Canadian Food Inspection Agency | Agence canadienne d'inspection des aliments

GUIDANCE FOR INDUSTRY

TESTING OF RESIDUAL MOISTURE

VICH GL 26

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VICH Canada Coordinating Secretariat
Veterinary Drugs Directorate, HPFB, Health Canada
Guidance Document

FOREWORD

This guideline has been developed by the responsible VICH Expert Working Groups. The VICH Steering Committee has endorsed this guideline and it has already been accepted by the regulatory bodies of the European Union, Japan and USA.

In adopting this VICH guideline, Government of Canada endorses the principles and practices described therein. This document should be read in conjunction with the relevant sections of other applicable guidelines.

Guidelines are meant to provide assistance to industry and health care professionals on how to comply with Government of Canada's policies and governing statutes and regulations. They also serve to provide review and compliance guidance to Government of Canada staff, thereby ensuring that the policies and guidelines are implemented in a fair, consistent and effective manner

Guidelines are administrative tools that do not have the force of law and, as such, some flexibility in approach is allowed. Alternative approaches to the principles and practices described in these documents may be acceptable provided they are supported by adequate scientific justification. Alternative approaches should be discussed in advance to avoid the possible determination through evaluations that applicable statutory or regulatory requirements have not been met.

It is important to note that Government of Canada reserves the right to request information or material, or define conditions not specifically described in this guidance, in order to allow the evaluators to adequately assess the safety, efficacy or quality of a veterinary drug. Government of Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

INTRODUCTION

1) Objective of Guideline

Freeze-dried veterinary vaccines always contain some water, commonly known as residual moisture (RM). It is important to determine the level of RM in final products, since a satisfactory test gives assurance of an adequate shelf life and that the manufacturer's freeze-dry cycle was properly controlled. The RM test should confirm that moisture level is consistently within the manufacturer's specification.

This document provides a guideline on the general requirements for residual moisture testing. The guideline leaves the flexibility for other test methods based on the specific scientific situations or characteristics of the target material. These variations must be stated in the manufacturer's production method and include equivalence data. It is recognized that the limits for the alternative equivalent assay may be different from the gravimetric assay.

2) Scope of Guideline

This guideline applies to final product testing for all freeze-dried new veterinary vaccines.

3) Background

Three common methods are generally recognized for use in determining residual moisture, these are:
- Titrimetric method, (Karl Fischer)
- Azeotropic method
- Gravimetric method.

Neither EU or USDA specify a test for residual moisture. The USA Code of Federal Regulations (9CFR 113.29) states " a suitable method used to determine the moisture content shall be described in an outline of production approved for filing by APHIS." The EU Directives/Guidelines state that each batch <of product> is tested for residual humidity and " Where applicable, the freeze-drying process is checked by a determination of water and shown to be within the limits set for the product." Japanese Standard Requirements specify the "loss on drying method."

4) General Principle

Residual moisture is determined by the gravimetric method as follows: Residual moisture is driven from the test product by heating under vacuum. The residual moisture content (as per cent) of the test product is calculated based the product weight loss during the drying cycle.

Residual Moisture Assay

1. Materials and equipment

1.1 Cylindrical weighing bottles--individually numbered with airtight glass stoppers.

1.2 Vacuum oven--equipped with validated thermometer and thermostat. A suitableair-drying device must be attached to the inlet valve.

1.3 Balance--capable of readability to 0.1 mg (rated precision ± 0.1 mg).

1.4 Desiccator--with phosphorus pentoxide, silica gel or equivalent

1.5 Sample--desiccated veterinary vaccine in original sealed vial.

2. Preparation for the test

2.1 Preparation for the test – Environment Conduct all operations in an environment with a relative humidity less than 45%.

2.2 Preparation for the test – Weighing bottles

Label the weighing bottle for sample(s). Thoroughly clean weighing bottles.

Place stopper at an angle on top of bottle and dry for a minimum of 30 minutes at 60˚ ± 3˚C under vacuum (<2.5 kPa). While hot, immediately transfer bottles and stoppers into a desiccator. Allow to cool to room temperature, close stopper, weigh and record the weights as “A”. Return bottles to desiccator.

2.3 Preparation of the sample. Retain sample, in original airtight containers at room temperature until use. Do not break the seal until ready to proceed.

3. Performance of the test

3.1 Procedure

3.1.1 Break sample container seal. Using a spatula, break up desiccated product and rapidly transfer (minimum of 100 mg or the amount required for a precise determination at the lower limit, use more than one vial for single dose products if needed) to a previously weighed bottle. Close stopper and immediately weigh. Record the weight as “B”.

3.1.2 Place the bottle with the stopper at an angle in the vacuum oven. Set vacuum to <2.5 kPa and the temperature to 60˚ ± 3˚C.

3.1.3 After a minimum of 3 hrs, turn off the vacuum pump and bleed dry air into the oven until the pressure inside of the oven is equalized with the atmosphere.

3.1.4 While the bottle is still warm, stopper bottle and transfer to desiccator, and allow to cool to room temperature (for a minimum of two hours or a time validated to yield a constant weight). Weigh, and record the weight as “C”.

4. Calculations and Results

Calculate the residual moisture (%) as ((B - C) / (B - A)) X (100)
A is tare weight of bottle.
B minus A is weight of sample before assay.
B minus C is weight equivalent to residual moisture of sample.