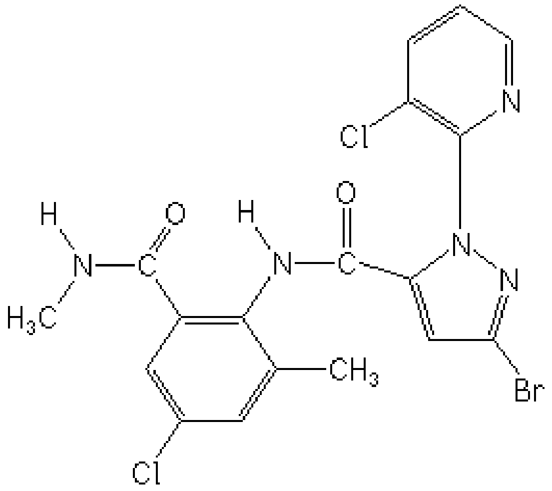
CIPAC STATUS REPORT

11.08.2024



0794 *chlorantraniliprole*

Allocated to ESPAC

CIPAC methods published in:

CIPAC

CIPAC 59th meeting, June 2015 in Athens

Mrs McNally presented the results (5008, 5009) of a **small scale** collaborative study on the determination of chlorantraniliprole in technical material, FS, WG and SC formulations using HPLC-UV with a reversed phase C18 column, UV-detection at 275 nm, and internal and external standard calibration. One participating laboratory reported an extreme high HPLC column back-pressure and tested another type of C18 HPLC column. Other participating laboratories also recorded a high back pressure; however, they were able to continue. One technical, one FS, one WG, and two SC products were investigated by six laboratories.
Five out of six laboratories used both internal and external calibration methods. After the initial evaluation, the calculated reproducibility standard deviation (RSD_R) met the Horowitz criteria for both the technical and all four of the formulations examined using the internal standard calibration method. When a second column was employed using the same HPLC conditions and internal standard calibration and these results were treated as an additional laboratory in the calculations, the calculated RSD_R also met the Horowitz criteria for both the technical and all four of the formulations examined.
For the external standard calibration, six laboratories evaluated the method. After the initial evaluation, the calculated RSD_R met the Horowitz criteria for three of the four formulations examined, the FS, the WG and one of the SCs. When a second column was employed using the same HPLC conditions and external standard calibration and these results were treated as an additional laboratory in the calculations, the calculated RSD_R also met the Horowitz criteria for the same three formulations.
After comparing both calibration methods, the internal calibration method delivered better quantitative results.
Mrs McNally proposed to move to a full CIPAC collaborative trial.

The following comments were received from the meeting:

- A high HPLC column back pressure was notified by all participants; one participant reported a back pressure (at the recommended flow rate) far beyond the pressure limit of the HPLC column. It was advised to investigate the possibility of testing alternative HPLC columns before commencing to the full CIPAC collaborative trial. This was accepted by Mrs McNally.

- Can THF be replaced by another solvent in the stationary phase? E.g. by methanol? This was not recommended by Mrs McNally.
- The calibration curve consists of seven points; it was advised to remove the lowest and highest points.
- The internal standard can be added by pipetting or by weighing. Mrs McNally preferred to use weighing as it results in lower errors. Proposal was made to use also the possibility of filling to the volume.
- The importance of removing outliers is clearly shown in this data set as one laboratory was failing when applying external standard calibration.
- Comment was made not to report results above 100%

Closed Meeting:
The meeting discussed the comments received during the open meeting.
The high back pressure of the HPLC column at the recommended flow rate was of concern to the meeting. It was advised to add the possibility of using a 2nd HPLC column to the method in order to broaden the applicability and robustness of the method. This should be incorporated in the method by adding “or equivalent” when describing the HPLC column. Equivalence should be proven and accepted if the separation between the active substance and interfering compounds is adequate. In this respect, so-called Kinetex columns were mentioned, and also the possibility of adjusting the flow rate was mentioned. Another option consists of rinsing the column carefully before analysis. In this particular case, the use of an alternative column was discussed with DuPont (Mrs McNally), however DuPont did not want to change the HPLC column.
As there were clear differences between quantification according to internal and external calibration procedures, it was discussed which method should be used during the full CIPAC trial. It was concluded that both possibilities should be possible therefore an internal standard should be incorporated in the method.
Several remarks which were given by the participants were not presented by Mrs McNally. Also chromatograms were not shown.
It was also advised to change the seven-point calibration curve in a five-point calibration curve by removing the lowest and highest points.

CIPAC 60th meeting, June 2016 in Tokyo

Chlorantraniliprole by Mrs. Mary-Ellen McNally (5034, 5035)
Ms McNally presented the results of a full scale collaborative study on the determination of chlorantraniliprole in technical material, FS, WG and SC formulations using HPLC-UV with a reversed phase C18 column, UV-detection at 275 nm, and internal standard calibration. The recommended HPLC column was an ACE C18 3µm-particle size, 4.6x150 mm column. As a result of ESPAC small scale study in 2015, the proposed column can be substituted with a 2.6 µm particle size, 4.6 x 100 mm Kinetex® C18 column or a 2.7 µm particle size, 4.6 x 100 mm Restek Raptor® C18 column. These three HPLC columns were validated for the method under good laboratory practices, for linearity, accuracy, precision and specificity. There were some comments from the participating laboratories on the high number of calibration points and high back pressure on the column during the chromatographic run.
Twenty-four laboratories received samples for this collaborative trial and twenty-one laboratories submitted the results.
The statistical evaluation was carried out according to the guidelines in the CIPAC document “Guideline for CIPAC collaborative studies Procedure for Assessment of Performance of Analytical Methods”. The data were tested for outliers firstly using Cochran’s test on the within laboratory variance and then using Grubbs test on laboratory means to test the between laboratory variance.
Using the proposed internal standard calibration method for chlorantraniliprole, the technical material and all of the formulations met the Horwitz criteria when the one Grubbs outlier was eliminated for the 35 WG formulation.
Based on these results, Ms McNally recommended that the chlorantraniliprole method to be accepted as provisional CIPAC method.

The following comments were received from the meeting:

- A high column back pressure was notified at the specified flow rate by one participant, who asked to mention in the trial protocol that stainless steel capillary connections should be used during the measurements instead of PEEK tubing.
- There were some comments on sending the collaborative trial results, the participants did not receive the report before the CIPAC meeting
- The Secretary explained that results were received late by CIPAC, it was not enough time to distribute them among the participants
- Sending the samples of the trial encountered also some problems

Closed Meeting:
The meeting discussed the comments received during the open meeting. A high column back pressure was notified at the specified flow rate by one participant, who asked to mention in the trial protocol that stainless steel capillary connections should be used during the measurements instead of PEEK tubing. I was agreed that the problem of tubing of the HPLC instrument is a technical hardware problem and it is not closely related to the method. The method presented is a robust method. The key issue is the resolution between the a.s. and the impurity, the flow rate can be reduced because of the pressure if the resolution is maintained.
The method was accepted as **provisional CIPAC method**.

CIPAC 61th meeting, June 2017 in Rome

At the previous meeting, the method was accepted as provisional. No further comments were received.
The method can be promoted to a full CIPAC method.
The reversed phase HPLC method using internal standard (CIPAC/5034) for the determination of chlorantraniliprole in TC, FS, WG and SC formulations was accepted as a **full** CIPAC method.

CIPAC 67th meeting, June 2023 Braunschweig

Solvents in chlorantraniliprole by Ms Mary Ellen McNally (5351, 5352)

Ms McNally presented the results of a small scale trial for the determination of two solvents in chlorantraniliprole one TC material and one WG and three SC formulations by GC-FID on a capillary WAX column. Six laboratories participated resulting in seven datasets as one laboratory reported two independent results. All laboratories reported deviations but none were assessed as critical. After removing outliers/stragglers the HorRat ratios ranged from 0.46-1.6. The results from acetonitrile deviated a little bit more with a HorRat range of 1.4-4.3. Ms McNally explained the larger acetonitrile HorRat range by the low concentration of acetonitrile in the investigated products: in the WG formulation the encountered concentration was approximately 30 times lower than regulated and in the SC formulations the encountered concentration was approximately 10 times lower. Previous internal method validation with spiked solvents resulted in recoveries between 95% and 105% with low RSDs (0.3-8.0%).

Ms McNally therefore recommended continuation with a full scale collaborative trial.

No questions were asked by the meeting.

c to the presenter this was caused by the very low concentrations of the investigated solvents in the sample material. Although not relevant in a small scale trial high HorRat values will be relevant in a full scale trial.

The method was recommended to a **full scale** CIPAC trial. Mr De Rijk contacted the organizers in order to discuss other validation options.

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CIPAC 68th meeting, June 2024 Wageningen

Chlorantraniliprole relevant impurity by Ms M.E. McNally (5376, 5377)

Ms Mary Ellen McNally presented the results of a full scale collaborative trial of two relevant impurities (acetonitrile and 3-picoline) in two chlorantraniliprole SCs and one chlorantraniliprole TC. Fifteen laboratories participated and returned 15 results for the TC and 14 results for both SCs. The analysis was performed by GC-FID on a DB-Wax GC column (30 m × 0.250 mm, 0.50 µm), a temperature gradient of 60°C to 240°C, helium or hydrogen as carrier gas and internal standardization. Baseline separation was achieved for the two analytes and the internal standard. Several comments from the participating laboratories were discussed. However, none of them were assessed as critical. For 3-picoline the results were as follows: in the TC two Grubbs' outliers and stragglers were identified as were two Cochran's outliers and stragglers. In the 200 SC sample two Grubbs' outliers and stragglers were identified as were two Cochran's stragglers. In the 600 SC sample two Grubbs' outliers and stragglers were identified as were two Cochran's outliers and stragglers. After removing the Grubbs' outliers and stragglers HorRat values of 1.4 (TC) and 0.6-0.7 (SCs) were calculated. For acetonitrile the results were as follows: in the TC three Cochran's outliers and stragglers were identified. In the 200 SC sample two Cochran's outliers and stragglers were identified. And finally in the 600 SC sample one Cochran's outlier and straggler were identified. The accompanying HorRat values were 1.23 (TC) and 1.27 (200 SC) and 0.54 (600 SC) while no Cochran's outliers and stragglers were removed. The presence of the HorRat values 1.23 and 1.27 were explained as being caused by the low concentration of acetonitrile in the SC samples.
Ms Mary Ellen McNally recommended this method to be accepted as a provisional CIPAC method for the determination of acetonitrile and 3-picoline in chlorantraniliprole TC and SC.

Questions and remarks from the meeting.

- Two laboratories reported performed the analysis after dilution with *N*,*N*-dimethylformamide instead of the prescribed *N*, *N'*-dimethyl acetamide as solvent. Were these results excluded?
    - The statistical evaluation was performed with and without the results of both laboratories. There was no difference between both ways of calculation.
- The rel. 5% retention time deviation is too large if it is encountered within a measurement series. It is acceptable between series. This should be clear in the text.
    - The description of the method will be updated.

Closed Meeting:

Some remarks were given by the meeting.

- The presence of two HorRat values of around 1.2 for the SC formulations is fully acceptable.
- This might be the case but it cannot be explained by stating that the low concentration is responsible for that as HorRat value incorporates the actual concentration of the analyte in its calculation formula. So further explanation is required.
- It was asked what is the maximum acceptable number of removed outliers? Max 20%.
- The relevant impurity methods validated through CIPAC are available free of charge.

Conclusion: after further clarification of the HorRat values between 1 and 2 the method was **accepted** as relevant impurity method, freely available from the CIPAC site.