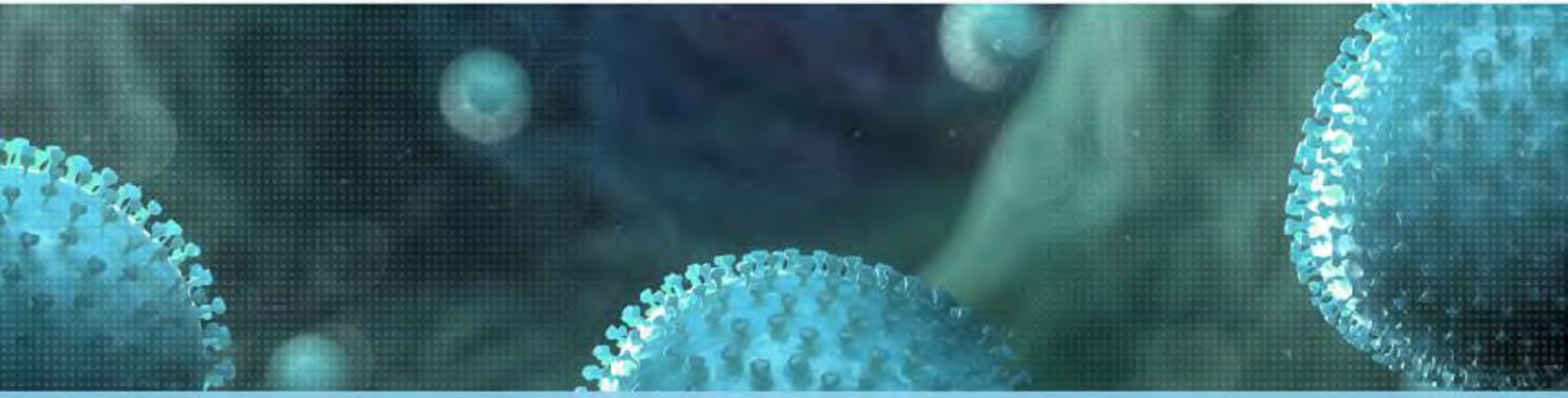
Erasmus MC

NSABB meeting, January 7 & 8, 2016

Viroscience lab

WHERE SKILLS MEET TO STUDY & PROTECT



Reflections on Gryphon Scientific's Risk and Benefit Analysis and NSABB WG's Draft Working Paper

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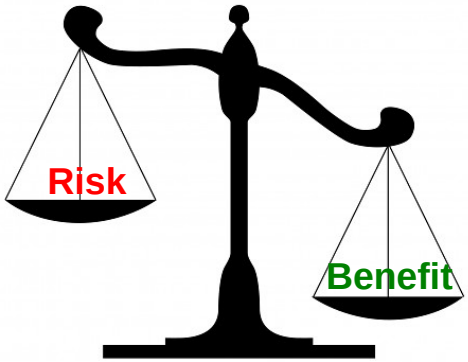
Professor Molecular Virology

Strengths and limitations of the RBA
- Gryphon Scientific Final Report Dec 2015 -

Strength: broad scope of benefit analysis (but excluding long-term benefits and blue-sky research) :
- Identifies "stringent limitations" of alt-GOF experiments as stand-alone tool
- Identifies situations where GOF experiments "provide unique benefits"
- Identifies instances where GOF "moderately contributes to overall risk"

Limitation: biosafety risk assessment
- Risk relative to "wildtype pathogen" (for which no major outbreaks occurred)
- Estimate of "absolute risk" is still "hypothetical"; no LAIs have been recorded
- Biosafety risk assessment (explicitly) ignores biosafety enhancements

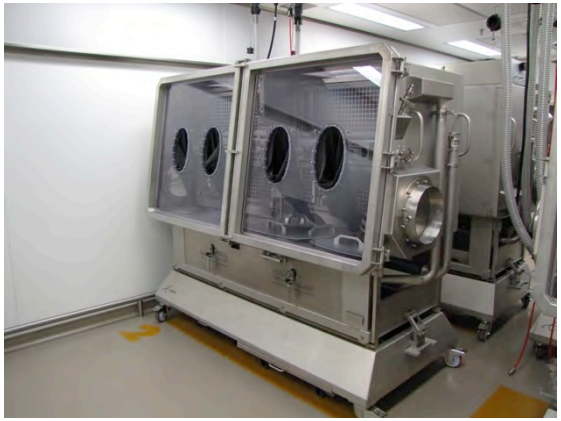


Risks: not quantified/quantifiable
Benefits: not quantified/quantifiable
Weighing: impossible/subjective

Biosafety 2.0 in agreement with Asilomar 1975
- Pathogen-specific enhancements -

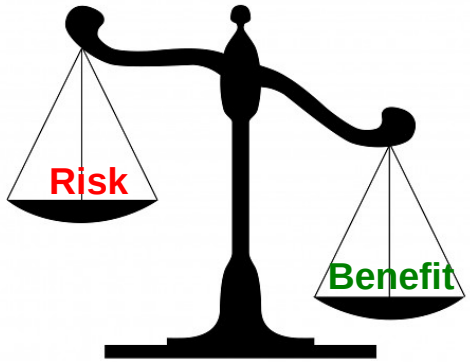
<u>Preventing the LAI</u>
- Class III units (monitored, validated)
- Extra layer of PPE
- Extensive training (incl incident response)
- Personnel work in pairs
- Vaccine use when possible
- Antiviral treatment upon any incident

> 140-fold risk reduction (very conservative)



<u>Preventing onward transmission from LAI</u>
- Reduce virus shedding (vaccine, drugs)
- Quarantine of personnel

> 20,000-fold risk reduction



Overall reduction of risk from very low to negligible

> 6 orders of magnitude risk reduction

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Fouchier RA, Studies on influenza virus transmission between ferrets: the public health risks revisited. MBio. 2015 Jan 23;6(1). pii: e02560-14.

Which GOF studies are of greatest concern?

- None (to date), relative to nature -

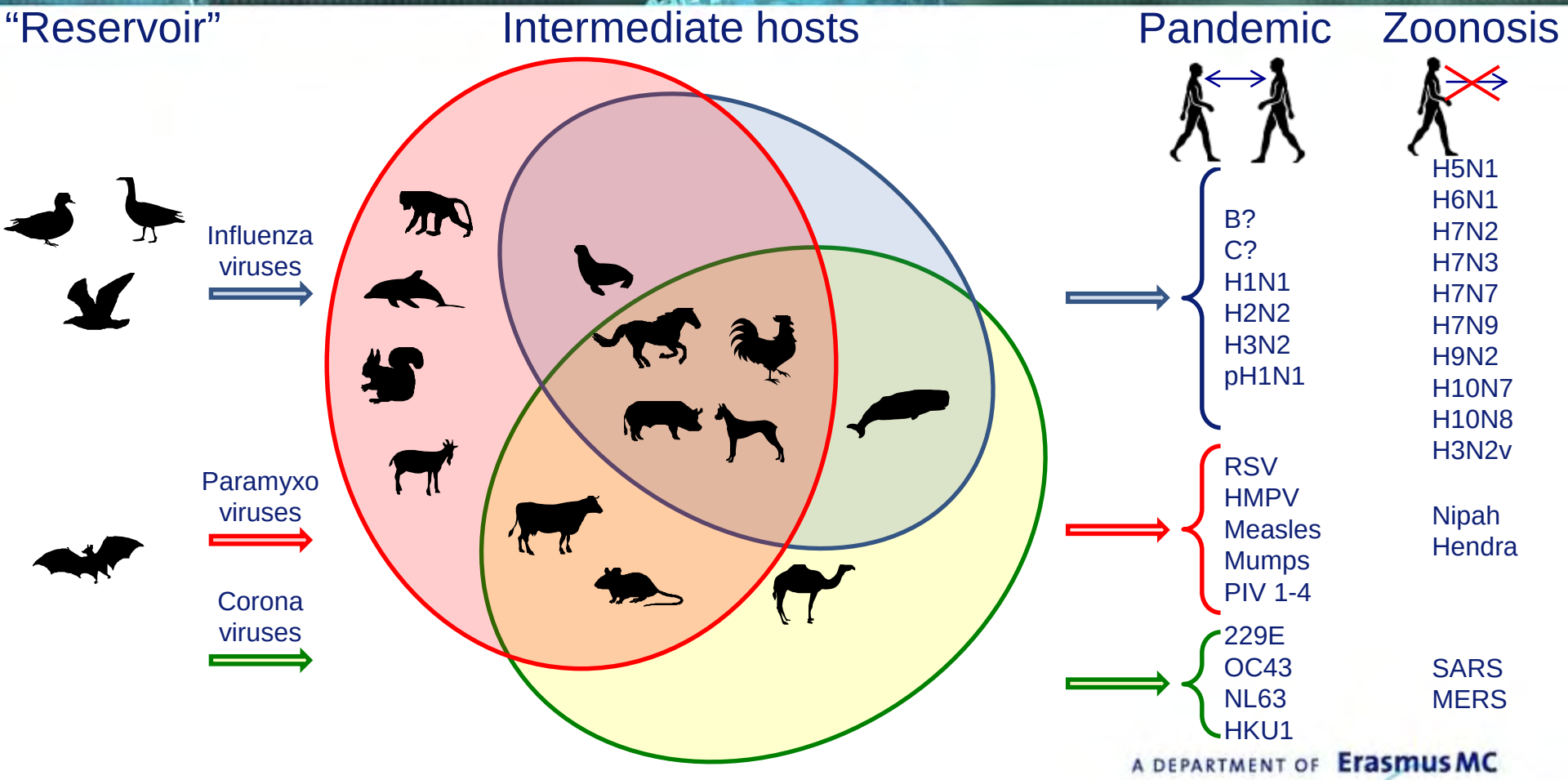

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Image: Herfst & Fouchier, Eurosurveillance 2014

Working paper NSABB WG
- Deliberative draft, December 2015 -

Thoughtful document, comprehensive and sound
Articulates limitations of RBA (lack of quantitation of risks and benefits)

Key Finding 1: There are many types of GOF studies and not all of them have the same level of risks. Only a small subset of GOF studies—GOF studies of concern—entail risks that are potentially significant enough to warrant additional oversight.

Key Finding 4. There are life sciences research studies that should not be conducted on ethical or public health grounds if the potential risks associated with the study are not justified by the potential benefits. Decisions about whether GOF studies of concern should be permitted will entail an assessment of the potential risks and anticipated benefits associated with the individual experiment in question. The scientific merit of a study is a central consideration during the review of proposed studies but other considerations and values are also important.

Recommendation 1. Research proposals involving GOF studies of concern entail the greatest risks and should be reviewed carefully for biosafety and biosecurity implications, as well as potential benefits, prior to determining whether they are acceptable for funding. If funded, such projects should be subject to ongoing oversight at the Federal and institutional levels.

Recommendation 3. The risk-benefit profile for GOF studies of concern may change over time and should be re-evaluated periodically to ensure that the risks associated with such research is adequately managed and the benefits are being realized.

Assumptions:
i) Risks are not negligible;
ii) Risks can be quantified;
iii) Benefits can be quantified;
iv) Risks & benefits can be weighed (objectively?)

Working paper NSABB WG
- Deliberative draft, December 2015 -

Proposed Conceptual Approach for Funding Potential GOF Studies of Concern

1. Identify proposals anticipated to involve GOF studies of concern, as described by the following attributes:

i. The pathogen generated is highly transmissible in a relevant mammalian model

ii. The pathogen generated is significantly virulent in a relevant mammalian model, and

iii. The pathogen generated is likely resistant to control measures or more capable of being spread among human populations than currently circulating strains of the pathogen.

2. Review proposal to determine whether they meet the following criteria:

i. The research proposal has been evaluated by a peer-review process and determined to be scientifically meritorious and has been assessed to be likely to exert a sustained, powerful influence on the research field(s) involved.

ii. An assessment of the overall potential risks and benefits associated with the project determines that the potential risks compared to the potential benefits are justified.

iii. There are no feasible, equally efficacious alternative methods to address the same scientific question in a manner that poses less risk than does the proposed approach.

iv. The investigator and institution proposing the research have the demonstrated capacity to carry it out safely and securely.

v. The research information is anticipated to be broadly and legally shared in order to realize its potential benefits to global health.

vi. The research will be supported through funding mechanisms that include appropriate oversight of: a) all aspects of the research including its conduct, b) the sharing of data and materials, and c) the communication of the research.

vii. The proposed research is ethically justifiable.

Proposals not meeting these criteria should not be funded.

3. Fund, do not fund, or fund with required additional risk mitigation measures or stipulations.

4. Conduct the research in accordance with applicable oversight policies and employ any additional risk mitigation strategies that were identified at the time of funding or that are deemed necessary during the course of the research.

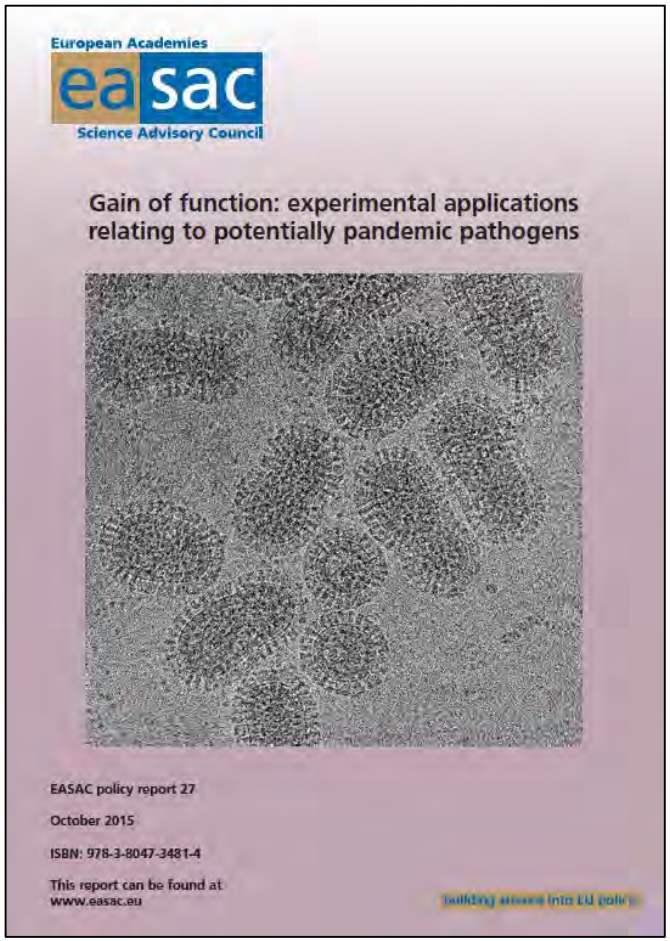
i. Research should be reviewed regularly at the institutional level

ii. Research should be reviewed regularly by the Federal funding agency

DRAFT

An EU perspective

- Laws, rules, regulations, codes are in place -



http://www.easac.eu/home/reports-and-statements/detail-view/article/easac-report-1.html

Fears R, Ter Meulen V. Elife 2015 Dec 30. pii: e13035 & J Virol 2015 Dec 23. pii: JVI.03045-15

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