Pre-licensing dialogue with Regulators

Developing Countries Vaccine Manufacturers Network Symposium,
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NIBSC Functions

• Standardisation
  – Leading WHO Collaborating Centre for International Standards (60th anniversary)

• Medicines Control
  – UK OMCL for Biologicals (EU network)

• Research
  – Biologics safety and efficacy: ~ 100 pubs/yr

  Regulatory Science

• Now operating as Centre with UK MHRA
Talking to Regulators

• Early dialogue extremely important
  – Benefits to both parties – helps company get it right, regulator do a better job

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Personal Experience

- Cantab Pharma (1990) – Camb University spin out
  - Strong science/great SAB but limited resource
- Lead products: TA-HPV & DISC HSV
  - rVV carrying 4 oncogenes from HPV
  - ‘single cycle’ herpes simplex virus as vaccine and vector
- Preclinical discussions with NIBSC/MCA/FDA
  - No insurmountable barriers, but watch out for:
    - Choice/history of master cell for growing viruses
    - Threat from BSE (serum sourcing)
    - Vector instability – recombination events leading to loss of inserts/recapture of replication competency
Value of Dialogue

• Advice built into company product design at the outset:
  – Incredibly valuable – saved huge amounts of time and money and possibly the company
  – Encouraging – much less conservative views than anticipated

• Helped shaped regulatory thinking
  – What are the real risks to be weighed against benefits?
  – What can be done to mitigate risk/offer the best chance of success?
  – What does the scientific evidence tell us and what further research is needed where there are gaps?
  – How should regulation best be shaped in future?

• Helped avoid unpleasant future surprises for both parties
Dialogue through Europe

• Encouragement to approach regulatory experts as early as possible

• Formal EMA system for providing official advice from CHMP (fees)
  – Distinction between scientific and regulatory
  – Mainly written system
  – Innovation Task Force to advise on novel product types
  – Expensive but provides synthesised view of 28 member states – very valuable if you are seeing EU licensure
  – SME fee reductions
  – Can ask for parallel advice from CHMP/FDA
In the UK

• Direct advice available from MHRA/NIBSC
  – Informal (free) or formal (fees) – face to face
  – All aspects of development (regulatory, non-clinical, quality and clinical)
  – Any stage of initial development before submission of a marketing authorisation application (MAA)
  – During the pre-submission period for a variation of an existing MAA
  – Advice/help on bioassays/standards/lot release (NIBSC)
    • Collaboration on release assay transfer
  – Opportunity for joint advice with other regulators
• Also from other EU regulators – compare/contrast views
Wider Engagement

• Maintenance of contact with individual manufacturers
  – E.g. regular NIBSC meetings with vaccine companies marketing in EU – what’s ahead?
• Dialogue with trade associations
  – E.g. UK BIA/MHRA run joint conferences on topics of mutual interest
  – NIBSC-hosted 6mthly meetings with global flu vaccine producers, ERLs, WHO CCs
• General contacts and scientific discussion between regulatory and company experts
• Potential for real or perceived conflicts of interest needs to be recognised and managed carefully
Summary

- Manufacturers and regulators are ‘on the same side’
- Constructive dialogue helps both to get it right in the interests of public health
- Pre-licensing discussion, as early as possible, is hugely beneficial