dashboard

- Intuitive interphase
- Share key data between project partners

Alarms/alerts

Identify animals that are at a higher risk of death based on surrogate indicators

Aim2:

REFINE predictors of animal going into a distressing, helpless, life threatening, irreversible or severe clinical stage – so that mitigating actions can be made and fish studies
REFINED



Marineholmen
RASLab



Project Group

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norecopa

