

FNUSA-ICRC Workshop 2016



Harm-Benefit Analysis: the AALAS-FELASA Working Group Proposal

Javier Guillén

Senior Director Europe and Latin America

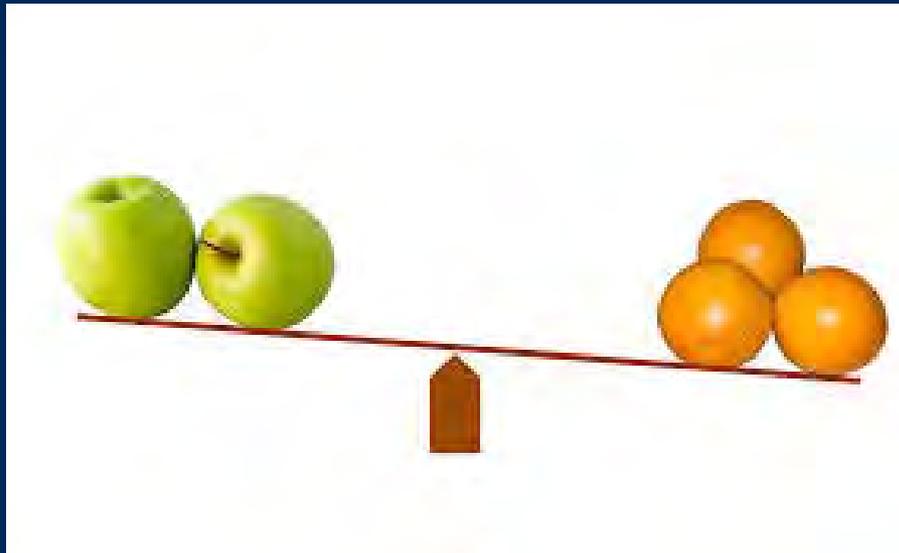
Aurora Brønstad

University of Bergen – Norway





Ethical Balance of Different Things



Risk – Benefit



Cost – Benefit



Harm – Benefit



Harm-Benefit Analysis Framework



Directive 2010/63/EU. Art. 38, 2, d.

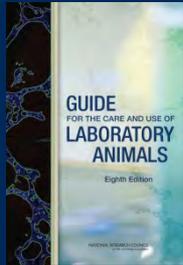
2. The project evaluation shall consist in particular of the following:

(a), (b), (c), (e), (f)

(d) **a harm-benefit analysis** of the project, to **assess whether the harm to the animals in terms of suffering, pain and distress is justified by the expected outcome** taking into account ethical considerations, and may ultimately benefit human beings, animals or the environment;



Harm-Benefit Analysis Framework

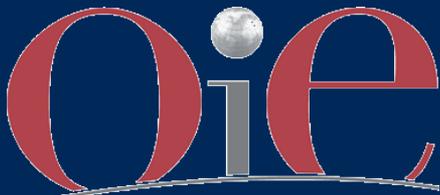


Guide for the Care and Use of Laboratory Animals
(NRC, 2011)

“...the IACUC is obliged to weigh the objectives of the study against potential animal welfare concerns.”



Harm-Benefit Analysis Framework



Terrestrial Code Chapter 7.8.

Use of Animals in Research and Education

Ethical review: means consideration of the validity and justification for using *animals* including: an **assessment and weighing of the potential harms for *animals* and likely benefits** of the use and how these balance;...

Harm-benefit analysis: means the process of **weighing the likely adverse effects (harms) to the *animals* against the benefits** likely to accrue as a result of the proposed project.

Project Proposal Review: ...(i) ethical considerations such as the application of the Three Rs and a **harm/benefit analysis**; the benefits should be maximised and the harms, in terms of pain and distress, should be minimized;



Harm-Benefit Analysis Framework



International Guiding Principles for Biomedical Research Involving Animals (2012)

P.I: “...Decisions regarding the welfare, care and use of animals should be guided by scientific knowledge and professional judgement, reflect ethical and societal values, and **consider the potential benefits and the impact on the well-being of the animals** involved”.

P.X: “The oversight framework... should promote a **harm-benefit analysis** for animal use, balancing the benefits derived from the research or educational activity with the potential for pain and/or distress experienced by the animal”.



Harm-Benefit Analysis Framework



http://www.aaalac.org/accreditation/faq_landing.cfm#B3)

AAALAC International expects that IACUC's (or comparable oversight body), as part of the protocol review process, will **weigh the potential adverse effects of the study against the potential benefits** that are likely to accrue as a result of the research. This analysis should be performed prior to the final approval of the protocol, and should be a primary consideration in the review process.



AALAS-FELASA Harm-Benefit WG



Christian Newcomer, VMD, DAACLAM
Executive Director, AAALAC
International

Jeffrey Everitt, DVM, DAACLAM, DACVP
GlaxoSmithKline

Kathy Laber, DVM, MS, DAACLAM
Animal Program Director, NIEHS/NIH

Aurora Brønstad, DVM, Ph.D.
Chief Veterinarian, University of Bergen

Thierry Decelle, DVM, M. Sc.
Director, Global Animal Welfare Officer
Sanofi Pasteur

Javier Guillén, DVM
Director Europe & Latin America
AAALAC International



AALAS-FELASA Harm-Benefit WG

Assigned Tasks

1. Review existing literature on harm-benefit analysis.
2. Define and describe the current concepts and elements of the harm-benefit analysis.
3. Recommend how it can be addressed by persons responsible of the protocol/project applications.
4. Define how the harm-benefit analysis can be implemented by committee members as part of the ethical evaluation.
5. Present practical cases that may exemplify common situations in the research environment.



Dimensions of Harm (literature)

- **Species**, choice of animals
- Sentience and consciousness
- Quality of animals
- Duration
- Duration related to lifespan
- **Number** of animals
- Origin, acquisition or transport
- Care, housing factors, handling, health care
- Possibility to express Normal Behaviour
- **Staff** competence and quality
- Hunger and Thirst
- Discomfort
- **Pain**
- Injury or Disease
- Fear, anxiety and distress
- Frequency of procedures
- Severity of procedures
- Risk of harm = probability x severity
- Deaths (caused by the experiment)

- Intrinsic value and animal rights
- Genetic modulation of animals - respect for nature

- **Aim, Realistic potential**
- **Scientific Quality**
- **Non-publishing of negative results**



Dimensions of Harm (literature)

The Five Freedoms

1. Freedom from Hunger and Thirst
2. Freedom from Discomfort
3. Freedom from Pain, Injury or Disease
4. Freedom to Express Normal Behaviour
5. Freedom from Fear and Distress

- **Brambell, R., Five Freedoms. 1965, Farm Animal Welfare Council**
- **Mellor&Reid, Concepts of animal well-being and predicting the impact of procedures on experimental animals 1994**

” There is a danger that with focus largely on suffering we could overlook a broader view of welfare which may be more informative and safeguard more effectively the interests of the experimental animals ”



Dimensions of Benefit (literature)

- **Benefits for humans**
- **Benefits for animals**
- **Benefits for environment**
- Economic interests
- **Health interests**
- **Safety interests**
- **Knowledge interests**
- **Educational interest**
- Primary (direct) versus secondary (indirect) benefits
- "Surrogate outcomes" versus "health outcomes"
- Originality
- Dissemination of results

- **Aim, Realistic potential**
- **Quality, "good science"**
- **Non-publishing of negative results**



Dimensions of Benefit (literature)

The benefits

What?

- Scientific outputs
- (short/long-term)

Who?

- Patients
- Other researchers

How?

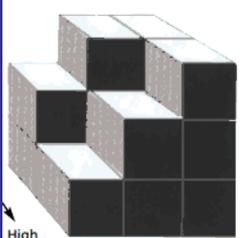
- Improved therapy, survival

When?

- In life-time of project
- Much later



Models of Harm-Benefit Analysis (literature)

	Strengths	Weaknesses
Tables, spreadsheet	Categories are useful to simplify a complex picture. Stimulate actions to avoid severe categories.	The categories do not fit all cases
$E = mc^2$ $\Sigma = \pi e^{HBA}$	Algorithms are helpful in <u>guiding</u> a decision	Moral dilemmas cannot/shall not be solved by arithmetic's
	Graphic representations have <u>pedagogic value</u> in visualizing the concept and relationship between harm and benefit	Depend on defined categories (eg. low-middle-high) Not operational (too simple?)
	Process oriented models <u>structure</u> the HBA process, how to <u>balance</u> different opinions and <u>question quality</u> of the analysis. Generic	Does not provide an answer on what model (as previous) to use or provide solutions for conclusions (too generic?)



Harm-Benefit Analysis Extensive Summary

- HBA is a systematic way to assess and compare harms, benefits and how they are balanced
- HBA must be transparent and verifiable
- HBA identifies harm – and stimulate researchers to seek alternative approaches
- HBA is a tool to make sure that animals are only used when it is justified because of potential benefit
- HBA clarifies if harm is necessary for achieving certain benefits
- HBA is important for public relations
- HBA is important to avoid uncritical use of animals even for the cause of the good
- HBA provides an ethical framework and is an essential part of the ethical review
- Harm Benefit analysis is based on utilitarian consequence ethics
- HBA stimulates ethical reflection and discussion
- HBA is dependent on and limited to the current context (external factors)
- HBA is influenced by subjective opinions (“affective heuristics”)



Working Party Report

Current concepts of Harm–Benefit Analysis of Animal Experiments – Report from the AALAS–FELASA Working Group on Harm–Benefit Analysis – Part 1

Aurora Brønstad¹, Christian E Newcomer², Thierry Decelle³, Jeffrey I Everitt⁴, Javier Guillen⁵ and Kathy Laber⁶

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The AALAS-FELASA WG Proposal

- The working group defines HBA as a **systematic, transparent** way to assess and compare harms, benefits of a particular animal study and how they are balanced.
- The WG has structured a **simple, systematic, and flexible** approach and developed a **tool** to perform a thorough HBA.
- Consideration of harms is based upon the Five Freedoms and a set of “modulating factors”
- Consideration of benefits is based upon a specific set of domains (what, who, how, when) and “modulating factors”.

KEY

Benefit = Domains
Social benefits <ul style="list-style-type: none"> • Human health • Animal health • Environmental health
Socioeconomic benefits
Scientific benefits
Educational benefits
Safety and efficacy

Harm = Impact on Five Freedoms
Freedom from Pain/Injury
Freedom from Fear/Distress
Freedom from Hunger/Thirst
Ability to express normal behavior
Freedom from Discomfort/appropriate husbandry

*Category:	Category Description:	Color Score:
Harm/Aggravating Factors	No impact	White
Benefit /Strength Factors	High Impact	
Harm/Aggravating Factors	Minimal	Pink
Benefit /Strength Factors	Moderate	
Harm/Aggravating Factors	Mild	Rose
Benefit /Strength Factors	Neutral	
Harm/Aggravating Factors	Moderate to Severe	Red
Benefit /Strength Factors	Minimal	
Harm/Aggravating Factors	Severe	Crimson
Benefit /Strength Factors	No positive impact	

HARM TABLE

HARM-Freedoms Impacted

Pain/Injury: _____

Fear/Distress: _____

Hunger/Thirst: _____

Ability to express normal behavior: _____

Discomfort/Husbandry: _____



Modulating Factors for HARM	Description	Mitigating Effect	Aggravating Effect	Summary Color
Animal—Species				Dark Red
Animal—Number				Light Red
Animal—Suited to environment				Red
Animal—Health status				White
Experimental-Intensity				Light Red
Experimental Duration				White
Experimental Cumulative Experience				Light Red
Experimental—Endpoint				White
Experimental Complication/Distribution Rate				White
Experimental Genetic Modulation				White
Environmental Housing/Husbandry				Red
Environmental Personnel competence/experience				Light Red

BENEFIT TABLE

BENEFIT DOMAINS

Social

- Human health: _____
- Animal health: _____
- Environment health: _____

Socioeconomic: _____

Scientific: _____

Educational: _____

Safety and Efficacy: _____



Modulating Factors for Benefit	Description Why/How/What /When	Summary Color/ Numeric Score
Importance of outcome		Red
Clarity of objectives		Light Red
Translational Potential		White
Likelihood of success		Light Red
Continuity of recognized scientific efforts		White
Quality of Experimental Design		White
Innovation Level		Red
Dissemination of Results		White



Working Group Report



Recommendations for Addressing Harm–Benefit Analysis and Implementation in Ethical Evaluation – Report from the AALAS–FELASA Working Group on Harm–Benefit Analysis – Part 2

Kathy Laber¹, Christian E Newcomer², Thierry Decelle³,
Jeffrey I Everitt⁴, Javier Guillen⁵ and Aurora Brønstad⁶

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