الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

# Testing of Residual Moisture

# VICH GL26

***Adopted from VICH***

**Version 1.0**

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**Version 1.0**

Saudi Food & Drug Authority

Drug Sector

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**Saudi Food and Drug Authority**

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## Vision

To be a leading international science-based regulator to protect and promote public health

## Mission

Protecting the community through regulations and effective controls to ensure the safety of food, drugs, medical devices, cosmetics, pesticides and feed

## Document Control

| Version | Author | Date | Comments |
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# 1. INTRODUCTION

## 1.1. 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.

## 1.2. Scope of Guideline

This guideline applies to final product testing for all freeze-dried new veterinary vaccines. Residual moisture testing is required both at the time of product release and during stability studies, as appropriate, to ensure the moisture level remains within specification throughout the product's shelf life. This is in alignment with international regulatory practices such as VICH GL10.

### 1.3. Background

Three common methods are generally recognized for use in determining residual moisture, these are:

- Titrimetric method, (Karl Fischer)
- Azeotropic method
- Gravimetric method.

### 1.4. 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 contents (as per cent) of the test product is calculated based the product weight loss during the drying cycle.

However, the guideline allows the use of other scientifically justified methods such as Karl Fischer titration or azeotropic distillation, provided they are validated and equivalence data are included in the production method.

## 2. 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 suitable airdrying 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. A commonly used drying condition is a vacuum of <2.5 kPa and a temperature of 60° ± 3°C for a minimum of 3 hours. Alternative conditions may be used if

scientifically justified and supported by validated data demonstrating equivalence in results, particularly for heat-sensitive products.

3.1.3 This approach is consistent with the flexibility allowed in VICH GL18 and EMA guidelines.

3.1.4 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.

3.1.5 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.