CIPAC MT46 STATUS REPORT

16/09/2020

MT 46 ACCELERATED STORAGE PROCEDURE

Allocated to DAPF

CIPAC methods published in:

CIPAC Handbook J p128ff (MT 46.3)

CIPAC 58th meeting, June 2014 in Liège

Mr Pigeon presented the results of a small scale collaborative study for the extension of CIPAC MT method MT 46.3, accelerated storage procedure to include sample preparation details for LN formulations.
4 laboratories participated and two samples of different LN products were provided:
Olyset®: Permethrin 20 g/kg incorporated LN, [WHO specification 331/LN (April 2014)]. The WHO specification for this product provides clauses for accelerated storage after 2 weeks at 54°C.
PermaNet® 2.0: Deltamethrin 1.4 g/kg coated LN [WHO specification 333/LN/1 (NETTING & NET) (July 2013)]. The WHO specification for this product provides clauses for accelerated storage after 8 weeks at 40 °C.
Each laboratory was asked to apply the following procedure:

- Carry out the accelerated storage according to the extension of CIPAC method MT 46.3 to LN.
    - Fold carefully once or twice in each direction 6 pieces of 25 cm x 25cm of LN, roll them, and put in a 1 L glass bottle
    - Fit the polyethylene insert into the cap, tightly seal the bottle, and keep it in an oven at the specified temperature and for the defined period of time
    - Remove the bottle from the oven and allow it to reach room temperature.
- Perform the test in duplicate (replicates 1 and 2).
- Determine (for each replicate) the wash resistance index using the CIPAC MT 195 and the relevant CIPAC methods for a.i. content
    - on the unstored net (before accelerated storage)
    - on the net after accelerated storage.

The following comments were received from the laboratories:
Laboratory 1: Deviations from the CIPAC analytical methods for active ingredient content for PermaNet® 2.0: extraction with 24 ml solvent instead of 14 ml, adaptation of the calibration curve, Phenomenex Luna CN, 5 µm, 250 mm x 4.6 mm instead of Lichrosorb Si60, 5 µm, 150 mm x 4.6 mm for the HPLC column, internal standard calibration.
Laboratory 2: Deviations from the CIPAC analytical methods for active ingredient content for Olyset® : extraction by refluxing with xylene, reconstitution with n-hexane and 1,4-dioxane (95:5, v/v) as mobile phase and determination by HPLC-DAD using deltamethrin as internal standard.
For PermaNet® 2.0 : extraction with n-hexane and 1,4-dioxane (95:5, v/v) and determination by HPLC-DAD using dibutyl phthalate as internal standard.
Laboratory 3: Folded carefully once in each direction 6 pieces of 25 cm × 25 cm of LN, rolled them, and put in a 1 L glass bottle.
Deviations from the CIPAC analytical methods for active ingredient content for PermaNet® 2.0: the mobile phase and the extraction solvent were substituted to tetrahydrofuran due to hazard classification of original solvent in the country of the laboratory. As it would be well suitable for LN to use IS-LC method to reduce the extraction error, CIPAC method 333/LN/(M)/3 was modified to the IS-LC method.
The result of the small scale trial showed:

- Mean active ingredient content of LNs after accelerated storage in good agreement in all labs and complies with the limits of the WHO specifications.
- RSD of the active ingredient content in the 3 net pieces analysed individually after accelerated storage was not significantly different from those measured before storage and was always lower than the maximum limit of 20% recommended by WHO.
- Wash resistance index after accelerated storage does not significantly differ from that measured before storage and still complies with the limit of the WHO specifications.
- These results confirm the applicability of the extension of the CIPAC method MT 46.3

(accelerated storage procedure) to LNs.
- Further confirmation of the performance of the CIPAC method MT 195.
- Mr Pigeon proposed to adopt the extension of MT 46.3 to LN as full CIPAC method called MT 46.3.4.

The following comments were received from the meeting:
- Is the method restricted to storing the samples in glass bottles or can we also use the sales pack? For ambient shelf-life studies the product has to be stored in the sales pack so we would prefer to be able to use the sales pack for accelerated storage too. Mr Pigeon replied that the method clarified that only glass bottles (inert) should be used to avoid any interaction between the net and the packaging. The first principle of accelerated storage studies according to the CIPAC method is to use an inert glass bottle. He agreed that for ambient studies for registration purposes the study should be performed in the sales pack but for accelerated the glass bottle is preferred.
- If the glass bottles have a screw cap and are air tight then the atmosphere in the bottle will reach saturation point so this will not reflect real conditions. Do we have to use glass bottles? Mr Pigeon replied that the purpose of the method is to standardise conditions and tests as much as possible for use in quality control.

Decision: The extension of the scope (CIPAC/4956) of CIPAC method MT 46.3 for the accelerated storage procedure of the LN formulations regarding determination of active ingredient content and retention index was accepted as a **provisional** CIPAC MT method..

CIPAC 59th meeting, June 2015 in Athens

At the 58th meeting, 2014 in Liège the method was adopted as provisional. No further comments were received.

Decision: The method can be promoted to a **full CIPAC method**.

CIPAC 60th meeting, June 2016 in Tokyo

Extension (applicability) of MT 46.3 to matrix release formulation by Mr Takashi Sasaki (5045, 5046)
Mr Sasaki presented a small scale collaborative trial on the extension of the CIPAC method MT 46.3 to MR formulation. This method is an extension to MR of the existing CIPAC method MT 46.3.1 Liquid formulations, MT 46.3.2 Solid formulations, MT 46.3.3 Solid formulations stored under pressure and MT 46.3.4 LN formulation for the accelerated storage procedure. The trial involved the testing of three different MRs (MR-Green, MR-Red, and MR-White).
The parameters tested show that:
- The mean pyriproxyfen content of pyriproxyfen MR after accelerated storage does not significantly differ from the content before storage and complies with the limit of the WHO specifications.
- The relative standard deviation (RSD) of the pyriproxyfen content in the 3 pieces of pyriproxyfen MR analysed individually after accelerated storage is not significantly different from the RSD before storage and unquestionably low.
- The pyriproxyfen retention rate after accelerated storage does not significantly differs from the retention rate before storage and complies with the limit of the WHO specifications.
These results confirm the applicability of the extension of the CIPAC method MT 46.3 (accelerated storage procedure) to MR. Mr Sasaki proposed that this method extension would be adopted as a full CIPAC method.

The following comments were received from the meeting:

- ➢ Why Al foil is used in the trial, is it really needed?
- ➢ How are the results affected by the use of Al foil?
  The answer was that it was easier to handle the sample if it was wrapped in the Al foil, as the formulation is very solid and difficult to cut. The active ingredient would be adsorbed less on Al foil than on the plastic bag.
- ➢ In CIPAC MT 46.3 the sample is placed in a glass bottle, why Al is used? The answer was that they did not want to cut the product.
- ➢ The objective was to check the storage stability in an inert container. The commercial package is still not available.
- ➢ How they checked that the extraction was complete?
- ➢ All the checked samples were too good if it is possible also a weaker formulation is needed for the tests.
- ➢ Several extensions of the methods are published in different handbooks (MT 46.1; 46.2; 46.3 etc.) it is difficult to handle them.

Closed Meeting:
Several extensions of the methods are published in different handbooks (MT 46.1; 46.2; 46.3 etc.) it is difficult to handle them. It was proposed to revise the old method and to include in it the MR method.
It was decided that Mr Pigeon will make a comparison of the existing variants of the MT 46.3 and the proposed decision will be communicated to the Company.
The method was accepted as a tentative CIPAC MT method.

CIPAC 61th meeting, June 2017 in Rome

Closed Meeting:
The method was tentative. It was promoted to full CIPAC method.
The extension of the scope (CIPAC/5045) of CIPAC method MT 46.3 for the accelerated storage procedure of the MR formulations regarding determination of active ingredient content and retention index was accepted as a **full** CIPAC MT method.

CIPAC 63rd meeting, June 2019 in Braunschweig

MT 46.4 Accelerated Storage Test by Mr Burkhard Wiese (5217)
Mr Wiese presented a DAPF proposal for the update of MT 46.4 Accelerated Storage Test. The conditions for storage were not changed however there was no requirement to store for two weeks at 54°C to support tropical conditions. Storage at e.g. 40°C may be fully sufficient. Furthermore, was proposed to delete the section about storage of solid formulations stored under pressure as this was already covered by CIPAC MT 172.2. And where the scope of MT 46.3 was limited to liquid and solid formulations, and LN and MR formulation types, the scope of MT 46.4 will be open to all formulation types. Another proposed change was that the storage containers are no longer described in detail. However, for some formulation types like Mosquito Coils or LN formulations relevant information should e.g. be added to the Specification Templates in the FAO/WHO Manual.

The organizers therefore proposed to accept MT 46.4 as provisional CIPAC MT as the changes compared to MT 46.3 are not significant with the remark that MT 46.4 supersedes MT 46.3 (incl. 46.3.4 for LN / 46.3.5 for MR).

During the work related to updating of MT methods DAPF encountered that differences exist in the way MT methods are updated. Updates can be added to or can supersede the previous versions of the MT method. In the first case the previous versions remain active and in the latter case the previous versions are made inactive. As it was not always clear which route was followed and DAPF suggests stating this clearly with each update.

The following comments were received from the meeting:

- Mrs Julinkova remarked that note 6 is no longer part of the new proposal. In the answer it was mentioned that all formulations should not have a boiling point at the storage temperature. I there would be a pressure, opening would cause problems for the operators.

Closed Meeting:
MT 46.4 can be promoted to **provisional**. It was proposed that the method supersedes all previous methods.

CIPAC 64th meeting, June 2020 virtual (Geneva, Corona)

The harmonized accelerated storage procedure for all formulation types (CIPAC/5217) was accepted as a **full** CIPAC method. MT 46.4 supersedes all previous versions of MT 46 for accelerated storage.