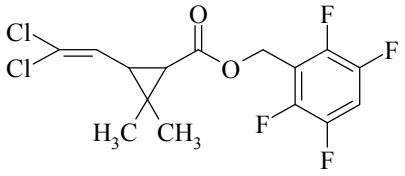
CIPAC STATUS REPORT

22/09/2018



0741 Transfluthrin

Allocated to D

CIPAC methods published in:

CIPAC K, p. 128

CIPAC 46th meeting, June 2002 in Rome

Dr Werner presented the results of a collaborative study of the capillary GC method for the determination of transfluthrin in technical material (2 TC) and formulations (3 VL vaporising liquids). Results were presented from 13 laboratories. The nature of the identity test was considered and it was questioned whether, providing transfluthrin was the mixture of trans isomers, the cis isomers would be separated under the gas chromatographic conditions. If the cis components were separated then this may remove the need for an enantiospecific identity test. The method for the VL formulations did not meet the accepted criteria for one of the formulations. Concern was expressed that the method was poor for the analysis of the formulated products. The meeting requested confirmation that the proposed identity test was capable of confirming the isomer composition of the active ingredient.
Decision The capillary GC method for transfluthrin technical and a vaporizer solution CIPAC/4291, has been accepted as provisional CIPAC method for the technical material and a tentative CIPAC method for the formulations.

CIPAC 47th meeting, June 2003 in Bucharest

Mr. T.Werner presented a stereospecific identity test for transfluthrin in response to the requirement, discussed at the 46th CIPAC Meeting in Rome, for the verification of the selectivity of the CIPAC method 741 for transfluthrin. Dr Müller asked if the technical material in which the stereoisomers are present at known concentrations could be available as a reference material for checking the performance of the GC column. Mr Werner replied that this could be arranged. Mr Fussel enquired about the commercial availability of stereoselective GC columns: it was confirmed that such columns are available.
Decision The capillary GC method for transfluthrin technical has been accepted as **full** CIPAC method and **provisional** CIPAC method (CIPAC/4291) for the VL (vaporizer solution) formulation.
The identity test was accepted with the provision that the racemic reference material to the testing laboratories for the validation of the resolution of the enantioselective GC columns will be made available on request.

CIPAC 48th meeting, June 2004 in Brno

Decision The capillary GC method (CIPAC/4291) for the VL (vaporizer solution) formulation has been accepted as **full** CIPAC method.

CIPAC 58th meeting, June 2014 in Liège

Mr Krautstrunk presented the results of a **peer validation** study for an enantioselective identity test for transfluthrin in technical material (TC).
Transfluthrin has 2 stereocentres leading to 4 isomers: 1*S*, *cis* and 1*R*, *cis*; 1*S*, *trans* and 1*R*, *trans*. The current CIPAC method 741/TC/M/- determines the stereoisomers by GC-FID.

The method uses a Phenomenex LUX Cellulose-1 column; 3 µm; 250 mm x 4.6 mm with hexane/ *iso*-propanol = 95:5 (v/v) mobile phase. Detection is at 230 nm.
Two laboratories took part in the peer validation for the TC using two different TC samples

- The method separates all four transfluthrin isomers and allows to determine the enantiomeric ratio of transfluthrin (1*R*-*trans*) and its enantiomer (1*S*-*trans*) in technical materials / TCs.
- The identity check was done successfully using certified reference standards for the two cis and the two trans transfluthrin isomers.
- Measurements were done according to CIPAC Doc. Nr. 4946 using 5 independent weighings for each sample (duplicate measurements).
- The validation showed excellent agreement between the measurements from the two participating laboratories.
- All measurements (presented as % ratio and enantiomer content) pass the acceptance criteria.

Mr Krautstrunk considered that the method is suitable and proposed it to be accepted as a new CIPAC method for the determination of the transfluthrin enantiomer ratio. He proposed to use the new chiral analytical method for permethrin technical materials in combination with CIPAC 741/ TC/m/- for the quantification of transfluthrin (1*R*-*trans*) and its enantiomer (1*S*-*trans*) in technical materials.
The following comments were received from the meeting:

- Do you propose to withdraw the current CIPAC stereo selective method as no longer supported? Mr Krautstrunk replied that although this had not been fully discussed internally in his company he suspects that this will be the proposal.
- Was there any evidence of isomerism during the sample manipulation? Mr Krautstrunk replied that there was none that they were aware of.

The meeting considered that sufficient information had been provided to demonstrate the method was acceptable
If was noted that if the current CIPAC method is withdrawn then any published WHO specification that refers to the current method will need to be revised. This will need to be co-ordinated between WHO and CIPAC.
However if this is a change to *a part* of the identity test which is mentioned in the CIPAC method then the actual method for determine of active ingredient content will not change and so the specifications do not need to change.
CIPAC will clarify with the company what is intended and then and confirm with FAO and WHO.

Decision: The chiral HPLC method (CIPAC/4948) for the determination of the enantiomeric ratio of the four transfluthrin stereoisomers in technical active substance was **accepted** as an enantioselective identity test.

CIPAC 59th meeting, June 2015 in Athens

At the 58th meeting, 2014 in Liège the enantio-selective method was accepted as an additional enantioselective identity test. It was noticed by the meeting that the prescribed stationary phase was no longer available and it was suggested to use the stationary phase described for 331 Permethrin. A double check should be performed whether two different stationary phases have to be applied. It should be clarified whether the existing method has limitations which cannot be fulfilled (availability of column) and based on the result to decide about its maintenance or removal.

CIPAC 62nd meeting, June 2018 in Panama City

Determination of permethric acid anhydride (PAA) in transfluthrin TCs by Mr Michael Haustein (5105, 5106)
Mr Haustein presented the outcome of a peer validation study for a method for the determination of 1R-trans-permethric acid anhydride (PAA) impurity in technical transfluthrin.
The samples were dissolved in acetonitrile and the PAA content was analysed by use of a 0.01 M phosphoric acid in water/acetonitrile gradient, reversed phase high performance liquid chromatography (Zorbax SB C8, 1.8 µm, 100 mm x 4.6 mm at 70°C), UV detection at 210 nm and external standard calibration. The retention time of PAA was approx. 4.6 min.
The identity of PAA was confirmed by comparison of the UV-spectrum and retention time with the UV-spectrum and retention time of the certified reference material. The specificity of the analytical

method for PAA was deemed sufficient as no interferences with known transfluthrin impurities were detected at the retention time of the analyte.
Initial validation with five samples spiked at 70 and 250 mg/kg under GLP conditions resulted in a proven linearity ranging from 53-530 mg/kg, and an acceptable precision and accuracy.
A peer validation followed with three participants in which the identity of PAA, the specificity of the method, and the linearity were confirmed by all participants. Each participant received three technical material samples (spiked at 70, 140, and 350 mg/kg respectively) and they were requested to analyze the samples in fourfold. The data presented in the statistical summary showed that the method is suitable to gain accurate and reproducible results for all test items tested.
The organizers recommend the acceptance of the proposed method for the determination of the relevant impurity 1R-trans-permethric acid anhydride in technical transfluthrin.

The following comments were received from the meeting:

- Mr di Loreto asked about the vulnerability of PAA in glass vials as the use polypropylene HPLC vials was recommended whereas all other vials used in the preparation of calibration solutions and extracts were made of glass. Mr Haustein replied that degradation of PAA was encountered once; however, it was not encountered again in later experiments.

Closed Meeting:
The method was noted and adopted.