

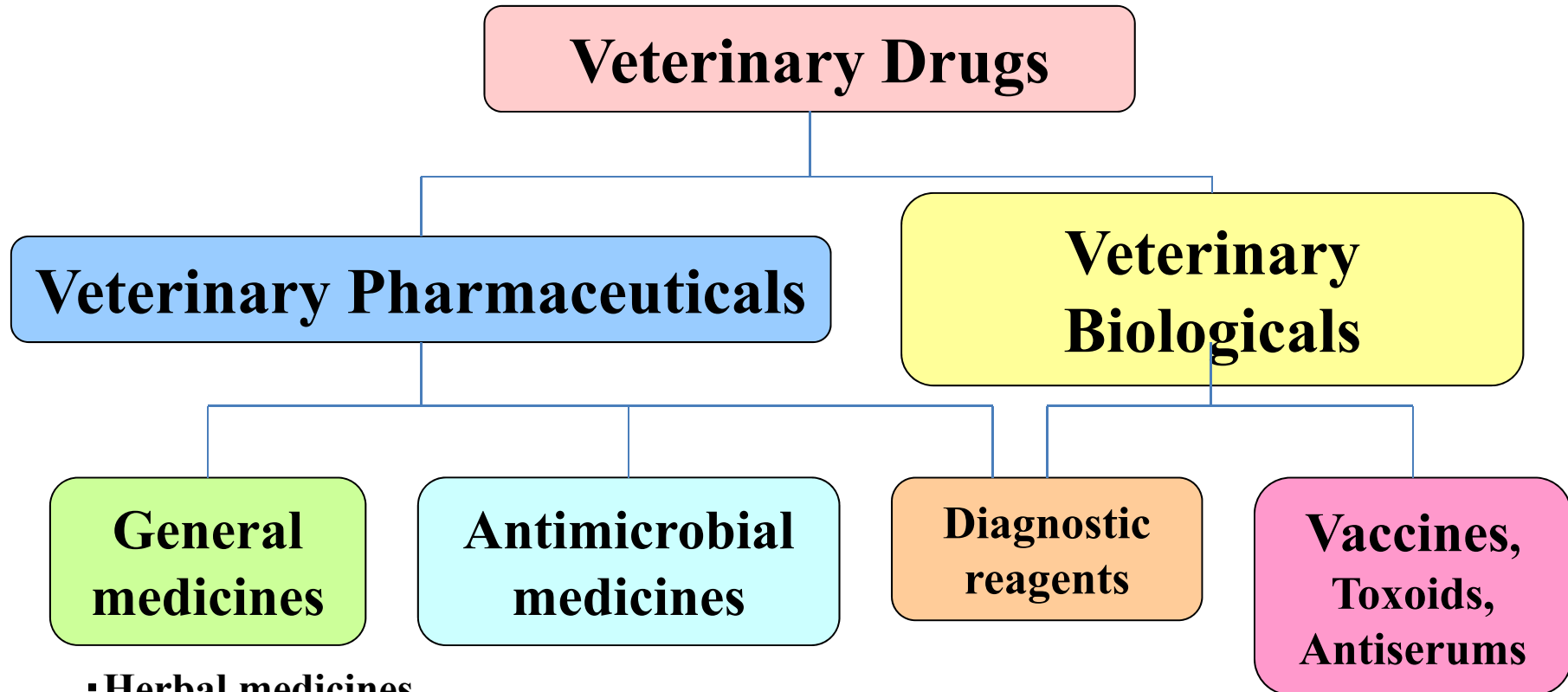


Herbal Medicine for Animal Use in JAPAN

Quality Assay Section,
Assay Division II,
National Veterinary Assay Laboratory

21 Dec. 2016

Veterinary Drugs



- Herbal medicines
- Vitamins
- Hormones
- Digestive medicines
- Anti-inflammatory agents
- Disinfectants / Antiseptics
- Pesticides for animal etc.

Risk Management of Veterinary Drugs

Pre Marketing

- Marketing Approval System

Post Marketing.

Manufacturing & Quality Control

- License of the Manufacturer
- License of the Marketing Authorization Holders

Distribution Control

- License of the Retailer
- System for Drugs Requiring Veterinary Consultation
- Prescription system

Use Control

- Restrictions on the Usage of Veterinary Drugs

Review of Marketing Approval

- Reexamination & Reevaluation
- Reporting Adverse Reactions

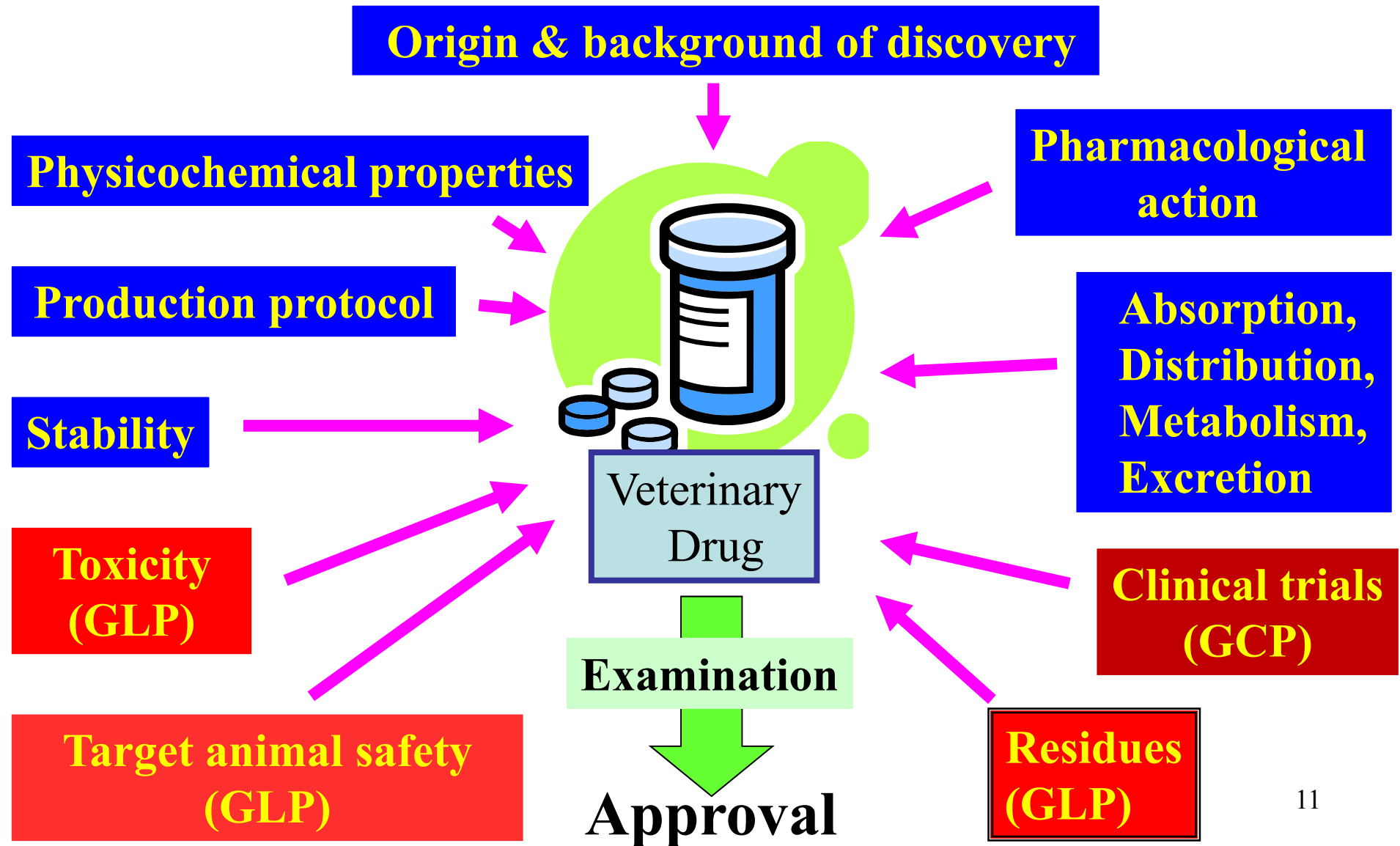
Marketing Approval System

Nobody can sell veterinary drugs without Marketing Approval.

Requirements of the approval

- ✓ License of the Marketing Authorization Holders
- ✓ License of the Manufacturer
- ✓ Management of manufacture conformed to GMP (Good Manufacturing Practice)
- ✓ Data for Marketing Approval
 - Data conformed to GLP (Good Laboratory Practice)
 - Data conformed to GCP (Good Clinical Practice)

Data Required for Marketing Approval of a Veterinary Drug in Japan



Data No.	Data category		(A) New herbal medicine	(B) New compositions	(C) New administration route	(D) New dosage/indications	(E) Generic
1	Origin & background of discovery		○	○	○	○	×
2	Physicochemical properties		○	○	△	△	○
3	Production protocol		△	△	△	△	△
5	Stability		○	○	△	△	○
6	Toxicity	Acute	△	×	×	×	×
7		Repeat (Chronic etc.)	△	×	×	×	×
8		Specific	△	△	△	×	×
9	Target animal safety		△	△	△	△	×
10	Pharmacological action	Efficacy	△	×	×	×	×
11		General	△	×	×	×	×
12	Absorption, distribution, metabolism & excretion		△	△	△	△	×
14	Clinical trial		○	○	○	○	×
15	Residue		△	△	△	△	×

(note) ○: Data must be attached

△: It shall not be necessary to attach the data

×: Data shall not be necessary to attach

Distribution Control

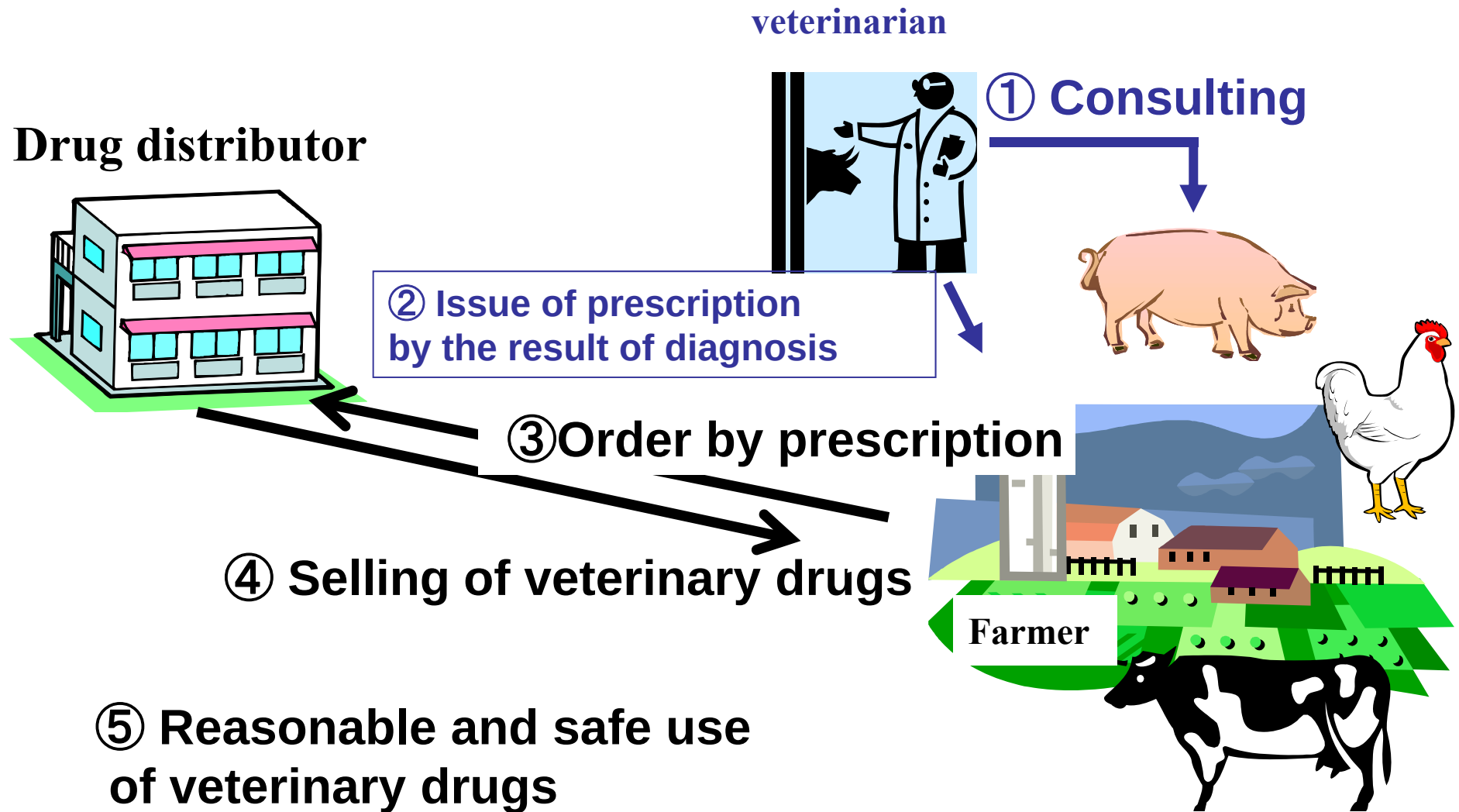
System for Drugs Requiring Veterinary Consultation

No veterinarian should provide or prescribe poisonous or powerful drugs, etc., without providing consultation by themselves.

- ① Poisonous drugs
- ② Powerful drugs
- ③ Biologics (vaccines, serums)
- ④ Prescription drugs
(Vaccines, Antimicrobial medicines, Hormonal products, etc.)
- ⑤ Drugs regulated for use on animals
(Antimicrobial medicines, Hormonal products)

Veterinary drugs used for fish is not included in this system.

Prescription System



Veterinary drugs used for fish is not included in this system.

Use Control

Restrictions on the Usage of Veterinary Drugs

Standards governing restrictions on the usage of veterinary drugs used for food-producing animals

to assure public health safety in administration of antimicrobial preparations, etc.

to meat or milk-producing animals,
poultry, fish/crustacea or bees,

to specify drugs that can be used,
and their administration, dosages, and
prohibition periods for use in the animals concerned.

Example of Standards of Restriction for Usage of Veterinary Drugs

Drugs	Target animal	Dosage	Prohibition period for use
Ampicillin (in feed)	Cattle (not more than 6 months old))	- Administrate not more than 24 mg/kg bw /day	5 days before slaughter
	Pigs	- Administrate not more than 24 mg/kg bw /day	5 days before slaughter
	Chickens	- Administrate not more than 40 mg/kg bw/day	2 days before slaughter

Ampicillin level in beef should not exceed its MRL!

Regulation of Veterinary drug Residues in Food

Marketing Approval System

- FSC : ADI (Risk assessment)
- MHLW : MRL
- MAFF : Withdrawal Period
 - **Establishment of Appropriate Withdrawal Period**

Distribution Control

- System for Drugs Requiring Veterinary Consultation
- Prescription System
 - **Appropriate Use of Drugs under the veterinarian's control.**

Use Control

- Restrictions on the Usage of Veterinary Drugs
 - **These regulations will prevent the veterinary drug over MRL from remaining in food**

Countermeasures against Antimicrobial Resistance (AMR)

Marketing Approval System

- FSC : Risk Assessment of AMR
- MAFF : Approval (included specifying method of administration, dose, precautions for use)

Distribution Control

- System for Drugs Requiring Veterinary Consultation
- Prescription System

Use Control

- Restrictions on the Usage of Veterinary Drugs

Other

- Second Choice Drug System
- Enlightenment of Prudent Use

→ **These regulations will manage AMR**

Question items : appendix_1.vaccine part

9. How many aquatic vaccines and herbal medicine have been licensed and permitted for using in Japan?

➤ Herbal medicine : about 50 products

How many batches you have to inspect aquatic vaccine and herbal medicine per year?

➤ Herbal medicine : about 0 products
(once in several years)

Question items : appendix_2 drug part

1. Are there any specified test item in veterinary drugs need to done in registration? (in various dosage forms)

➤ See VICH GL39

“Test Procedures and Acceptance Criteria for New Veterinary Drug Substances and New Medicinal Products: Chemical Substances”

(<http://www.vichsec.org/guidelines/pharmaceuticals/pharma-quality/pharma-specifications.html>)

Question items : appendix_2 drug part

2. Does endotoxin test or particulate matter test need to perform in veterinary drugs injections?

➤ See VICH GL39

Endotoxins/Pyrogens: A test procedure and acceptance criterion for endotoxins, using a procedure such as the limulus amoebocyte lysate test, should be included in the specification in accordance with regional requirements. Pyrogenicity testing may be proposed as an alternative to endotoxin testing where justified.

Japan

injection and vehicles attached to preparations, other than those exclusively for intracutaneous, subcutaneous or intramuscular administration

- See The Japanese Pharmacopoeia 17th Edition
(<https://www.pmda.go.jp/files/000213750.pdf>)

GENERAL RULES FOR PREPARATIONS

[3] Monographs for Preparations

3. Preparations for Injection

3-1. Injections

(9) Unless otherwise specified, Injections and vehicles attached to preparations other than those used exclusively for intracutaneous, subcutaneous or intramuscular administration meet the requirements of **Bacterial Endotoxins Test** <4.01>. In the case where the Bacterial Endotoxins Test <4.01> is not applicable, Pyrogen Test <4.04> may be applied instead.

Question items : appendix_2 drug part

2. Does endotoxin test or particulate matter test need to perform in veterinary drugs injections?

➤ See VICH GL39

Particulate matter: Parenteral products should have appropriate acceptance criteria for particulate matter. This will normally include acceptance criteria for visible particulates and / or clarity of solution, as well as for sub-visible particulates as appropriate.

Japan

Unless otherwise specified, Injections and vehicles attached to preparations meet the requirements of Insoluble Particulate Matter Test for Injections

- See The Japanese Pharmacopoeia 17th Edition
(<https://www.pmda.go.jp/files/000213750.pdf>)

GENERAL RULES FOR PREPARATIONS

[3] Monographs for Preparations

3. Preparations for Injection

3-1. Injections

(13) Unless otherwise specified, Injections and vehicles attached to preparations meet the requirements of **Foreign Insoluble Matter Test** for Injections

(14) Unless otherwise specified, Injections and vehicles attached to preparations meet the requirements of Insoluble **Particulate Matter Test** for Injections

Question items : appendix_2 drug part

3. Can you provide animal drug regulations about unqualified products of control and punishment?

- Nobody can sell veterinary drugs without marketing approval.
- The user must observe “Standards governing restrictions on the usage of veterinary drugs used for food-producing animals”.
- Nobody can use anything other than veterinary drugs which have been already approved to food-producing animals.
- Punishment : Penal servitude three years or less, penalty that is less than 3 million yen or both

Question items: appendix_2 drug part

4. Are there any aquatic animal drug or formulas had been approved especially for using in ornamental fish and food fish?

➤ See following site (food fish)

養殖業者の皆様へ

水産用医薬品の使用について

第29報

消費・安全局 畜水産安全管理課

http://www.maff.go.jp/j/syouan/suisan/suisan_yobo/pdf/29.pdf

➤ See following site (ornamental fish)

動物用医薬品等
データベース

● 農林水産省動物医薬品検査所トップページ
● 更新情報 ● お問い合わせ ● 検索ヘルプ

農林水産省
動物医薬品検査所

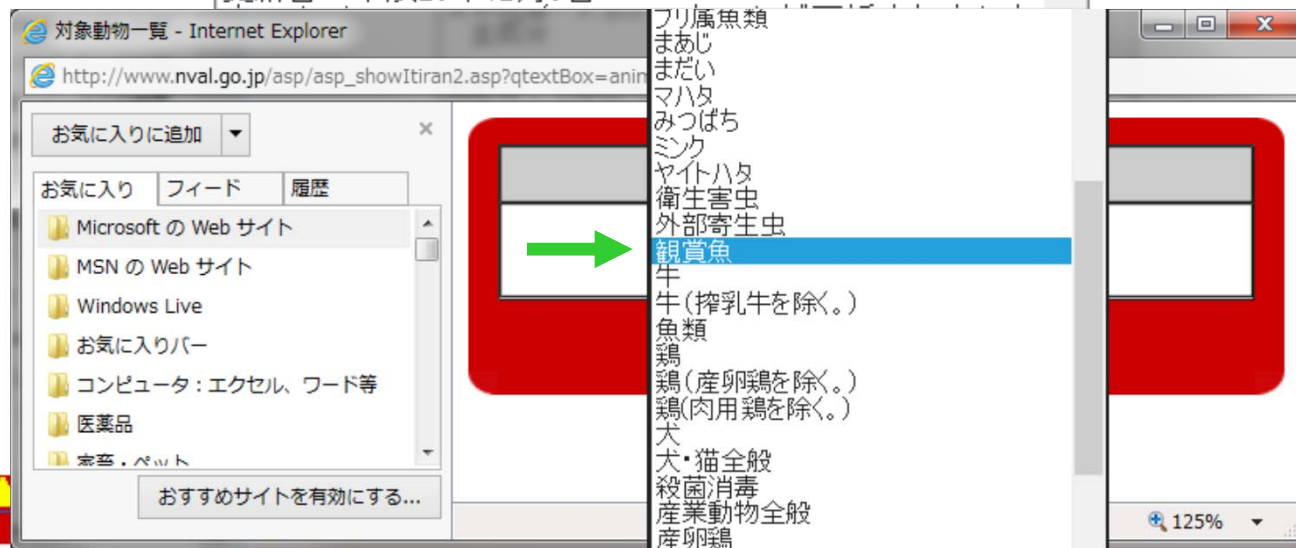
更新情報

動物用医薬品データベースが更新されました。

更新日：平成28年12月5日
AR抗原-K Bが更新されました
主成分

更新日：平成28年12月5日
ビオイムバスター錠が更新されました

更新日：平成28年12月5日



? 検索のヘルプ

以下の条件で検索

商品名称 (一覧)

製造販売業者名 (一覧)

主成分 (一覧)

対象動物 (一覧)

製剤区分 (一覧)

詳細指定をする ☐

検索条件入力に戻る

(http://www.nval.go.jp/asp/asp_dbDR_idx.asp)

Question items : appendix_2 drug part

5. Can you provide Japanese aquatic animal drug or formulas inspection standards about executing value effect, toxicological tests, and drugs residue tests etc. to us? And also, do testing fish type is object of host fish or other typical fish to do the tests?

➤ See VICH web site

(<http://www.vichsec.org/>)

➤ NVAL Home Page

(http://www.maff.go.jp/nval/hourei_tuuti/pdf/160805_betten2.pdf)

Question items : appendix_2 drug part

7. Are there any traditional medicine (like herbs or traditional Chinese medicine) already using in veterinary drugs?

How about the regulation on registration, test item or reference?

- Yes
- As stated above

Question items : appendix_2 drug part

9. Is the disinfectant for farm used outlined in animal drugs or environmental drugs?

And, does this disinfectant used for specific virus (for instant AI, ND, FMD etc.) to do killing tests?

If you do, could you provide your testing references to us?

- The disinfectant for animal farm used is outlined in animal drugs.
- usually No, if necessary Yes, but *in vitro* test only.
- We cannot provide you the data which were submitted by an applicant.

Thank you for your attention!!

