Challenges in developing research infrastructures for preclinical animal related research

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Background

- Preclinical research using animals is essential in R&D of novel health initiatives.
- This is a global issue dependent on open collaborations between international partners.
- Barriers to collaborations crucially impact the success of preclinical research globally.



Develop RIs for sharing animals and animal data

- <u>Mice</u> mouse models in health sciences are essential to understanding functional basis of human disease. Thousands of GA mice are being created globally but existing capacities lagging for phenotyping, archiving and distribution of models.
- Infrafrontier Research Infrastructure (ESFRI) initiative is addressing through:
 - <u>Capacity building</u> scientific platforms and services for individual small projects (bottom up) and for large scale (top down) projects e.g. IMPC;
 - <u>Single point of entry</u> for users underpinned by common quality standards, taxonomy and procedures, global capacity and risk management, and user training.
- <u>Non-human primates</u> Unique as models of human disease; moral value plus research utility demands infrastructure for global sharing of data, models & tissues.
 - ILAR proposal for International Primate Plan demands e-infrastructure
 - Primate Portal funded by NIH; EUPRIM-Net funded by EU; poor global synergy
 - Common standards and definitions (e.g. genetic & microbiological) and sharing are crucial;
 - Genetic definition of macaques being led by China with US research partners
- <u>Challenges in securing sustainable funding</u> for bio-informatics structures and datasharing; mouse production centres, repositories and phenotyping centres; crucial to be supported by Horizon 2020;
 - Emerging similar issues for <u>zebrafish.</u>
- <u>Veto on international transport of animals</u> due to pressure on airlines and ferries by animal rights activists is a major impediment to collaboration - needs co-ordinated action globally – governments & NGOs (e.g. IATA and OIE).



Create systems for harmonisation of animal use

- Lack of global harmonisation of animal research standards and reporting impacts:
 - confidence in research outcomes using animal models
 - effectiveness of global collaborations.
- Meta-analysis of animal research data essential part of:
 - Evaluating global research outcomes
 - Validating usefulness of animal models.
 - Dependent on <u>harmonising</u> standards of performing and reporting studies.
- Infrastructures needed to deliver harmonisation of:
 - <u>Standards</u>: Experimental design and care & welfare standards vary significantly globally.
 - □ Focus on the impact of lack of harmonisation on research outcomes.
 - ILAR (2004-2012) Reviews of scientific basis for research animal housing and care standards.
 - OIE (World Organisation for Animal Health, 2010) establishing standards for 178 countries. ILAR developing Collaborating Centre status with OIE.
 - <u>Reporting</u> initiatives (ILAR, 2011 & NC3Rs' ARRIVE Guidelines, 2011) are leading to improved standards both of designing and reporting of *in vivo* experiments.



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Promote alternatives – the 3Rs (Replacement, Reduction, Refinement)

No informatics infrastructures exist for alternatives but essential for encouraging alternatives to be used wherever possible.

- Directive 2010/63/EU One of the three key objectives in reviewing use of animals in scientific procedures.
 - Reflects public concern and expectation
 - Competent authorities are obliged to consider alternatives when authorising projects – but how?

Where to focus 3Rs infrastructure?

- Need <u>science led</u> approaches focused on <u>scientific benefits</u> of developing alternatives (NC3Rs).
- Regulatory safety testing been the focus of ECVAM. Progress very slow - validation step critical.
- <u>Fundamental & Applied research</u> is the greater challenge includes >75% of animal use so potential rewards high.



Conclusions

- The following challenges need to be addressed as a priority in future EU funding strategies:
 - To develop improved infrastructures for sharing animals and animal data.
 - Focus on Mice and Non-human Primates (zebrafish)
 - Sustainable funding mechanisms
 - To create systems for harmonisation of animal use
 - Standards & Reporting focus on outcomes
 - To promote implementation of alternatives (the 3Rs)
 - Focus on fundamental and applied research

