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Laboratory Animals at GSK –

- Industry is in a state of rapid change – from blockbuster to individualised medicine. Research is now exploring the inner workings of the cell
- Portfolio shift to “Biopharm-like” products up to 20% (2010-2015)
- The “Biopharm paradigm” is representative of the way biomedical science changes direction and the use of animals – species and numbers vary as new data is acquired
- Focus on cellular processes – iRNA – we are entering the cell and developing drugs that operate at the level of regulating protein mechanisms
- Understanding of how our DNA and regulation interacts with the environment – the birth of Epigenetics
- Entire animals are indispensable as we chart unknown and new scientific waters
- GSK is recoginsant of the fact that there is no replacement for these animals – we do not yet know what can be replaced.
- GSK is totally committed to Reducing and Refining – core principles

Alternatives and Replacements – Semantics?

- Research and Testing – Context?
- GSK – Between 60 and 80%of all animals are used in discovery research – we have a hypothesis of what we are seeking – the proof of which will be proven and leads to a drug. There is no alternative since there is nothing to alternate from. We can reduce and refine however but not replace – we do not yet know what to replace
- Testing encompasses the remaining use 20 to 40%.The research phase passes to development. We know what we have and there are legion opportunities for replacement, reduction and refinement – we have an overarching commitment to the 3R's in testing i.e. developing the drug for use in humans and animals.
- Globally – academia and industry the major use of animals occurs in basic (academia) and discovery (pharma) research.
- Innovation implies uncharted territory – the world of biomedical research will continue to be based on the use of animals for as long as there are unknown or novel biological processes!

GSK's commitment to the 3R's – Good Science

- We recognise that for the unforeseeable future animals are an indispensable part of our biomedical research and development effort
- We have implemented many animal free methods in development – in-vitro, in-silico, isolated organs etc.
- The challenge is to seek reduction and refinement in all areas of discovery research.
  - Use only those animals that are scientifically necessary
  - Use only those species that will respond correctly to the question being asked – avoid ethical conundrums
  - Design experiments correctly so that results are relevant, reproducible and reliable – Systematic application of Statistics before and after the study
  - Create an environment for the animal that allows it to express its behaviours in the most physiologically optimal way – reduce "noise"

GSK and the 3R's

- The GSK 3R's initiative
  - Dedicated senior management role – Gianni Dal Negro
  - Commitment at the corporate and science direction level
  - Model review underway to understand which models have been critical in project progress
  - Identify cutting edge models – the newest and most relevant
  - Challenge investigators on the choice of model/species
  - 3R's model database that ultimately will allow understanding of which models have had most impact retrospectively
  - Database will also allow access to models that have had a critical impact on project outcomes and relate this to new areas of research
  - Metrics on animal use related to discovery effort and model criticality

Replacement

- Very much in the domain of drug development – toxicology
- Plethora of methods – skin replacement, artificial cornea down to Ames test and cell cultures
- Less so in regulatory pharmacokinetics
  - Understanding of how a drug distributes and is metabolised in an animal needs just that - an entire animal
- Design however has Reduction potential - implicit here the judicious re-use of animals in Pharmacokinetic studies
- The cascade of methods used in the pathway from discovery to development has many steps that do not use animals e.g. cell based receptor binding tests, Quantitative Structure Relationships (computer modelling), In-silico Early Safety Prediction and so on.
- Non-animal models used for mechanistic purposes in support of the regulatory package are very often embraced by the Regulatory Authorities

Refinement

- Environmental enrichment
- Transgenic animals (but numbers may and have gone up)
- Imaging (studies in live animals that in some cases are not anaesthetised)
- Bioluminescence – seeing how cells migrate and congregate in live animals that do not have to be killed in order to study the same effect
- Translation – does it apply to the human condition
- In-vivo bile collection (GSK 3R's award 2009) obviates the need to surgically cannulate the bile duct

Conclusion

- GSK and other Pharma companies recognise that animals will continue to be used in discovery research.
- We seek, wherever possible, to replace these animals with scientifically valuable non-animal approaches
- The use use of animals by the Pharma Industry is not a trivial issue
- Reduction and Refinement are top priority goals for those animals that continue to be used
- We welcome initiatives such as EPAA and will continue to work towards a goal of Best Science Couple with Best Welfare.