Ceva Santé Animale	Rabitec	03/2021

Rabitec

Report on viral titer stability testing in field conditions

2F.2.3 Short-term stability studies/ stress tests

Short-term stress tests on the vaccine embedded in baits were done to cover the conditions during distribution of the baits (transport, storage short before distribution and climatic condition in the field).

Two commonly used climatic conditions (+25°C and +40°C) were chosen.

Results:

The results of the stress test are given in Table 2F.7 and Table 2F.8 .

2F.2.3.1 Stress (accelerated) test at +25°C

Table 2F.1: Virus titre of vaccine in baits, stored at +25°C for 7 days

Batch no	VM 0010814-A	VM 0020814-A	VM 0030814-A	VM 0030814-B
Storage time	Virus titre requirement: ≥ $10^{6.6}$ FFU/ml			
0	$10^{6.6}$	$10^{6.7}$	$10^{7.0}$	$10^{7.1}$
1 day	$10^{6.8}$	$10^{7.0}$	$10^{7.4}$	$10^{7.3}$
2 days	$10^{6.8}$	$10^{7.2}$	$10^{7.4}$	$10^{7.3}$
3 days	$10^{6.4}$	$10^{6.7}$	$10^{6.9}$	$10^{6.8}$
4 days	$10^{6.6}$	$10^{7.1}$	$10^{7.2}$	$10^{7.1}$
5 days	$10^{6.6}$	$10^{7.0}$	$10^{7.1}$	$10^{6.9}$
7 days	$10^{6.4}$	$10^{6.7}$	$10^{6.8}$	$10^{6.6}$

2F.2.3.2 Stress (accelerated) test at +40°C

Table 2F.2: Virus titre of vaccine in baits, stored at +40°C for 7 days

Batch no	VM 0010814-A	VM 0020814-A	VM 0030814-A	VM 0030814-B
Storage time	Virus titre requirement: ⩾ $10^{6.6}$ FFU/ml			
0	$10^{6.6}$	$10^{6.7}$	$10^{7.0}$	$10^{7.1}$
1 day	$10^{6.7}$	$10^{6.7}$	$10^{7.4}$	$10^{7.2}$
2 days	$10^{6.5}$	$10^{6.8}$	$10^{7.1}$	$10^{7.2}$
3 days	$10^{4.7}$	$10^{4.7}$	$10^{5.4}$	$10^{5.6}$
4 days	$10^{4.9}$	$10^{4.7}$	$10^{5.7}$	$10^{5.6}$
5 days	$10^{4.5}$	$10^{4.5}$	$10^{5.3}$	$10^{5.2}$
7 days	$10^{4.8}$	$10^{4.7}$	$10^{5.7}$	$10^{5.5}$

2F.2.3.3 Stress test (accelerated) at +25 °C after different storage conditions before stress test

Stability data supporting the intermediate storage for up to 7 days at 2-8°C is provided for 3 batches.
These 3 batches were first stored at -20°C.
After thawing they were stored for 7 days at 2-8°C followed by 5 days at 25°C.
The maximum loss in virus titre between thawing (study day 0) and end of the study (study day 12) was 0.1 FFU/ml (batch VM 0110616_A). However, this can be considered to be caused by the normal variation of the titration method.
The stability data about the combined storage at 2-8°C and 25°C is shown in the table below.

Table 2F.9: Virus titer (FFU/ml) of 3 batches stored at 2-8°C followed by stress test at 25°C

Temperature	-20°C	2-8°C	25°C	
Study Day	0	7	0	5
Cumulated Duration	**0**	**7**		**12**
VM 0030814-A (30 months at ≤ -18°C)	7.0	7.1		7.2
VM 0050616-A (7 months at ≤ -18°C)	7.2	7.0		7.1
VM 0110616-A (5 months at ≤ -18°C	7.0	6.9		7.1

Summary and conclusion:

The stability test results of the vaccine baits stored under stressed conditions at a temperature of 25°C for seven days demonstrate that the finished product remains stable and in accordance with the product specification.

The stability study of the vaccine stored at extreme stressed conditions (+40°C) shows that the vaccine can be exposed to high temperatures for some hours without appreciable loss of the minimum effective virus titre.

The combi test demonstrates that the vaccine is also stable and can be used if stored for 7 days at 2-8°C (e.g. during transport and time of bait distribution) followed by 5 days stress at 25°C.