Multicentre **P**reclinical **A**nimal **R**esearch **T**eam

WP4: Regulation and Ethics

Tasks

1. Identify relevant regulatory authorities across countries
2. Examine existing ethical approval processes across participating countries
3. Establish ethical review process for Multi-PART studies
4. Co-ordinate with WP2 Task 1 (Stroke models)
5. Explore the potential to establish a single point of contact and approval for preclinical studies
6. Explore the role of other regulatory bodies

Task 4.1 Identify relevant regulatory authorities

- Meeting with National Contact Point for UK and Kathy Ryder (HO Inspector: now on Advisory Board)

- Discussed key issues relating to project, EU directive and having common application

- UK Contact Point presented MultiPART to EC meeting where all regulatory authorities represented

Task 4.5 Potential to establish single point approval

Is there scope for multicentre animal studies to have a **single sponsor** within the EU with a single ethical application?

No – each member state (MS) is required to authorise projects within the MS, but Project Evaluation shall be performed "with a degree of detail appropriate to type of project"

Could be grounds for cooperation between authorities in multiple MS applications for the same study?

Could a single or common application for regulatory approval be developed?

Yes

Task 4.5 Potential to establish single point approval

What are the views of national and regional organisations implementing directive 2010/63/EU across Europe?

If improves scientific outcomes and performed to high welfare standards ….then positive

Possibility of "consistent authorisation" of standard procedure for single pre-clinical study across EU?

If so, what reassurances/ information are required? How can such applications be identified?

Next stage

- Requested to provide an example application to be reviewed by the EC member state meeting of National Contact Points
- Check regulation in Australia (and USA?)
- Set up remit of ethical review committee (ERC)
- Establish membership of ERC

Ethical issues

- Objective of Multi-PART is to benefit patients , but taking into consideration ethics and welfare of animals used
- Identified causes of translational failure include issues with the design and conduct of animal studies – could these have concealed issues with the models themselves?
- Choice of models has scientific and ethical implications
- Artificially separated WP4 but overlaps with most WPs

How to justify inclusion of specific models (assay + species + outcomes)?

- Starting point: models established in the consortium (WP2)
- Ideally, strong evidence base for each model included in the core set - several possibilities:
- Only include models for which there is evidence of predictivity
  - Evidence of predictivity already exists
  - Additional studies to gather such evidence
  - No evidence of lack of predictivity or construct validity is enough
- Secondary aim of multi-PART is to test models
  - Reflected in the design and statistical model
  - Validate multi-PART paradigm with interventions of known clinical effect
  - Validation carried out with candidate interventions

How to justify inclusion of specific models (assay + species + outcomes)?

- Establish distinct sets of models based on type of intervention?
- Inclusion of models using higher species – justify advantages over rodents
- Training/experience with the model – minimum period of time model has been used in a particular lab?

Scientific justification of the program

- When to put an intervention forward to a multi centre trial
- How much evidence should be available?
- How should that evidence be assessed?
  - Compulsory systematic review before every application
  - Delphi process
  - Other?