Pre-licensing dialogue with Regulators

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Stephen Inglis, National Institute for Biological Standards and Control, UK

Medicines and Healthcare Products Regulatory Agency

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


NIBSC

EUROPEAN OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE FOR MEDICINAL PRODUCTS DERIVED FROM HUMAN BLOOD OR PLASMA –Finished Product

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

➢ Good regulators make good companies

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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