Central Administration of Pharmaceutical Products
General Administration for Stability

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 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 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 aluminum 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: What is the freeze-thaw-freeze cycle stability study & when its required?

A12: 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 nature of 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.

Q13: Is the antimicrobial effectiveness test (AET) required for veterinary medicinal products?

A13: 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, In-use conditions.

Q14: What is the meaning of excursion studies?

A14: Excursion studies: studies carried out to evaluate the effect of short-term deviations from labeled storage conditions.

Q15: When are excursion studies required?

A15: Excursion stability study evaluate 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 labelling claims, justifying extending shelf life after an event, and help establishing action plans for real world –handling mishaps using data from accelerated studies or specific excursion labelling.

Q16: When photostability studies can be waived?

A16: when it is stated in one of the officially recognized pharmacopeias that the product should be “protected from light” in such cases it is sufficient to state “protect from light "on labelling in lieu of conducting photostability studies & when the container closure system (CCS) is demonstrated to be light protective.

Q17: What is the appropriate In-Use Stability Studies design for Multiple-Dose Injectable Animal Drug Products?

A17: 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 be applicable 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.

Q18: How to design in -use stability study for multispecies dosage form in veterinary products?

A18: 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).

Q19: What are the Test Parameters of in use stability studies?

A19: 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 which 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.

Q20: If an in-use study is required; what length is appropriate?

A20: 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 in respect of 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.

Q21: Can an open dish stability study be used to assess in-use stability?

A21: 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

Q22: What is the maximum allowable loss on drying for premixes?

A22: 15.0% (unless otherwise justified and authorized).

Q23: What are the three main types of in-use labeling statements?

A23:
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.”

Q24: How do animal drug products differ from human multiple-dose injectables?

A24: Animal products often come in larger volumes, with smaller doses per species, meaning more punctures and potentially longer in-use periods.

Q25: How should needle gauge be selected for in-use stability studies?

A25: Use the largest gauge normally used in practice for the intended species.

Q26: What is the “theoretical maximum number of punctures”?

A26: The maximum punctures based on the smallest dose and largest container size for the labeled species.

Q27: What if the stopper cannot withstand the theoretical maximum punctures?

A27: According to FDA requirements labeling restrictions (e.g., maximum punctures) are acceptable or recommend multi-dosing equipment.

Q28: What are the different types of medicated premixes?

A28: **Type A Medicated Article:**
The most concentrated form, a premix containing a drug intended for further mixing to make animal feed. It's not fed directly to animals. It’s used to manufacture Type B or Type C feeds.
Type B Medicated Article:
An intermediate feed made by mixing a Type A article with feed ingredients. Also not fed directly, it’s further diluted to make Type C feed. It contains a substantial quantity of nutrients including vitamins and/or minerals and/or other nutritional ingredients in an amount not less than 25 percent of the weight.
Type C Medicated Feed: The final feed product, ready to be fed directly to animals, Provides the approved therapeutic or nutritional level of medication.

Q29: What excursion stability studies are recommended in the absence of an accelerated storage condition for freezer-stored substances, and why is it necessary?

A29: 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 re-test 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.

Q30: When is it needed to evaluate potential water loss in FPS?

A30: 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 necessitates testing at the intermediate storage condition, however data should be provided to demonstrate that the medicinal product will not have significant water loss throughout the proposed shelf life.

Q31: Is it acceptable to have more than 5% water loss?

A31: 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 40C may be accepted.

Q32: How can water loss at reference relative humidity be estimated if tested at a different humidity?

A32: By experimentally determining the permeation coefficient or by using a calculated ratio of water loss rates between tested and reference humidifies at the same temperature.

Q33: Must stability studies be conducted in the market container?

A33: Yes, stability must be demonstrated in the intended market container.

Q34: What container properties are required?

A34: 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.

Q35: Are special studies required for liquid and semi solid containers?

A35: Yes. Liquids must be stored upright and inverted to evaluate interactions with

Q36: How do we know that one plastic container is Semipermeable?

A36: Based on ICHQ1A Stability testing of new drug substances and drug products Semipermeable containers 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.

Q37: When are new stability studies required due to container changes?

A37:

- Change in container material → new stability studies required
- Change in size/shape → case-by-case
- New container/closure

Q38: What are the acceptable references for setting the specifications for veterinary products?

A38: 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)

Q39: How are impurities and degradation products in veterinary medicinal products controlled, and what thresholds apply for identification, reporting, and qualification?

A39: 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.

Q40. Which veterinary products require bacterial endotoxin testing?

A40: 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.

Q41. Are there specific bacterial endotoxin limits defined only for veterinary products?

A41: 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

Q42.Is it necessary to study both upright and inverted storage positions when conducting stability studies for liquid, semi-solid, or suspension drug products?

A42: 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 pressurized metered dose inhalers).

Annex I

Requirements for Physical Analysis

File assessment for physical analysis of any dosage form will be performed according to the following tables:

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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.

1-Topical Preparations
(Creams, Ointments, Gels, Solutions, Spot-ons, Pour-ons, Topical powders, Lotions, Pastes and sticks)

Physical Character including Appearance-Homogeneity- Color -Clarity, Powder fineness (for topical powder) Content for single-dose cutaneous powders,
Uniformity of mass, Minimum fill, Apparent viscosity, pH, Water content, Freeze and thaw cycles.
Sterility (applies to otic preparations, Lotions (must pass suspendability tests), Microbial limits (including total microbial count, molds and yeasts, and specified pathogens), Preservative content must ensure microbiological quality (Acceptance criteria depend on the minimum level needed to maintain microbiological quality throughout the product's usage and shelf-life).

2-Eye 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)

Physical Character including Appearance, color, homogeneity
Minimum fill -Specific gravity/ viscosity - Globule size (ophthalmic emulsion)- Mass uniformity (Powders for eye-drops and powders for eye lotions (single-dose)- Particle size distribution (semi-solid ophthalmic preparations, suspensions) - Suspendability (ophthalmic suspensions).
Osmolality (in case of the addition of isotonic agent in the composition)-Particulate matter (ophthalmic solution)- pH (O/W cream)
Dissolution (Powder reconstituted to form sustained ophthalmic suspension)

Microbial testing- Sterility - Bacterial endotoxin testing - Antimicrobial preservative content.

3-Oral Liquids preparations (Solutions and Suspensions)

(Oral liquid, Oral suspension, Buccal solution)

Physical Character including Appearance- Clarity- Color
Viscosity -Minimum fill - Deliverable volume- Redispersibility (for suspensions to ensure proper resuspension)- Suspendability (for suspension after reconstitution)- pH - Specific gravity/ viscosity testing- Uniformity of mass of delivered doses (for Multidose oral suspensions with a measuring device)- Visual foreign matter- Freeze thaw cycles., microbial limits testing (Total microbial count, total mold and yeast, Specified pathogens)- Antimicrobial preservative content -Antioxidant preservative content.

4-Liquid preparations for cutaneous application (dip concentrate- and diluted preparations)

Liquid preparations for cutaneous application (0927).

(Non pressuerized cutaneous medicated foams, dip concentrates, shampoos, pour-on preparations, sprays, teat dips, teat sprays, udder washes, and spot-on preparations, Mastitis preparations, Preparations for Irrigation)
Physical Character including Appearance, delivered dose uniformity -Relative foam density (Medicated Foams)- Suspendability-pH- Minimum fill -Specific gravity, viscosity and freeze thaw cycles, Sterility testing (applies to sterile products)- Antimicrobial preservative efficacy, antioxidant, preservative content.

5- Parenteral Preparations

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

Physical Character including Appearance-Clarity-Color- Visual foreign matter

Specific Gravity/Viscosity- Particulate matter -Particle size distribution (for injectable suspensions)-Reconstitution time (for powders to be reconstituted)

Uniformity of mass (for reconstituted powders)- Osmolality (when tonicity appears on labelling)- pH -Redispersibility (for injectable suspensions which settle on storage) -Phase separation (for injectable emulsions)- Water content (For non-

aqueous parenteral, and for parenteral products for reconstitution)- Syringeability where appropriate ,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 containers.

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

For Implants; Hardness, Release rate, Friability.

6-Tablets

(Ph. Eur. monograph 0478)

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

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)

7-Capsules

(Oral and intrauterine capsules)

Appearance- Color (and the 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).

Mass uniformity of capsule - Disintegration testing -Dissolution testing is required for all capsules, using USP or BP monographs or an approved in-house method (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- Water content (when required), microbial testing .

8-Vet Semi Solid preparations for oral use (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 bodyweight.

Antimicrobial effectiveness- Microbial quality of non-sterile pharmaceutical preparations, pH- Dissolution- Uniformity of mass of delivered doses- Freeze and thaw cycles, container content (syringes)

9-Herbal Drug Extracts

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

Microbial Quality, heavy metals, Relative density

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

Microbiological quality, Heavy metals, Aflatoxins - Ochratoxin A - Pesticide residues (2.8.13)

10-Premixes (Feed or Water):

Medicated articles premixes, medicated feed - Products Can be pelleted forms.

Test for premixes

Physical characters of the formulation; appearance, colour, odour, Viscosity, and pH, chemical identification and assay.

LOD – moisture content, microbial quality for non-sterile products

Medicated feed products, Medicated premixes:

Testing for Moisture Content- Assay based on moisture and recovery.

Interference studies when added to multiple API

Content uniformity of the API across the (bulk or bagged materials)

Homogenity Studies- specifically for small quantities less than 75 mls is to be added to feed to make a ton, homogeneity is critical aspect.

Type B and C medicated liquid feed supplements / liquid feed supplements (LFS)

•To ensure that the drug substance is chemically stable in general in LFS matrices

•To ensure the drug substance is homogeneously distributed or positionally stable

(in general) in LFS matrices during on-site storage before and at the time of use.

Test for (LFS) Liquid feed supplement:

The physical characteristics of the formulation: Appearance, Color, Odor, viscosity if applicable , pH

The chemical characteristics of the formulation identification and assay of the active ingredient

A short freeze-thaw study for period of at least 5 days should be conducted to indicate the effect of freezing.

11-Vet Oral Powders (Soluble Powders, Medicated drinking water, Oral Drenches, Medicated milk replacers, Emulsion, granules for oral solution, powder for oral solution, concentrate for oral solution, suspensions for oral solution, for in drinking water use)

They are intended for oral administration, usually after dilution in the feed or drinking water. Veterinary Oral Powders may be in the form of soluble or wettable

powders.
Completeness of solution or dispersion- Particle Size distribution- where solid products are measured volumetrically (e.g. by means of a measuring scoop), the bulk density of the product should be controlled.

Dissolution time, in water of a specified quality, of granules, powders and suspensions should be presented. Dispersion time, in water of a specified quality, for emulsions should be presented.
Where pack sizes of the product and instructions are such that the total contents of a pack will be used in the preparation of the medicated drinking water, 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.

Soluble Powders

Medicated soluble powders testing for drug strength, moisture content, solubility (dissolution of the powder in a solvent), caking, and pH of solution.

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, 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 as a drug dosage form, 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.

Powders and Granules for Oral Solution or Suspension

Color- Appearance of powders or granules-Visual clarity (after reconstitution)

Specific gravity /Viscosity (after reconstitution)-Uniformity of mass of delivered doses (for multidose containers) - pH (applies only after reconstitution)- Deliverable volume testing for reconstituted products - Dissolution testing (dry powder or granules for resuspension dry powder or granules for resuspension)-Minimum fill-

Reconstitution time - Suspendability- Water content (For suspension after reconstitution)

Microbial testing (Total microbial count, Total mold and yeast, Specified pathogens)

12 - Rectal Preparations

Rectal preparations (1145)

(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)

Physical Character including Appearance, Color -Homogeneity-Clarity- Visible foreign matter
Uniformity of mass (solid single-dose rectal preparations)- Dissolution (required for solid preparations)- Softening time (for lipophilic suppositories) -Disintegration (Rectal capsules and suppositories)- Minimum fill (for Rectal solutions, suspensions, and emulsions) - Viscosity -Specific gravity (applies to rectal solutions)-pH- Water content
Microbial limits -Antimicrobial preservative content (for multidose products and sterile single dose products)

13 - Intrauterine Preparations

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

Physical Character including Shape, uniformity of mass- Dissolution testing (solid single-dose intrauterine preparations)-Disintegration (intrauterine tablets and capsules) -pH -Water content -Hardness and friability (uncoated tablet)-Specific gravity and viscosity (intrauterine emulsions and suspensions)-
Antimicrobial preservatives content- Sterility (for sterile products)

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

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)-Sterility (required where applicable)-Dosage unit uniformity.

Osmolality (when tonicity is declared)-Net fill weight (Aerosols, Sprays, foam)-Delivery rate (Continuous valve Aerosol products)- Valve Delivery and valve Corrosion (FDA)-Delivered Amount- Relative Density (Uncollapsed Foam)- Water content (If applicable)

Aerodynamic particle size (Inhalation aerosol)- Particle size distribution (particle size in case of suspended solid drug substance or globule size in case of an emulsion)-Number of deliveries per inhaler- Uniformity of delivered dose- Spray pattern/ Plume geometry (Shape and size of evolving spray)

15 -Transdermal Delivery Systems (Transdermal patches, cutaneous patches)

Description -Dimension testing -Additional TDS-specific tests include peel adhesion, release liner peel, tack test, cold flow test, and shear testing per manufacturer requirements.

Water content (Need justification to skip test)-Dissolution testing -Particle size (suspension in reservoir)-Dosage unit uniformity.

References

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7-VICH GL8 stability testing of medicated premixes.
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