Veterinary gene modified vaccines in the EU

Anja Holm
Danish Medicines Agency

”Genetic vaccines”
Oslo, 2008

Veterinary GMO vaccines

- Legal basis for authorisation
- Special ”double” environmental assessment
- Authorised GMO products

Legal basis for authorisation

- Regulation 726/2004, article 31 (2)+(3).
  - GMOs shall comply with Dir. 2001/18/EC.
  - Annex: Products developed by recombinant DNA technology, controlled expression of proteins, etc: Application must go via EMEA (centralised procedure).
- Directive 2001/18/EC (environmental risk assessment)
- Guidance in Notice to Applicants, March 2006: ”Guidance on environmental risk assessment…GMOs…”

(+ the normal authorisation by Dir. 2001/81/EC and 2004/28/EC, etc)

Environmental assessment

For development and research:

- the Manufacturer/Applicant must get a formal written consent for deliberate release from the Competent Authority of the Member State where the study is conducted, before start of the study.
- This consent must be included in the application dossier.

Environmental assessment

For Marketing Authorisation:

- the Applicant submits a dossier, including part II-H (environmental part) to EMEA.
- EMEA informs the Environmental Agencies in all Member States about the application.
- The Environmental Agencies can then ask EMEA for a copy of part II-H, which will be provided by the Applicant.
- Env. Agencies may send comments and questions, - these may go via a “leading” consulted Env. Agency.

Environmental assessment, cont.

- The Rapporteurs (from CVMP) of the procedure will then take such comments and questions into account in their own assessment of the environmental part and in the List of Questions.
- The Rapporteurs provide assessment of the Applicant´s responses to the questions.
- EMEA will give feedback to Env. Agencies and send Applicant´s responses and Rapporteurs´ assessment
- The final opinion is up to CVMP.
- The authorisation is given by the Commission

GMO products / Commission Decision

Product Name	Status
Suvaxyn Aujeszky 783 o/w	CD 7 August 1998
Purevax FeLV	CD 13 April 2000
(Eurifel RCP FeLV	CD 8 March 2002)
Vaxxitek HVT+IBD	CD 9 August 2002
Proteq Flu	CD 6 March 2003
Proteq Flu-Te	CD 6 March 2003
Equilis StrepE	CD 7 May 2004
Purevax RCCP FeLV	CD 23 February 2005
Purevax RCP FeLV	CD 23 February 2005

Suvaxyn Aujeszky 783 o/w

Vaccine for pigs, Pseudo-rabies:

- Live attenuated Aujeszky's disease virus
- Developed at DLO institute, The Netherlands
- Deletion of thymidine kinase gene (increases safety)
- Deletion of glycoprotein E gene (allows for differentiation between vaccinated animals and field-virus infected animals)

Purevax FeLV

Purevax RCCP FeLV
Purevax RCP FeLV
(Eurifel RCP FeLV)

Vaccines for cats, Leukaemia:

- Live recombinant canary-pox virus
  - Canary-pox: Live virus vector system
  - Does not multiply in mammals
  - Apathogenic for chickens and canaries
  - Expresses antigens from inserted genes of Feline Leukaemia Virus (Subgroup FeLV-A; env, gag and part of pol genes encoded)
  - Antibody and T-cell response against FeLV

Vaxxitek HVT+IBD

Vaccine for chicken, Mareks disease & Gumboro disease:

- Recombinant Turkey Herpes Virus expressing the VP2 gene of Infectious Bursal Disease Virus
- HVT
  - protects chickens against Mareks disease: (lymphoproliferation)
  - Does not replicate in mammals, apathogenic in all species.
- IBDV:
  - Gumboro Disease (immune suppression, diarrhoea, muscle hemorrhages), very virulent virus sub-types.
  - Early vaccination necessary (day-old chickens or eggs)
  - (Attenuated IBDV-vaccines often cause disease).

Proteq Flu

Proteq Flu-Te

Vaccine for horses, Influenza:

- 2 recombinant Canarypox virus vectors
- Expressing HA-gene from 2 different equine influenza strains
- Same vector as described above
  - Does not replicate in non-avian cell cultures, and apathogenic in chickens and canaries.

Equilis StrepE

Vaccine for horses, Strangles:

- Live streptococcus equi bacteria
- Deletion mutant strain, i.e. important gene missing
  - Needs specific media to survive
  - Replication in horses is very low

- No other Strangles vaccine is available
  - vaccines developed by normal attenuation: often unsafe
  - vaccines developed by inactivation: often inefficacious

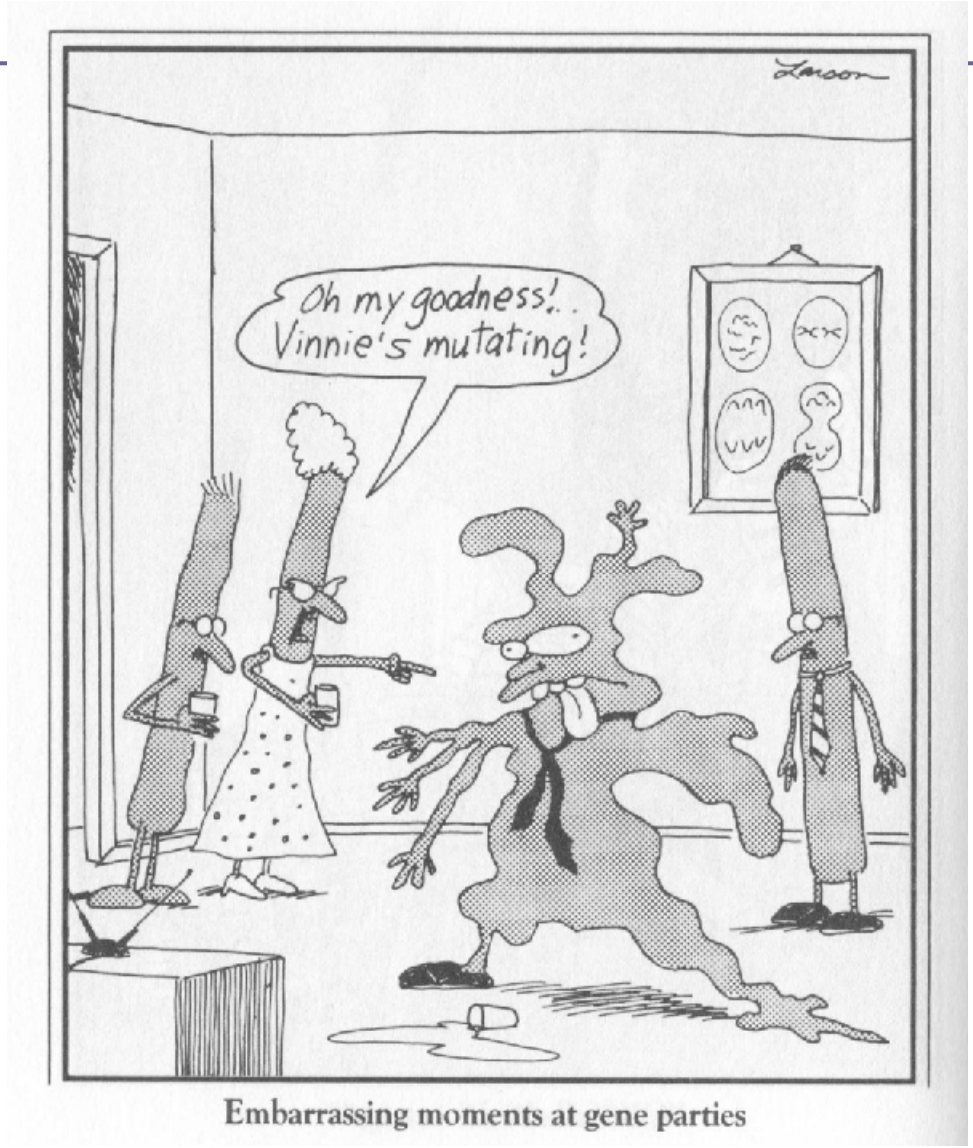
Conclusions

GMOs as veterinary medicinal products

- Strictly regulated legislative basis
- Application must go via EMEA-CVMP
- ”Double” environmental evaluation
- Several GMO-vaccines authorised for swine, chicken, horses and cats.

Note: Several other non-GMO products developed by biotechnology processes are authorised, eg. proteins or modified toxins produced in GMOs (E. coli).

Thank you for your attention



Embarrassing moments at gene parties