BOS 4

Rob Hemmings preliminary comments

AZ - Modelling to guide Regulatory Guidelines and decision making during development

- M&S is important, not only in individual drug projects, but also to understand a disease area and how the Regulatory requirements determines the feasibility for clinical development of a new compound. Agree
- At what stage of development is it suitable to have industry-Regulatory interactions? Any, including pre-Phase I
  - What should be the requirements of M&S work in such a situation?
  - Is there a potential for collaboration across companies? Yes
- M&S can help guide the development of future Regulatory Guidelines in terms of suitable endpoints in clinical trials (early & late stage) and requirements for registration and label claims. Agree in principle
- How to facilitate discussions, based on M&S, between industry and Regulatory agencies regarding new Guidelines? Good question

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- High impact
  - ≠ controversy, but on reg decision
- "Design of PhIII to meet patient, regulatory and payer needs (incl claims) - population, endpoints, type of studies, comparator, sample size…"
  - What is 'conflict of interest here'? Display and critique of assumptions is critical
  - Adds objectivity to predominately subjective exercise
- Investigate feasibility - also of Conditional MA
- "We choose to focus on aortic diameter (AD), which guides the current clinical management of the disease."
  - Presume that regulatory interaction could also inform this

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- Can this be presented in a form that the regulators can understand and enter dialogue to test their own assumptions?

- Model disease and model potential effects of treatment on disease to guage effect sizes required
  - from basic pharmacology?
  - or from assumed response?

- ITF meetings / Scientific advice – perhaps both.