Central Administration of Pharmaceutical Products
General Administration For Stability

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FAQ on stability studies for veterinary products

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Q1: What is the reference adapted for generating stability studies of veterinary products to EDA?
A1: To generate stability data in accordance with VICH GL3, VICH GL 4, with long-term conditions compliant with VICH GL58 for Climatic Zones III/IV, to support shelf-life assignment and storage conditions.

Q2: What is a stability protocol, and when should it be submitted?
A2: A stability protocol outlines the plan for generating stability data and may be submitted before initiating studies for EDA comment.

Q3: What information should a stability protocol include?
A3:

- Product description
- Sampling plan and frequency
- Number of samples and replicates
- Storage conditions
- Container/closure system
- Analytical methods and validation data
- Other relevant tests

Q4: How should stability testing of veterinary drug substances and medicinal products be conducted with respect to the container closure system and specifications for shelf life?
A4: Stability testing should be carried out on the dosage form packaged in the container closure system proposed for marketing, including any secondary packaging and labels. A smaller or simulated system may be acceptable, but justification must be provided. Supporting studies on products outside their immediate containers or in other packaging materials can be valuable as stress testing data.
Shelf-life acceptance criteria should be derived from all available stability data. Justifiable differences may exist between release and shelf-life criteria.

Q5: Is it acceptable to have differences between release & shelf-life acceptance criteria for antimicrobial preservative content?
A5: Shelf-life acceptance criteria should be derived from consideration of all available stability information. It may be appropriate to have justifiable differences between the shelf life and release acceptance criteria based on the stability evaluation and the changes observed on storage. For example, any differences between the release and shelf-life acceptance criteria for antimicrobial preservative content should be supported by data demonstrating preservative effectiveness of a development batch of the proposed formulation artificially prepared to contain the lowest permitted levels of the antimicrobial preservative(s) according to the shelf-life specification. A single primary stability batch of the medicinal product should be tested for antimicrobial preservative effectiveness (in addition to preservative content) at the proposed shelf life for verification purposes, regardless of whether there is a difference between the release and shelf-life acceptance criteria for preservative content.

Q6: What is the purpose of stress testing a drug substance? How is it typically conducted, and what conditions should be evaluated?
A6: The primary purpose of stress testing is to gain insight into the intrinsic stability of the drug substance, identify likely degradation products, and clarify degradation pathways. This information is crucial not only for understanding the molecule's stability profile but also for validating stability-indicating analytical procedures.
Stress testing is generally performed on a single batch of the drug substance with a percentage of degradation 10%-30%. It should cover a variety of conditions that simulate severe environmental stress, including:

- Elevated temperatures: usually applied in 10°C increments above the accelerated testing condition (e.g., 50°C, 60°C, etc.).
- High humidity: e.g., ≥ 75% RH, where moisture sensitivity is a concern.
- Oxidative stress: exposure to oxidative conditions to reveal susceptibility to degradation by oxygen.
- Photolysis: exposure to light to assess photo-degradation.
- Hydrolysis: evaluation across a wide pH range when the substance is in solution or suspension. (Acid Hydrolysis-Base hydrolysis).

Q7: Why are supportive stability studies at elevated temperature and extremes of humidity may be required?

A7: Special transportation and climatic conditions outside the storage conditions recommended in this guideline should be justified based on the results from studies in accelerated conditions (i.e., short excursions out of the long-term conditions), and if necessary, be supported by additional data under more stressful conditions. For example, these data can be obtained from studies on one batch of drug product conducted for up to 3 months at 50°C/ambient humidity to cover hot and dry conditions and at 25°C/80% RH to cover extremely high humidity conditions. In case of exportation to countries in zone IVB, it is recommended that permeable containers should not be used for long-term storage of products intended to be marketed in territories with extremely high humidity conditions, such as in climatic Zone IVB, unless stability data is available to support such storage conditions.

Q8: What happens if stability cannot be demonstrated under recommended conditions?

A8: Available options:

1. Reduced retest period or shelf life
2. More protective container closure system

Q9: How should significant changes observed within the first 3 months of accelerated stability testing be addressed in case of products stored in refrigerators, and what additional studies should be added?

A9: If a significant change occurs within the first 3 months of accelerated stability testing, the concern is that the drug substance may not tolerate short-term excursions outside its proposed label storage conditions (e.g., during shipping or handling). In such cases, the guidelines require the applicant to provide a discussion explaining the impact of these excursions on product quality.

This discussion can be strengthened by conducting additional testing:

- Performed on a single batch of the drug substance.
- Conducted over a shorter duration than 3 months.
- Using a higher frequency of sampling than standard stability studies.

Q10: How should the stability of drug substances/medicinal products intended for storage in a freezer be evaluated, and what storage conditions apply?

A10: Drug substances that are intended to be stored in a freezer must undergo long-term stability testing at
-20°C ± 5°C. The duration of this testing should cover at least 12 months at the time of submission, and the data obtained from these studies form the basis for establishing the re-test period. Unlike substances stored at room temperature or under refrigeration, there is no defined accelerated storage condition for freezer-stored substances. Therefore, the re-test period is determined solely from the real-time, long-term stability data collected under the specified freezer conditions.

Q11: Under what circumstances is photostability testing required for veterinary medicinal products? What is the standard that defines photostability testing for veterinary products?

A11: The photostability characteristics should be confirmed on a single batch selected if the product is clearly photostable or photolabile. If the results of the confirmatory study are equivocal, testing of up to two additional batches should be conducted. For some products where it has been demonstrated that the immediate pack is completely impenetrable to light, such as aluminium tubes or cans, testing should normally only be conducted on directly exposed drug products. It may be appropriate to test certain products, such as infusion liquids, dermal creams, etc., to support their photostability in-use. The extent of this testing should depend on and relate to the directions for use and is left to the applicant's discretion.
Normally, the studies on drug products should be carried out in a sequential manner.
-Starting with testing the fully exposed product, then progressing as necessary to the product in the immediate pack, and then in the marketing pack.
-Testing should progress until the results demonstrate that the drug product is adequately protected from exposure to light.

Q12: When can photostability studies be waived?

A12: When it is stated in one of the officially recognized pharmacopeia that the product should be “protected from light,” in such cases, it is sufficient to state “protect from light "on labeling instead of conducting photostability studies & when the container closure system (CCS) is demonstrated to be light protective.

Q13: What is the freeze-thaw-freeze cycle stability study & when is it required?

A13: Freeze-thaw stability studies are stress tests that evaluate a drug product's ability to withstand repeated freezing and thawing cycles without degradation.
They are required for any product intended for long-term frozen storage (e.g., below -20°C) and are strongly recommended for refrigerated or temperature-sensitive products (like liquids & semisolid products) to assess risks from accidental freezing during transport or handling. The studies check for physical changes (e.g., precipitation, aggregation) and chemical stability. Freezing temperature should be 0°C (32°F) or below.
Test schedule: 0(initial).....7 days.
Reconstituted Products:
Time element and schedule will depend upon the nature of the product, active ingredient, proposed expiration date, and/or other related factors.
Example: A powder dissolved in a solvent to be held for 14 days should be tested at the recommended storage temperature (room, elevated, and/or refrigerated temperature stations) According to the following schedule: 0 (initial),3,7,11,14 days.

Q14: Is the antimicrobial effectiveness test (AET) required for veterinary medicinal products?

A14: AET is mandatory when a product contains an antimicrobial preservative, but it may also be required for preservative-free products to demonstrate that the formulation itself is capable of controlling microbial growth during its shelf life and in-use period. The requirement depends on: Dosage form, Route of administration, risk of microbial contamination, and in-use conditions.

Q15: What are criteria for the determination of Antimicrobial preservative content in a veterinary medicinal product?

A15: For oral liquid dosage forms needing an antimicrobial preservative, acceptance criteria for preservative content should be based upon the lowest specified concentration of antimicrobial preservative necessary to maintain microbiological quality of the product at all stages throughout its proposed usage and shelf-life. This should be demonstrated by using a pharmacopoeial antimicrobial preservative effectiveness test.

Q16: What is the meaning of excursion studies?

A16: Excursion studies: studies carried out to evaluate the effect of short-term deviations from labeled storage conditions.

Q17: When are excursion studies required?

A17: Excursion stability study evaluates how a pharmaceutical or sensitive product withstands short-term deviations (temperature, humidity, light) outside its labelled storage condition, often during shipping, to determine if the product remains safe & effective after these temporary stresses.

These studies support labeling claims, justifying extending shelf life after an event, and help establish action plans for real-world handling mishaps using data from accelerated studies or specific excursion labeling.

Q18: What is the appropriate In-Use Stability Studies design for Multiple-Dose Injectable Animal Drug Products?

A18: Multiple-dose injectable animal drug products have no volume limit and are often packaged in much larger containers. In addition, some animal species weigh less than humans and, thus, individual doses are often smaller than those used in humans. As such, more punctures and a longer in-use period may apply to multiple-dose injectable animal drug products compared with their human counterparts.

All multiple-dose injectable animal drug products should have an in-use statement on the labeling.

IN-USE STABILITY STUDY DESIGN

A. Testing for Chemically Preserved Products:

If the drug product contains a chemical preservative system, full stability testing should be monitored at each test interval, with the following considerations:

- Assay of the preservative should be part of the testing parameters, and the minimum preservative assay acceptance criterion should be supported by

antimicrobial effectiveness testing (AET) data at the lowest acceptable preservative concentration.

•Sterility Testing and Bacterial Endotoxins Testing are not necessary

B. Testing for Self-Preserved Products

If the drug product contains no chemical preservative(s) and is designated self-preserving, full stability testing should be monitored at each test interval, with the following considerations:

• Antimicrobial effectiveness testing (AET) should be performed at the end of the in-use period.

• Sterility Testing may be substituted for AET. If sterility testing is substituted for AET, at a minimum, there should be one-time AET data (or similar microbial challenge study data) to support the exclusion of AET during the in-use stability study.

• Bacterial Endotoxins Testing is not necessary.

Q19: How to design an in-use stability study for a multispecies dosage form in veterinary products?

A19: Multi-species Dosage Forms

-For products intended for multiple animal species, stability testing must reflect the largest container size and maximum in-use period to cover the worst-case scenario

(Is the most unfavorable or severe possible outcome of a situation considering known risks).

Q20: What are the Test Parameters of in-use stability studies?

A20: The appropriate physical, chemical, and microbial properties of the product susceptible to change during use should be monitored. The parameters tested must be appropriate to individual formulations, but examples of the types of parameters that may need to be studied are given below:

Physical: color, clarity, closure integrity, presence of particulate matter, particle size.

Chemical: active substance level(s), antimicrobial and chemical preservative level(s), degradation product level(s), pH.

Microbial: Total viable count, antimicrobial preservative efficacy: single challenge (Ph.Eur) or repeat challenge, depending on the nature of the product.

Q21: If an in-use study is required, what length is appropriate?
A21: Only one multi-dose container will be needed for the treatment; the in-use studies should cover at least the length of the treatment. The study should cover the worst-case scenario with respect to the container closure system size.
If the treatment is of definite length and the content of one multi-dose container will not suffice, or if the treatment is continuous without a defined end, the studies should cover at least the time necessary to consume the content of two containers to accommodate a situation where the patient takes doses from two containers in parallel.
If the treatment is intermittent with the dosing instruction "when needed", the in-use studies should be designed with the aim of finding the time-point where the in-use stability fails.
The study could be designed with a less than daily opening of the container.
If no relevant change is observed in the in-use study after 6 months for a product in its immediate packaging, the study does not need to be continued, and no in-use shelf life should be set.

Q22: What are the three main types of in-use labeling statements?
A22:
Time-Limited → "Use within XX days of first puncture."
Puncture-Limited → "Use within XX days and puncture a maximum of YY times."
No In-Use Restrictions → "When used as labeled, there is no limit on punctures throughout expiry**."**

Q23: Can an open dish stability study be used to assess in-use stability?
A23: Yes. Storage without the protection of the immediate container is considered (e.g., solid dosage forms) as a worst-case scenario, and can, in some instances, be used to assess the need for an in-use shelf life. If no relevant change is observed after 3 months of open dish storage, no in-use shelf life is necessary. If there are relevant changes, normal in-use studies with repeated opening and closing of the container as outlined above are required to establish an in-use shelf life. The conditions of the open dish studies should be controlled for the results to be comparable.
Open-dish studies at 30 °C/65% RH are considered to be acceptable without further justification, as constant exposure to humidity can be regarded as a worst-case scenario

Parameter	Recommendation
Study type	Open dish (uncovered)
Conditions	30 °C / 65 % RH
Minimum duration	3 months
Pass criterion	No significant change → no in-use shelf life
Fail criterion	Any relevant change → full in-use study needed

Q24: What is the maximum allowable loss on drying for premixes?
A24: 15.0% (unless otherwise justified and authorized).

Q25: How do animal drug products differ from human multiple-dose injectables?
A25: Animal products often come in larger volumes, with smaller doses per species, meaning more punctures and potentially longer in-use periods.

Q26: How should the needle gauge be selected for in-use stability studies?
A26: Use the largest gauge normally used in practice for the intended species.

Q27: What is the "theoretical maximum number of punctures"?
A27: The maximum punctures based on the smallest dose and largest container size for the labeled species.

Q28: What if the stopper cannot withstand the theoretical maximum punctures?
A28: According to FDA requirements, labeling restrictions (e.g., maximum punctures) are acceptable or recommend multi-dosing equipment.

Q29: What are the different types of veterinary pharmaceutical dosage forms that can be added to drinking water?
A29: Emulsion for drinking water use; granule for oral solution for in drinking water use; powder for oral solution for in drinking water use; concentrate for oral solution for in drinking water use; suspensions for oral solution for in drinking water use.

Q30: What excursion stability studies are recommended in the absence of an accelerated storage condition for freezer-stored substances, and why is it necessary?

A30: Since no accelerated storage condition is defined for substances stored in a freezer, applicants are required to conduct additional studies on a single batch of the drug substance at an elevated temperature (typically 5°C ± 3°C or 30°C ± 2°C) for an appropriate, shorter duration. The purpose of this testing is not to establish the long-term retest period, but to provide evidence of how the drug substance withstands short-term excursions outside its proposed label storage condition. These excursions can realistically occur during shipping, distribution, or handling before the substance reaches its destination. Such data ensure that any temporary deviations from the recommended freezer storage (e.g., exposure to refrigerated or room temperatures for limited periods) do not compromise the substance's quality, safety, or efficacy.

Q31: When is it needed to evaluate potential water loss in FPS?

A31: For aqueous-based products packaged in semi-permeable containers, water loss can be evaluated in addition to physical, chemical, biological & microbiological stability. a 5% loss of water from the initial value after the equivalent of 3 months' storage at 40°C/NMT 25% RH is considered a significant change.

A significant change in water loss alone at the accelerated storage condition does not necessitate testing at the intermediate storage condition; data should be provided to demonstrate that the medicinal product will not have significant water loss throughout the proposed shelf life.

Q32: Is it acceptable to have more than 5% water loss?

A32: Yes, exceptions may apply for small containers (1 mL or less) or unit-dose products; a water loss of 5% or more after an equivalent of 3 months storage at 40 °C may be accepted.

Q33: How can water loss at reference relative humidity be estimated if tested at a different humidity?

A33: By experimentally determining the permeation coefficient or by using a calculated ratio of water loss rates between the tested and reference humidities at the same temperature.

Q34: Should stability studies be conducted using the market container?
A34: Yes, stability must be demonstrated in the intended market container.
N.B: In Case of premixes the use of comparable containers smaller than the actual market packaging may be justified.

Q35: What container properties are required?
A35: Containers must not be reactive, additive, or absorptive and must protect the product from contamination and deterioration. (More details are mentioned in USP chapters 660,661 & 671.

Q36: Are special studies required for liquid containers?
A36: Yes, to ensure the container-closure system does not adversely affect the product. These studies evaluate compatibility, stability, and potential interactions between the liquid and its packaging:
a. Inverted/upright Stability Studies: to test the closure system's integrity
b. Water Loss Evaluation: Aqueous-based products in semi-permeable containers (e.g., plastic bottles, pouches) must be evaluated for potential water loss, often under low relative humidity conditions.
c. In-Use Stability Studies: These are required for multi-dose products to determine the storage conditions and shelf-life after the container has been opened

Q37: How do we know that one plastic container is Semipermeable?
A37: Based on ICHQ1A Stability testing of new drug substances and drug products, Semipermeable containers are defined as the following:
Containers that allow the passage of solvent, usually water, while preventing solute loss. Examples of semi-permeable containers include plastic bags and semi-rigid, low-density polyethylene (LDPE) pouches for large volume parenteral (LVPs), and LDPE ampoules, bottles, and vials.

Q38: When are new stability studies required due to container changes?
A38:
- Change in container material → new stability studies required
- Change in size/shape → case-by-case
- New container/closure

Q39: What are the acceptable references for setting the specifications for veterinary products?

A39: In stability testing, a Specification refers to the set of tests, analytical procedures, and acceptance criteria that a drug substance or medicinal product must meet to be considered of acceptable quality throughout its shelf life or re-test period. It defines the quality standards against which the product is evaluated during development, release, and stability studies.

For detailed requirements on specifications, reference should be made to:

- VICH GL39: Specifications – Test Procedures and Acceptance Criteria for New Veterinary Drug Substances and New Medicinal Products: Chemical Substances.
- Pharmacopoeia monographs, where applicable. (Please read annex I for more details)

Q40: How are impurities and degradation products in veterinary medicinal products controlled, and what thresholds apply for identification, reporting, and qualification?

A40: Impurities & degradation products in veterinary medicinal products should comply with Pharmacopoeia monographs if present or with VICH GL 10 (in case of API) & GL 11 (in case of FPP) limits should include reporting threshold, identification threshold & qualification threshold.

Q41. Which veterinary products require bacterial endotoxin testing?

A41: Bacterial endotoxin testing is required for:

- Parenteral veterinary medicinal products (injectables, infusions)

Parenteral preparations for veterinary use comply with a suitable test for pyrogenicity when the volume to be injected in a single dose is 15 ml or more, & its equivalent to a dose of 0.2 ml or more / kg body weight.

- Sterile veterinary products intended for systemic administration
- Certain ophthalmic or intrathecal preparations (if applicable)

Non-parenteral products (e.g., oral solids, topical non-sterile products) generally do not require BET, unless specifically justified.

Q42. Are there specific bacterial endotoxin limits defined only for veterinary products?

A42: No. Based on USP chapter 85, there are no separate veterinary-only numerical endotoxin limits. Veterinary products follow the same endotoxin limit principles as human medicinal products, as defined in pharmacopoeia standards, with limits calculated based on:

- Route of administration
- Maximum dose administered per kilogram body weight

Q43.Is it necessary to study both upright and inverted storage positions when conducting stability studies for liquid, semi-solid drug products?

A43: Changes in the quality of a product may occur due to the interactions between the drug substance or drug product and the respective container closure system, and the effect of such interactions on product stability should be evaluated. Any impact of container orientation on the critical quality attributes of the drug product should be assessed based on prior knowledge gained through development and/or as part of stability studies. For primary batches of liquids, solutions, semi-solids and suspensions, the product should be placed into an inverted (or horizontal) position and an upright (or vertical) position unless a worst-case orientation is justified with supporting data. However, when drug product-container closure interactions cannot be excluded; stability studies should include samples maintained in both the inverted (or horizontal) position, as well as in the upright (or vertical) position (e.g., when storage orientation can have a significant effect on the delivered dose/repriming period of pressurised metered dose inhalers).

Annex I

VICH GL 39 classifies veterinary dosage forms into solid oral medicinal products, liquid oral medicinal products, and parenterals (small and large volume). While the other classification systems of veterinary dosage forms were adopted from BP volume VI, the FDA, and EMA veterinary guidelines

Tables Index

Dosage form	Page no.
1. Herbal Drug Extracts (liquid extraction preparations, semi-solid (soft extracts and oleoresins) or solid (dry extracts) preparations obtained from Herbal drugs (1433) using suitable solvents)	**18**
2. Intrauterine Preparations (Tablets, capsules, foams, suspensions, solutions, and semi-solid intrauterine products, foams, sticks, tablets for intrauterine solution and suspension)	**18**
3. Medicated Topical Preparations (Creams, Ointments, Gels, Topical powders, Lotions, Pastes, and sticks)	**18-19**
4. Medicated veterinary Liquid preparations for cutaneous application (Non-pressurized cutaneous medicated foams, dip concentrates, shampoos, pour-on preparations, sprays, teat dips, teat sprays, udder washes, spot-on preparations, Mastitis preparations, Preparations for Irrigation)	**19**
5. Ophthalmic Preparations (Eye drops, Eye lotions, Powders for eye drops, semi-solid for eye preparation like creams and ointments, and ophthalmic inserts)	**19**
6. Oral Capsules (soft and hard gelatin capsules)	**20**
7. Oral Tablets (Boluses) (Uncoated, coated, gastro-resistant, modified-release, effervescent, dispersible, soluble, chewable, orodispersible tablets, and oral lyophilizates)	**20**

8. Parenteral Preparations (Injections, infusions, concentrates, powders for injection or infusion, gels for injection, Implants, and intravitreal preparations and intramammary infusions)	**20-21**
9. Premixes	**21**
10.Pharmaceutical Pressurized Preparation (Non-metered products like foam and metered products like aerosols, sprays, powder, solution, suspension, and inhalation products.)	**21**
11.Rectal preparations (Suppositories, rectal capsules, rectal solutions and enemas, suspensions and emulsions, foams, powders and tablets for rectal solutions or suspensions, semi-solid rectal preparations and tampons)	**22**
12.Transdermal Delivery Systems (Transdermal patches, cutaneous patches)	**22**
13.Veterinary Oral liquids preparations (solution, suspension, emulsion)	**23**
14.Veterinary Oral Powders (Soluble Powders, powder and granules for oral solution or suspension).	**23-24**
15.Veterinary Oral semi-solid preparations (pastes or gels)	**24**

Annex I – Testing parameters for the stability studies of veterinary products
Section I for Active Pharmaceutical Ingredients:

In stability studies of active pharmaceutical ingredients (APIs) for veterinary products, it is essential to evaluate parameters such as appearance, assay, and degradation products. Since certain related substances may only be detected as degradation products during stability testing, all specified impurities should be monitored throughout the study. Additionally, other characteristics of the API that could change over time should be assessed when relevant—for example, particle size distribution or polymorphic form in the case of low-solubility APIs (more details are clarified in VICH GL39).

Section II for the Finished Pharmaceutical Products:

For each dosage form, the following parameters provide guidance on the types of tests to include in stability studies for veterinary products. Appearance, assay, and degradation products should be assessed for all dosage forms, along with preservative and antioxidant content when relevant, according to VICH GL 39, VICH GL 58 & pharmacopeia requirements.
The microbiological quality of multi-dose sterile and non-sterile products must be controlled. Antimicrobial preservative tests should be conducted at least at the start and end of the shelf life. These are typically part of pharmaceutical development (e.g., primary stability studies) and do not need to be repeated in later studies unless a change (e.g. change in composition or pack) occurs that could affect microbiological safety.
It is not expected that every test be performed at each stability time point. For example, sterility testing may be limited to the beginning and end of the study period. A validated container-closure integrity test may be used instead of sterility testing. Bacterial endotoxin tests may be restricted to the time of product release. Sterile dosage forms containing dry materials (such as powders or lyophilized products) and solutions packaged in sealed glass ampoules may not require further microbiological testing beyond the initial time point. However, liquids packaged in glass containers with flexible seals or in plastic containers should be tested for microbial contamination at least at the beginning and end of the stability study. Weight loss from plastic containers should be monitored and reported throughout the shelf life.

The list of tests is not exhaustive, nor is it expected that every test be included in a stability protocol for a given veterinary finished pharmaceutical product (FPP). Finally, storage orientation (upright versus inverted) may need to be considered in the protocol when product contact with the closure system could influence stability (e.g., liquids or semisolids), or when the container-closure system has been modified.

Section III Veterinary Dosage Forms

1. Herbal Drug Extracts

Liquid extraction preparations, semi-solid (soft extracts and oleoresins) or solid (dry extracts) preparations obtained from Herbal drugs (1433) using suitable solvents.

FPS general tests include Residual Solvent, Microbiological quality and Relative density.

Specific Tests:

Volatile oil content: measure the oil volume, composition, and purity analysis.

Heavy metals: to ensure safety from toxic elements like Lead (Pb), Cadmium (Cd), Arsenic (As), and Mercury (Hg)

Aflatoxins: to detect carcinogenic molds that contaminate the herb by HPLC-MS

Ochratoxin A: a toxic mold byproduct resulting from improper drying or storage

Testing for Ochratoxin A (OTA) detected by methods like HPLC or ELISA

Pesticide residues (2.8.13): GC-MS, LC-MS

2. Intrauterine Preparations

(tablets, capsules, suspensions, solutions, and semi-solid intrauterine products, sticks, tablets for intrauterine solution and suspension)

FPS general tests include Shape, uniformity of mass- Dissolution (solid single dose), disintegration, pH -Water content/ water loss -Antimicrobial preservatives content- Sterility (for sterile products)

Specific Tests:

Hardness and friability (uncoated tablet)

Specific gravity/viscosity (intrauterine emulsions and suspensions)-

For vaginal capsule: see Ph. Eur. monograph 1164

3. Medicated Topical Preparations

(Creams, Ointments, Gels, Topical powders, Lotions, Pastes, and sticks)

FPS general tests include Appearance, Homogeneity, Color, Clarity, Uniformity of mass, Minimum fill, pH, Water content / Water loss, Freeze and thaw cycles.

Microbial limits (including total microbial count, molds and yeasts, and specified pathogens), and preservative content.
Specific Tests:
Powder fineness and Uniformity of content for single dose (for topical cutaneous powder).
Apparent viscosity (creams, ointments, gels, and pastes)
Sterility (applies to otic preparations)
Lotions (must pass suspendability tests)

4. Medicated veterinary Liquid preparations for cutaneous application (Ph. Eur. monograph 1808)
(Non-pressurized cutaneous medicated foams, dip concentrates, shampoos, pour-on and spot-on preparations, diluted preparations, teat dips, teat udder washes, Mastitis preparations, and Preparations for Irrigation
FPS general tests include Appearance, delivered dose uniformity - pH- Minimum fill -Specific gravity/ viscosity- Water content / Water loss and freeze thaw cycles, Sterility testing (applies to sterile products)- Antimicrobial preservative efficacy, antioxidant, preservative content.
Specific Tests:
Relative foam density (Medicated Foams)- Suspendability.

5. Ophthalmic Preparations
(Ph. Eur. monograph 1163)
(Eye drops, Eye lotions, Powders for eye drops, semi-solid for eye preparation like creams and ointments, and ophthalmic inserts)
FPS general tests include Appearance, color, homogeneity- Minimum fill - Specific gravity/ viscosity – Water Content/water loss- Microbial testing- Sterility - Bacterial endotoxin testing - Antimicrobial preservative content.
Specific Tests:
Globule size (ophthalmic emulsion)
Mass uniformity (Powders for eye-drops and eye lotions (single-dose)
Particle size distribution (semi-solid ophthalmic preparations, suspensions)
Suspendability (ophthalmic suspensions).
Osmolality (in case of addition of isotonic agent in the composition)
Particulate matter (ophthalmic solution)
pH (O/W cream)

6. Oral Capsules
(Soft and hard gelatin capsule)

FPS general tests include: Appearance- Color (color of both the cap and body in addition to the contents color according to the supplier)- Type of capsule (hard or soft gelatin)-Size- Visual inspection for brittleness (for hard gelatin capsules) and Leaks (for soft gelatin capsules)- Water content (when required)- Mass uniformity - Disintegration- Dissolution is required for all capsules, (N.B: For rapidly dissolving products that meet specific solubility criteria across physiological pH ranges, disintegration may substitute dissolution.) as in decision tree 7 in VICH 39-, microbial testing.

7. Oral Tablets (Boluses)
(Ph. Eur. monograph 0478)

(Uncoated, coated, gastro-resistant, modified-release, effervescent, dispersible, soluble, chewable, orodispersible tablets, and oral lyophilizates)

FPS general tests include: Physical Character, including Shape, Scoring, Biconvex/flat, color, and color of coat and core if coated. - Friability for uncoated tablets - Hardness for uncoated tablets.

Dissolution testing -Disintegration -Uniformity of mass -Uniformity of dosage units- Water content - Subdivision testing (applies to functional scored tablets)

Microbial limits (includes total aerobic microbial count, total yeast and mold count, and absence of specified pathogens)

8. Parenteral Preparations
(Injections, infusions, concentrates for injection, powders for injection or infusion, gels for injection, Implants, intravitreal preparations and intramammary infusions)

Intramammary infusions which are intended for administration to lactating animals (Lactating Cow) and those intended for administration to animals at the end of lactation or during the non-lactating period (Dry Cow) used for the prevention or treatment of infections during the dry period. Follows all quality aspects for the parenteral injections.

FPS general tests include Appearance- Clarity- Color- Visual foreign matter- Specific Gravity/Viscosity-Water content when required - Particulate matter- pH - Sterility testing - Bacterial endotoxin - Antimicrobial preservative content - Microbial testing - Antioxidant preservative content, container content for injections - Container closure integrity- Multiple insertion/withdrawal – Testing of inverted and upright position.

Specific Tests:

Particle size distribution (for injectable suspensions)
Reconstitution time, Uniformity of mass (for powders to be reconstituted)
Osmolality (when tonicity appears on labeling)
Redispersibility (for injectable suspensions that settle on storage)
Phase separation (for injectable emulsions)
Water content (For non-aqueous parenteral, and for parenteral products for reconstitution)
Syringeability (where appropriate)
Release rate, Hardness, Friability (Implants; specifically for implantable tablets, pellets, or rods to ensure they remain intact during handling while still releasing the drug correctly)

9. Premixes:

FPS general tests include Appearance, color, odor, pH, chemical identification and assay- water content, microbial quality for non-, sterile products, and content uniformity across the bulk or bagged materials

10. Pharmaceutical Pressurized Preparations

(Non-metered products like foam and metered products like aerosols, sprays, powder, solution, suspension, and inhalation products.)

FPS general tests include Sterility (required where applicable)- Dosage unit uniformity- Uniformity of delivered dose

Specific Tests:

Leak rate (for Metered dose inhalation and nasal aerosol, topical aerosols fitted with continuous valves)
Propellant analysis (for aerosols)
Pressure in canisters (for aerosols)
pH (collapsed foam)
Relative Density (Uncollapsed Foam)
Osmolality (when tonicity is declared)
Net fill weight (Aerosols, Sprays, foam)
Delivery rate (Continuous valve Aerosol products)
Water content (If applicable)
Aerodynamic particle size (Inhalation aerosol)
Particle size distribution (particle size in case of suspended solid drug or globule size in case of an emulsion)

Functionality tests include Valve Delivery and valve Corrosion (FDA)- Delivered Amount-Number of deliveries per inhaler- - Spray pattern/ Plume geometry (Shape and size of evolving spray).

11. Rectal Preparations

Rectal preparations (1145)

(suppositories, rectal capsules, rectal solutions and enemas, foams, powders, and tablets for rectal solutions or suspensions, and semi-solid rectal preparations)

FPS general tests include Appearance, Color -Homogeneity-Clarity- Visible foreign matter- Uniformity of mass (solid single-dose) -pH- Water content
Microbial limits -Antimicrobial preservative content (for multidose products and sterile single-dose products)

Specific Tests:

Dissolution (solid preparations)
Softening time (lipophilic suppositories)
Disintegration (Rectal capsules and suppositories)
Minimum fill (Rectal solutions, suspensions, and emulsions) Viscosity/Specific gravity (applies to rectal solutions)

12. Transdermal Delivery Systems (Transdermal patches, cutaneous patches)

FPS general tests include Description -Dimension Testing-Water content (Need justification to skip test)- Dissolution testing -Particle size (suspension in reservoir)-Dosage unit uniformity.

Specific Tests:

Include peel adhesion, release liner peel, tack test, cold flow test, and shear testing per manufacturer requirements.

13. Veterinary Oral Liquids preparations

(solution, suspension, emulsion)

FPS general tests include Appearance- Color- Minimum fill - Deliverable volume- pH- water loss if required- Freeze thaw cycles, microbial limits testing (Total microbial count, total mold and yeast, specified pathogens)- Antimicrobial preservative content -Antioxidant preservative content.

Specific Tests:

Visual foreign matter- Clarity- Specific gravity (Oral Solution)

Viscosity and uniformity of mass of delivered doses in case of Multidose preparations with a measuring device. (Oral suspension and emulsion)

N.B: Redispersibility and Suspendability is a specific test for oral suspension preparations.

14. Vet Oral Powders

(Soluble Powders, powder and granules for oral solution or suspension).

Veterinary Oral Powders may be in the form of soluble or wettable powders.

Required testing before reconstitution:

FPS general tests include Color- Appearance of powders or granules- Particle Size distribution- water content- Testing for drug strength (assay)

Specific Tests:

Lower and upper limits for fill weight are required; in such cases, the limits should not usually be wider than 98 - 102% of the declared weight of contents, unless otherwise justified, and bulk density for solid products that are measured volumetrically (Powders to be used in drinking water)

After Reconstitution:

Medicated Drinking Water

Oral drenches

Drenches for oral administration may be available either as powders or as concentrated solutions or suspensions. They may also appear as solutions or suspensions ready for use.

Chemical stability and physical integrity, such as the absence of caking, sticking, gross discoloration, or irreversible loss of suspension or solution of the product.

Medicated Milk replacers

For the stability of the product, recovery data should be submitted to show that the drug to be used as a milk replacer is stable in solution for the length of time stated on the label

Required testing after reconstitution includes:

FPS general tests include Color and Appearance of the solution, suspension, or dispersion after reconstitution, Specific gravity/Viscosity, pH of solution, deliverable volume, and Microbial testing (Total microbial count, Total mold and yeast, Specified pathogens)

Specific Tests:

Visual Clarity (Oral solution)

Uniformity of mass of delivered doses in multidose containers (Oral suspensions)

Completeness of solution/solubility (soluble powders)

Dispersion time /reconstitution time (dispersion and/or suspension).

15. Vet Oral Semi-Solid preparations

(pastes or gels)

They are administered to the oral cavity and are intended to be swallowed for delivery of active substances to the gastrointestinal tract.

Veterinary Oral Pastes are presented in multi-dose containers, which are designed to allow the accurate dosing of animals according to their body weight.

FPS general tests include Uniformity of mass of delivered doses- Freeze and thaw cycles, container content (syringes)- Antimicrobial effectiveness- Microbial quality of non-sterile pharmaceutical preparations- pH- Viscosity- Water content (if required).

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