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# Approval process for veterinary medicinal products in Japan

**Evaluation and Organization Section,**
Planning and Coordination Division
**National Veterinary Assay Laboratory (NVAL)**

# The Law on Securing Quality, Efficacy and Safety of Products including Pharmaceuticals and Medical Devices

The title of the 'Pharmaceutical Affairs Law' was revised at 25, Nov., 2014

Article 1 (Objectives) *

- This law is intended to provide regulations required to ensure the quality, efficacy and safety of drugs, quasi-drugs, cosmetics and medical devices and to improve the public health and hygiene through necessary measures taken to promote the research and development of drugs and medical devices which are of particular importance to the medical practice.


* This English text of law is the previous text before revision.

The Law on Securing Quality, Efficacy and Safety of Products including Pharmaceuticals and Medical Devices

# Article 14*1

- A person intending to market a drug*2 , a quasi-drug*3, a cosmetic containing the ingredients designated by the Minister or a medical device*4 shall, for each product, obtain marketing approval of the Minister with respect to its marketing.

*1 This English text of law is the previous text before revision.
*2 Excluding drugs with the standards specified and designated by the Minister and in vitro diagnostic reagents specified under Article 23-2, Paragraph 1
*3 Excluding those with the standards established by the Minister
*4 Excluding general medical devices and controlled medical devices designated by the Minister pursuant to the provisions of the same paragraph

# Form for Approval application

Application for Marketing Approval

1 Name and Address of Company
2 License No. & Address of Marketing Approval Holder
3 Type of License
4 Name of Drug Product
5 Ingredients and Quantities
6 Manufacturing Method
7 Administration and dosage
8 Indications and effects
9 Condition for storage
10 Period of validity
11 Standards and Test Methods
12 Reference

# Appendixes

App. 1: Origin and background of the discovery

App. 2: Physicochemical properties

App. 3: Production protocol

App. 5: Stability

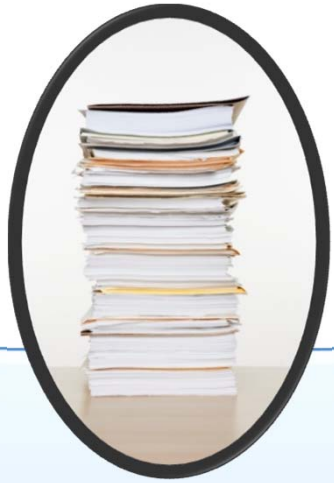
App. 6: Toxicity (acute toxicity)

App. 7: Toxicity (sub acute and chronic toxicity)

App. 8: Toxicity (special toxicity (e.g. mutagenicity, local irritation, etc.)

* App. 4 is only for Medical Device.

# Appendixes



App. 9: Target Animal Safety
App.10: Pharmacology related to efficacy
App.11: General pharmacology
App.12: ADME (absorption, distribution, metabolism and excretion)
App.14: Clinical trial
App.15: Residue for food producing animals

* App. 13 is only for Medical Device.

## Application for Marketing Approval

1 Name and Address of Company
2 License No. & Address of Marketing Approval Holder
3 Type of License
4 Name of Drug
5 Ingredients and Quantities
6 Manufacturing Method
7 Administration and dosage
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Must be attached → Appendixes

Appendix 1

# The origin and background of the development

- **Origin and background of development**
- **Condition of outbreaks and coping process in Japan**
- **Necessity of the application items**
- **Condition of use in foreign countries**
- **Adverse effect for human**
- **Public and animal hygiene (antimicrobial resistance; AMR)**

**etc.**

# VICH


- **I**nternational **C**ooperation on **H**armonisation of Technical Requirements for Registration of **V**eterinary Medicinal Products
- Trilateral (EU-Japan-USA) programme aimed at harmonising technical requirements for veterinary product registration
- To minimize the need to perform separate studies for regulatory authorities of different countries
- Final Guideline (GL) 1-54 (at July 2016)
- http://www.vichsec.org/

Appendix 2

# Physicochemical properties (VICH GL39)

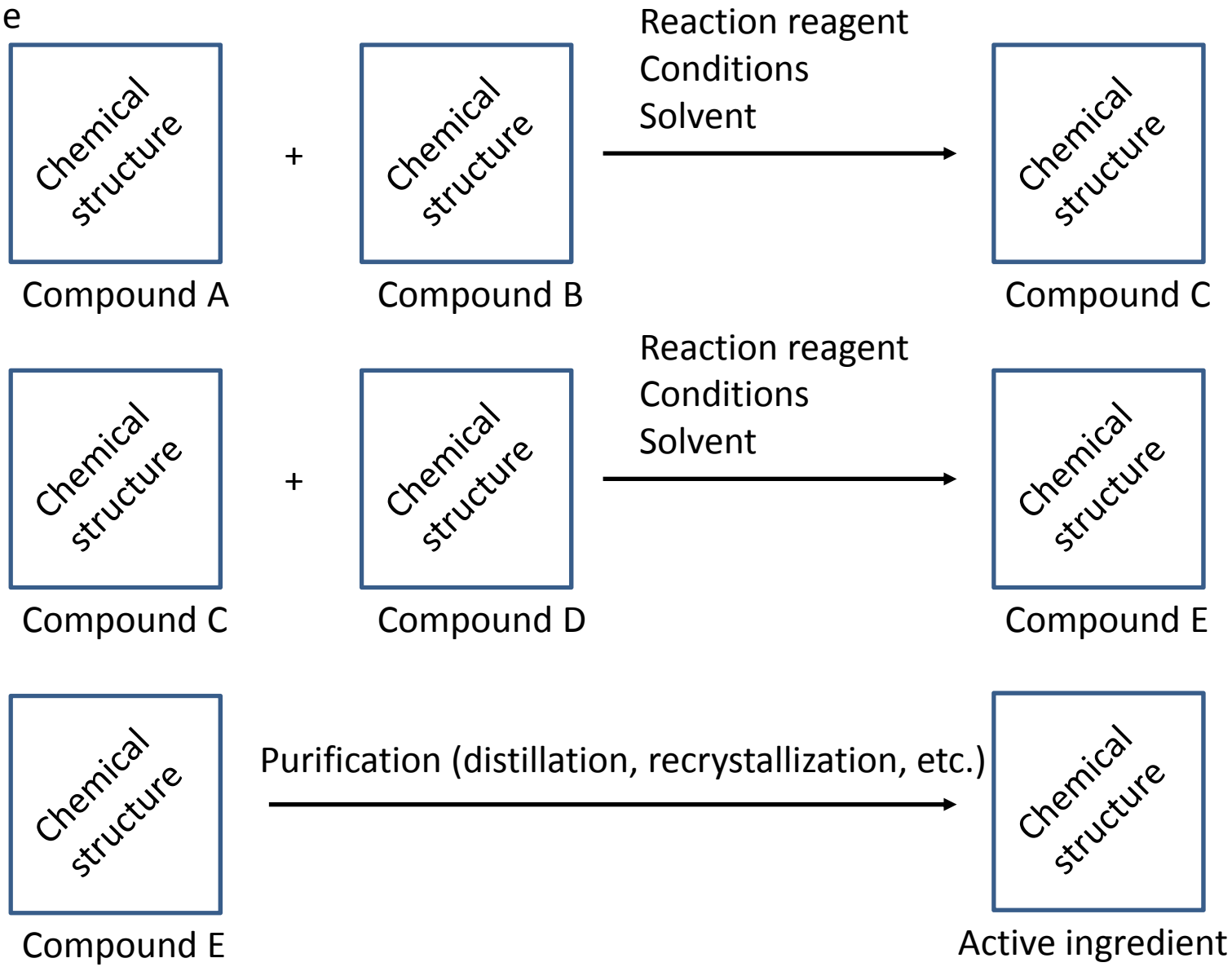
- Name of active ingredient and chemical structure
- Information of chemical structure (MS, NMR, UV, IR, optical rotation, etc.)
- Standard and test methods (active ingredient and final product)
- Evaluation of environmental impact

etc.

Appendix 3

# Production protocol -1

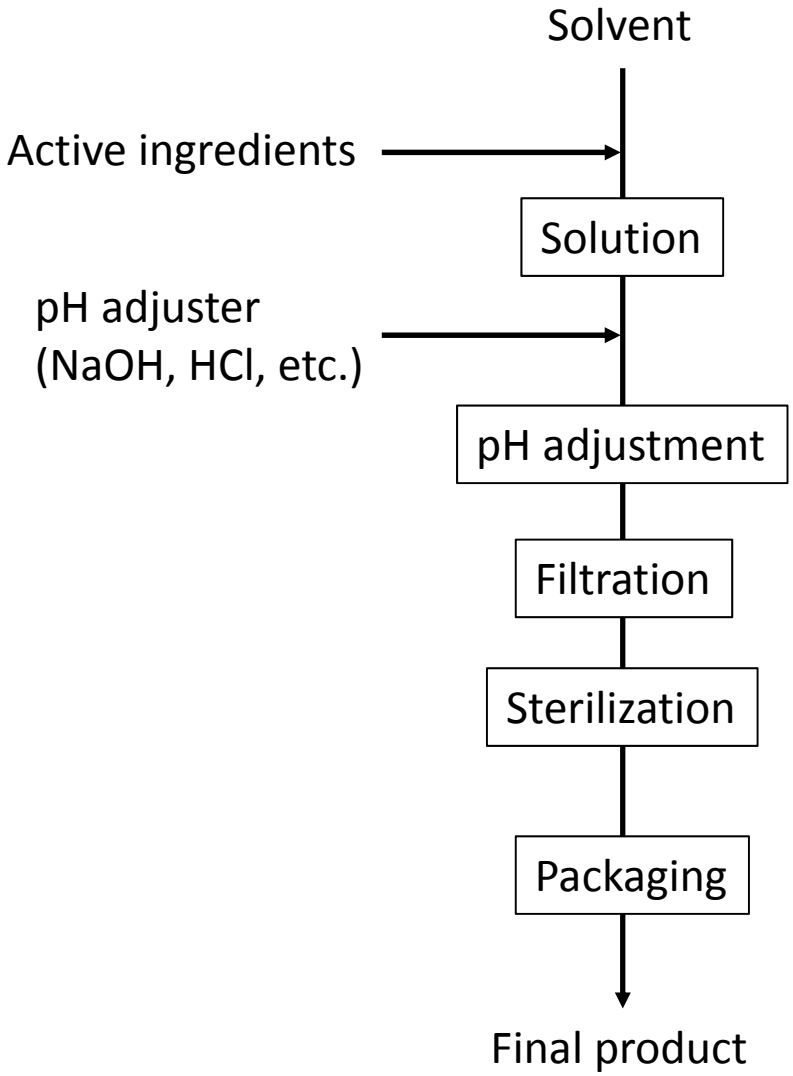
Example



Appendix 3

# Production protocol -2

Example for injectable slution



Appendix 5

# Stability

- Active ingredient

  Guideline: VICH GL3(R)

  - Long term
  - Accelerated
  - Photostability (VICH GL5)

- Final product

  Guideline: VICH GL3(R)

  - Long term
  - Accelerated
  - Photostability (VICH GL5)

- Other GLs(GL4, GL8, GL17, GL45, GL51)

Appendix 6-8

# Toxicity

- General approach to testing (VICH GL33)
- Acute toxicity
- Sub acute and chronic toxicity (VICH GL31, GL37)
- Reproduction toxicity (VICH GL22)
- Developmental toxicity (VICH GL32)
- Genotoxicity (VICH GL23)
- Additional tests if needed

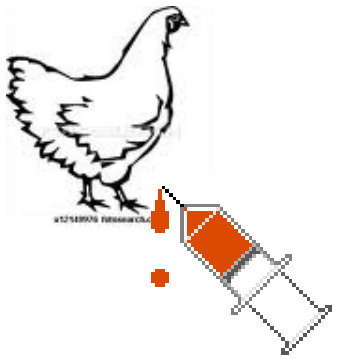
Appendix 9

# Target animal Safety test

- Objective

  - To evaluate adverse effects in target animals.

- Method: VICH GL43, 44



# Good Laboratory Practice (GLP)

- Non-clinical study (App.6-9 and 15) should be met GLP
- Target drug product ：drug product fulfilled under the following all conditions;
  - new active ingredient
  - new combination of active ingredients
  - new administration route
  - new target animal

- Outline of the assessment：
  - assess every facility
  - assess test equipments, buildings and manpower
  - assess compliance with required documents（SOP etc.），
  - record（test record, maintenance log etc.）

Appendix 10

# Efficacy

- Mechanism of action
- Minimum effective dose
- Basis of administration route and dosage

Appendix 11

# General pharmacology

Effects for

-central nervous system,

-autonomic nervous system,

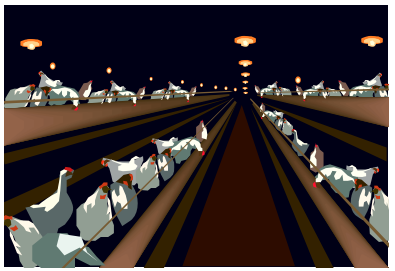
-respiratory system,

-circulatory system and

-gastrointestinal system

Appendix 14

# Clinical trial



- Objective :
  - To evaluate the efficacy and safety of the final product in the field
- Samples: Final product
- Number of test sites: More than 2 sites
- Number of Animals:
  - ≥ 200 chickens
  - ≥ 60 head for mammals
- Test period:
  - Adequate period for evaluation of efficacy and safety

# Good Clinical Practice (GCP)

- Clinical study should be met GCP
- Target drug product：drug product fulfilled under the following all conditions;
  - new active ingredient
  - new combination of active ingredients
  - new administration route
  - new target animal
- Outline of the assessment：
  - assess every facility
  - assess test equipments, buildings and manpower
  - assess compliance with required documents（SOP etc.），
  - record（test record, maintenance log etc.）

Appendix 15

# Residue for food producing animal

- Objective :
  - To evaluate the residue of active ingredient in the food producing animals when the veterinary drug product administrates with maximum dose and maximum period. This study will be used for establish of MRL and withdrawal period.
- Method: VICH GL46-49

# Council and Commission

# Council and Commission

- Article 14, paragraph 8
  - When any one of the following items is met, the Minister shall seek the opinion of Pharmaceutical Affairs and Food Sanitation Council (PAFSC) before granting the approval specified in Paragraph 1.
    - (1) …
    - (2) …
  - The expert of veterinary medicine, pharmaceutical sciences, toxicology, bacteriology, etc.


- Drugs for food producing animals
  - drug residues
    - PAFSC
  - Human health safety
    - Food Safety Commission of Cabinet Office(FSC)

# References

- VICH's website

  http://www.vichsec.org/
- NVAL's website

  http://www.maff.go.jp/nval/english/
- Food Safety Commission cabinet office's website

  http://www.fsc.go.jp/english/index.html
- MHLW's website

  http://www.mhlw.go.jp/english/index.html


Mt. FUJI from NVAL
Thank you.
Have a good trip in Japan !