Outline of Risk Analysis for Veterinary Vaccines in Japan

Shigeyuki NAKAMURA, DVM, Ph.D
National Veterinary Assay Laboratory
Ministry of Agriculture, Forestry and Fisheries
1-15-1 Tokura, Kokubunji, Tokyo, 185-8511 Japan
Veterinary Drugs in Japan

Veterinary Drugs

Veterinary Medicine
- General products
- Antibiotics

Veterinary Biologics
- Diagnostic reagents
- Vaccines, toxoids, antiserums
The legal hierarchy of Pharmaceutical Affairs in Japan

- The Pharmaceutical Affairs Law (Law No. 145, Series of 1960)
- Enforcement ordinance (No. 11, Series of 1961)
- Regulatory rules for Veterinary Products (Law No. 107, Series of 2004)
- Ordinances concerning GLP, GCP, GMP, etc.
- Ministerial announcements
- Ministerial notices
- Ministerial memoranda
- Biological products standard
- National testing standard, etc.
Risk Analysis of Veterinary Vaccines from Development to Evaluation Stage
Development Stage
Marketing Approvals

Data Required for marketing approval of veterinary vaccines

- Background of vaccine
- Production protocols
- Stability
- Safety of the target animal
- Physicochemical properties
- Efficacy
- Results of clinical trials

Veterinary Vaccines
Examination
Approval
Flow from application to approval

- Application
- Pharmaceutical Council (Examination for approval)
- The Food Safety Commission (Decision of ADI)
- MHLW (Decision of MRL)
- Approval
Standards for Biological Materials

The source materials standards of biological products for animal use

1. Standards for raw materials of animal origin
   - Prohibition of the use of raw materials of animal origin contaminated with pathogenic microbes.
   - Veterinary drugs that use unprocessed internal organs of animals should be of healthy animal origin.

2. Standards for raw materials of ruminant origin
   - Prohibition of raw materials of ruminant origin sourced from countries with high BSE levels.
   - List of internal organs of ruminant origin that can be used.
   - Ruminant-origin internal organs must be processed subject to the conditions described in the OIE International Animal Health Code.
Development Stage
Marketing Approvals

Standards for materials for manufacturing
Minimum Requirements for Biological Products

Materials for live vaccines
Regulations governing the use of *embryonated eggs*
Regulations governing the use of *SPF animals*
Regulations governing the use of *cultured cells*
Regulations governing the use of *bovine serum, etc.*
Development Stage

Manufacturing business license
(Accreditation of overseas manufacturers)

The manufacturing plant of a veterinary vaccine must be in compliance with the Ministerial Ordinance on Structure and Facilities to qualify for licensing or accreditation.
Manufacturing Stage

Manufacturing in compliance with GMP
Manufacturing in compliance with the Ministerial Ordinance Concerning Handling of Veterinary Biological Products

- If microorganisms other than the active ingredient are maintained in an active state, do not store them in the final container.
- Do not ship stock solution or final bulk before confirming absence of contamination by microorganisms and confirming full loss of activation, etc.
Manufacturing Stage

Quality control tests during the manufacturing process and in products

- Extraneous virus test
- Sterility test (bacteria, fungi)
- Mycoplasma test
- Salmonella test

→ These tests are described in the Minimum Requirements for Biological Products as general test methods. Harmonization of these test methods is designated in the VICH

Required to meet Good Quality Practice (GQP)
Manufacturing Stage

National Assay

The assay is performed on each lot/batch of veterinary biological products in NVAL, according to the Provisions of the Ministerial Notice.
Distribution Stage

Reporting of adverse drug reactions

- If marketing license holders or veterinarians come to know of any adverse reactions, infections, etc., they must report them to the Minister.
- Information on adverse drug reactions and recalls is added to the database, which is open to the public on the NVAL homepage.

Required to meet GVP

Good Vigilance Practice
Distribution Stage

Drugs whose use requires prior consultation with a veterinarian

1. Poisonous drugs
2. Active drugs
3. Biologics (vaccines, sera)
4. Prescription drugs (including 1. and 2.)
5. Drugs whose use in animals is regulated
Evaluation Stage
Post-Marketing Surveillance of Drugs

Reexamination: reviewing the efficacy and safety of a new drug

Period: 6 years after initial approval
Data to be attached to a reexamination application:
  a. Results of clinical use of the drug
  b. Spontaneous adverse drug reactions
  c. Investigation of how the drug is being used overseas
  d. Literature surveys

Required to meet GPSP
Good Post-marketing Study Practice
Reevaluation: regular survey of the efficacy and safety of a drug

Period of screening work: every 5 years

Data for screening:
  a. Spontaneous adverse drug reactions
  b. Literature surveys

Required to meet GPSP
Good Post-marketing Study Practice
Risk Analysis of Veterinary Vaccines from Development to Evaluation Stage

Development
- Marketing approval
- Standards for biological materials
- Standards for materials for manufacturing
- Manufacturing business license

Manufacturing
- Manufacturing with GMP
- Quality control with GQP
- National assay

Distribution
- Reporting of adverse drug reactions with GVP
- Consultation of veterinarian

Evaluation
- Reexamination and Reevaluation with GPSP
Data-gathering, filing and provision

① Making a database of veterinary drugs, adverse effect information, responses to user complaints, acquisition of antigenic information on field epidemic strains, etc.

② Release of this available information