IP issues arising in the development of avian influenza vaccines and standardisation of vaccines

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Outline

• Introduction to influenza seed strain derivation
• Introduction to reverse genetics
• The issues encountered by NIBSC
• Update on where we are today
• Key points
Influenza seed strain derivation

• NIBSC & WHO Global influenza Surv Network
• Conventional vaccine development:
  – Reassortment in hens’ eggs
  – Prepare stock and
  – distribute for validation as seed
• Would always envisage conventional route, but may be circumstances where:
  – Does not work
  – No antigenically similar non-pathogenic strain available
  – Where it is dangerous
  – Where a quicker and less hit and miss process, generating a better controlled material is useful
• Then need to assemble antigenically relevant high growth reassortant, i.e. use Reverse Genetics
Introduction to reverse genetics

• Wild-type RNA used to clone segments:
  – HA - haemagglutinin
  – NA - neuraminidase

• Above then cloned into plasmids (HA polybasic aa motif removed apathogenic)

• Transferred to Vero cells with helper and backbone plasmids

• Infectious supernate used to inoculate eggs

• Prepare stock and

• distribute for validation as seed
Issues encountered by NIBSC

• Right to operate who owns IPRs?
  – Plasmids co-developed bet. MSSM/Oxford
  – Medimmune now holder of RG patents
  – Further IPR from St Jude
  – Wisconsin IPR?

• How do we get strains accepted by Mfrs?
  – Royalties on already low margin vaccines
  – Interpandemic use ideal (↑ familiarity)
  – Inertia without urgency, but when urgent too late?
Update on where we are today

- ✓ 22/4/03 Covenant not to sue from MedImmune (covers WHO/contractees)
- ✓ MTA from MSSM covering plasmids
- ✓ MTA agreed with MSSM to cover NIBSC sending out material derived with plasmids
- ✓ MTA from AvP covering Vero cells
- ✓ MedImmune has offered/granted licences to mfrs on a case by case basis
- ✓ NIBRG-12: H5N1 vaccine reference strain generated by reverse genetics
- Next steps: NIBSC MTAs in place with recipients
Key points

• Good co-operation received from institutes and companies alike

• Progress was slower than ideal: complex web of IPR

• Difficult to get proactive adoption of an enabling technology:
  – Who is leading effort?
  – Economic case not compelling
  – Public health justification most acute when its too late