

BT-08

Ver 0.3

Homogeneity and cross-contamination





DOCUMENT HISTORY

Version and date of approval	Reason for revision	Revision scope	Ultimate application date
0.0 03/07/2008	Start of new GMP: new provisions	Entire document	01/01/2009
0.1 24/03/2009	Interpretation results homogeneity and explanations on methods	Point 2 Point 5.1.2 Point 5.1.3 Point 5.2.1	24/03/2009
0.2 19/12/2012	Approval of version 2.0 of the Auto-control Guide G-001: modification regarding the frequency of the homogeneity test	Point 3.1	1/01/2013
0.3 21/10/2016	New lay-out	Entire document	21/10/2016
	Modification of the designation (logo and standard)	Entire document	



Table of contents

1. INTRODUCTION	4
2. SCOPE	4
3. FREQUENCY	4
3.1. THE MEASURING OF HOMOGENEITY	4
3.2. THE MEASURING OF CROSS-CONTAMINATION.....	4
4. ANALYSES	5
5. MEASUREMENT OF HOMOGENEITY	5
5.1. GENERAL	5
5.1.1. <i>Direct methods</i>	5
5.1.2. <i>Indirect methods</i>	5
5.1.3. <i>Interpretation of results</i>	5
5.2. METHODS	6
5.2.1. <i>Methods requiring the use of a tracer</i>	6
5.2.2. <i>Method « Protein - Manganese »</i>	7
5.2.3. <i>Method « analysis of the complete spectrum »</i>	7
6. SAFETY	7



BT-08: Homogeneity and cross-contamination

1. Introduction

This document specifies the control frequency and the methods authorized for measuring the homogeneity of an installation.

Additionally, the control frequency of the cross-contamination level is determined.

2. Scope

This document is applicable to all manufacturers of animal compound feed¹ or pre-mixtures, whether or not they make use of additives (unaltered or as an ingredient in pre-mixtures).

Manufacturers of animal compound feed or pre-mixtures must also apply the following provisions when producing products with and without GMOs in one and the same production line (adapt labeling).

This document also applies to producers of additives, if the process contains a mixing step (e.g. mixing with a carrier substance).

This document is supplementary to document 'AT-08: Cross-contamination'.

3. Frequency

The terms stated in items 3.1 and 3.2 must be calculated starting from the date when the last valid test took place.

3.1. The measuring of homogeneity

A homogeneity test should be performed on each mixing installation, and minimum:

- at the activation of the installation
- at every significant change to the installation
- every 4 years.

3.2. The measuring of cross-contamination

A cross-contamination test must be realized on each manufacturing installation, and minimum:

- at activation of the installation
- at every significant modification to the installation
- every 2 years for the manufacture of additives
- every 2 years for the manufacture of pre-mixtures
- every 2 years for the use of animal feed containing GMOs and subsequent use of animal feed not containing GMOs
- every 2 years for the manufacture of animal compound feed containing additives of the antibiotics group (use only possible for productions intended for export outside the European Union)
- every 2 years for the manufacture of animal compound feed containing additives of group 4-d of the « growth promoters » (use only possible for productions intended for export outside

¹ *Animal compound feed means : complete feeding stuffs, complementary feeding stuffs, mineral feeding stuffs, milk replacer feed, molassed feed, feed supplements and any other feed material mixtures, either with or without use of additives, intended for orally administered animal feeds under the form of complete or complementary feeding stuffs.*



the European Union except for potassium diformiate) or to group 5 of the « coccidiostats and other medicinal substances » (cfr. Community Register of Additives)

- every 2 years for the manufacture of animal compound feed containing medicated pre-mixtures.
- every 4 years for the manufacture of animal compound feed², under the form of meal, pelleted feed or lick blocks, and containing additives not belonging to the group of antibiotics, growth promoters nor to the « coccidiostats and other medicinal substances ».

4. Analyses

The tracer level in the samples taken must be determined by a laboratory complying with the prescribed OVOCOM requirements (see 'BT-11: Sample-taking and analyses').

5. Measurement of homogeneity

5.1. General

The measurement of homogeneity is evaluated statistically, according to two different methods, depending on the type of method applied (TNO Report – V 4909 – 8/01/2004).

5.1.1. Direct methods

The methods based on the counting of particles (Microtracer F or FSS) leading to a series of results analyzed as Poisson distributions, whereby the homogeneity is expressed in terms of probability (p).

Are considered as direct methods:

- Method with tracer Micro tracer F
- Method with tracer Micro tracer FSS

5.1.2. Indirect methods

These methods are based on the determination of a concentration (cobalt, Micro tracer RF Lake Blue, additive (Salinomycin-Sodium, « protein – manganese » and « complete spectrum »). The series of results are analyzed as being normal distributions, whereby the homogeneity is given by the coefficient of variation « CV ».

Are considered as indirect methods:

- Method with tracer Micro tracer RF Lake Blue
- Method with cobalt tracer
- Method with tracer composed of an additive (Salinomycin)
- Method « protein – manganese »
- Method « analysis of the complete spectrum »

5.1.3. Interpretation of results

Depending on the method used, the results should be interpreted either based on table 1 or on table 2.

² This cross-contamination test does not relate to the installations intended for the manufacture of granule mixtures or all-mash.

Direct methods	Assessment
Probability p	
$p \leq 1\%$	Unsatisfactory.
$1\% < p < 5\%$	No unambiguous statistical result. It is recommended to do the test again.
$5\% \leq p$	Good homogeneity.

Table 1: Determination of homogeneity with direct methods – Action limits

Indirect methods	Assessment
Coefficient of variation CV	
$CV \leq 8\%$	Good homogeneity
$8\% < CV < 12\%$	Acceptable homogeneity
$12\% \leq CV$	Insufficient

Table 2: Determination of homogeneity with indirect methods – Action limits

Whereby the homogeneity of the mixture is considered as insufficient, the the ~~GMP-certified~~ company certified for FCA must:

- Draft an internal report relating to:
 - The probable cause(s)
 - The measures taken
- Have performed a new homogeneity test in order to verify that the measures taken will lead to a good homogeneity.

5.2. Methods

5.2.1. Methods requiring the use of a tracer

The measuring methods implementing a tracer (Cobalt, Micro tracer or Salinomycin) are described in document 'AT-08: Cross-contamination'.

In the case where the homogeneity measuring is not done simultaneously with the cross-contamination measuring, the company will be allowed to replace the Cobalt-tracer by a selected trace element (concentration ≥ 100 ppm) of his choice.

In case of cross-contamination measuring with Micro tracer F and FSS (direct method), the calculation of homogeneity is described in document 'AT-08: Cross-contamination'.

For the methods with an additive (Salinomycin or other), Micro tracer RF or with cobalt, the homogeneity is determined by way of the coefficient of variation (indirect method).



5.2.2. Method « Protein - Manganese »

This method is described in document 'AT-08: Cross-contamination'.

One calculates the homogeneity by taking 10 samples of the manganese-rich mixture by analyzing them on their manganese level.

The homogeneity of the mixture is given by the coefficient of variation.

5.2.3. Method « analysis of the complete spectrum »

This method is applicable only to the measuring of the homogeneity of the following manufactures:

- all-mash
- mixture of minimum two unaltered ingredients
- mixture of granules showing different characteristics

« Complete spectrum », means: the analyses of the levels of crude protein, crude fiber and crude ash. These analyses are performed e.g. by means of the NIR-method (*Near Infra Red*).

The company must take 10 samples in the animal feed flow, at a level determined by the company, but situated after the mixing equipment. Sampling must take place at regular intervals, over the whole duration of the emptying of the installation.

It should be taken into account an increasing phenomenon of demixing arising from the mixer and up to the output of the installation (bagging, loading of bulk wagon, and even the unloading of the wagon).

The homogeneity of the mixture is given by the coefficient of variation.

6. Safety

The control procedure is usually carried out under practical circumstances in the company. For those who carry out the control procedure in a company (operators), the following safety rules apply:

- The operators must be made aware, before the start of the activities, of the safety instructions which are applicable within the company;
- During their stay in the company, the operators are bound to follow the safety instructions of the company;
- In case where use is made of a cobalt tracer, protective gloves and a respiratory protector in the form of a nose covering must be worn.