CIPAC

COLLABORATIVE INTERNATIONAL PESTICIDES ANALYTICAL COUNCIL LIMITED

Commission Internationale des Méthodes d'Analyse des Pesticides (CIMAP)

Minutes of the 59th Annual meeting

The 59th meeting was held on Wednesday 17th June 2015 in Royal Olympic Hotel, Athens, Greece.

Those attending

- Items 1 to 8 on 17th June: members, correspondents, observers and expert witnesses.
- Items 9 to 12 on 17th June: members, correspondents and observers (representatives of industry and commercial laboratories, by special invitation only)

1. Welcome and introductory remarks by the chairman

The Chairman, Mr R. Hänel, opened the 59th CIPAC meeting, and welcomed all the participants. As Mrs S. Tessier has resigned from CIPAC, the position of Assistant Secretary is vacant. Mr T. De Rijk will act as temporary Assistant Secretary during the meeting.

2. Apologies

Apologies were received from:
Mr W. Dobrat, Mrs L. Janeš, Mrs A. Kashouli-Kouppari, Mrs S. Marais, Mr A. Martijn, Mr M. Müller, Mr F. Sánchez-Rasero and Mrs J. Schlosserova.

3. Adoption of the agenda

The following amendments were made to the Agenda:
Item 5.3 was presented directly after adoption of the agenda.
Item 4.1 regarding the collaborative trial of chlorantraniliprole was added, and the presentation order was rescheduled as follows:

Item 4.2: fenazaquin,
Item 4.4: pyriproxyfen,
Item 4.3: silthiofam.

4. Reports of expert witnesses

4.1 Chlorantraniliprole by Mrs M.E. McNally (5008, 5009)

Mrs McNally presented the results 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%

4.2 Fenazaquin by Mr R. Cochran (5006, 5007)

Mr Cochran presented the results of a **small scale** trial on the determination of fenazaquin TC and SC formulations using HPLC-UV with a reversed phase C8 column, UV-detection at 260 nm, and external standard calibration. Mr Cochran also presented the results of a **small scale** trial on the determination of a fenazaquin EC formulation using HPLC-UV with a normal phase silica column, UV-detection at 260 nm, and external standard calibration.
One TC sample, one SC sample, one EC sample, one SC formulation blank, one EC formulation blank, and one fenazaquin reference standard were investigated by two laboratories.
One laboratory mentioned that the retention time of the major component was sensitive to the quality of iso-octane used in the mobile phase. Both laboratories mentioned sampling difficulties with the SC formulation due to static electricity build-up during sampling.
The statistical evaluation was carried out according to ISO 5725 and showed no Grubb's or Cochran's outliers or stragglers.
When all the data were included the Horwitz criteria for RSD_R were met. Mr Cochran proposed to skip the small scale collaborative trial and to go directly to a full CIPAC trial.
The following comments were received from the meeting:

- Why were two methods proposed as the EC formulation can also be analysed with reversed phase chromatography? Mr Cochran replied that this was caused by the nature of the solvent in the EC formulation, not compatible with the acetonitrile/water system.
- It was asked -it the 2 ml/min flow rate could be diminished. The answer was that this is

possible if in the same time the eluent ratio is changed. However this would imply different chromatographic profile with implications in the registration processes. Both methods were used for registration purposes and the company preferred to keep the original analytical methods.

- The lack of retention time stability was of concern for the meeting. Small differences in water content might be the cause of large retention time deviations.

It was suggested to perform a small scale trial to identify any problems, to solve the retention time problem. It was suggested to contact ESPAC if the decision is to conduct a small scale trial.

4.3 Pyriproxyfen by Mrs M. Mukumoto (4997, 4998)

Mrs Mukumoto presented the results of a **method extension** for the determination of pyriproxyfen in a matrix release formulation (MR).
The applicability of transferring the available CIPAC method 715/TC/M/3 for pyriproxyfen TC to a pyriproxyfen containing MR product was investigated. CIPAC method 715/TC/M/3 consisted of a reversed phase C18 HPLC column, UV-detection at 254 nm and internal standardization based quantification, and was developed for TC, EC, EW and GR type products. The concentration range of the MR product was not within the scope of the existing method. Furthermore the method had to be modified with respect to the extraction solvent and extraction procedure. After consultation with CIPAC the proposed changes (replacing acetonitrile with ethyl acetate and extracting for 24 hrs at room temperature instead of 4 hrs at 40°C) the modifications were considered to as minor. Specificity tests showed no interferences whereas a company validation (two participating laboratories) showed sufficient repeatability in three different MR products ($RSD_r < 0.2\%$) and an accuracy of 100.6% ($n = 3$, $RSD_r = 0.1\%$). The modified CIPAC 715/TC/M/3 is considered appropriate for determination of the pyriproxyfen content in Pyriproxyfen MR.
JAPAC proposed to extend the existing CIPAC method for Pyriproxyfen MR.
The following comments were received from the meeting:

- It was asked if ethyl acetate is miscible with the mobile phase, which was confirmed.

4.4 Silthiofam by Mr F. De Groof (5004, 5005)

Mr De Groof presented the results of a **full scale** trial for the determination of silthiofam in TC and FS formulations with a reversed phase C18 HPLC column and UV-detection at 260 nm. The calibration was performed both with external and internal standardization. After presenting the history of the development of the method (company validation and small scale collaborative study) the outline of the full scale collaborative trial was presented. Eighteen laboratories have participated and reported their results. The participating laboratories received a silthiofam reference standard, an internal standard diethyl phthalate, three TC samples, and five FS samples. A detailed protocol was added and the participating laboratories reported deviations in HPLC column type and column dimensions, flow-rate, addition of internal standard (volumetric or gravimetric), and sample preparation. One laboratory did not report results for day 2 and was excluded for further data analysis. The data analysis resulted in the following remarks, conclusions:

- Instrument repeatability (expressed as % RSD) using an internal standard is statistically significant lower than without using internal standard ($p = 0.008$).
- Several Box-plot, Cochran & Grubbs outliers were detected and removed (3.8% and 7.8% of the data points for internal standardization calculation and external standardization respectively).
- The Horwitz criteria for RSD_R were met, both using internal standardization and external standardization.
- Mr De Groof also compared statistical outlier detection methods (Box-plot, Cochran, Grubbs and Hampel) and showed that the Hampel outlier detection procedure resulted in

less removed results and small RSD_r and RSD_R while keeping the mean calculated content identical.
- The methodology using an internal standard is recommended for the final Silthiofam method.
- Request to recognize the presented Silthiofam analytical method as full CIPAC method.

The following comments were received from the meeting:
- Mr De Groof was thanked for introducing the improvements which were suggested after the small scale trial as presented in the 2014 CIPAC meeting.
- It was remarked that gravimetric addition (compared to volumetric addition) of internal standard was the best procedure, although it allegedly did not show up in this trial. A note can be included in the description of the method that volumetric addition of the internal standard is also possible.
- Can sonication replace shaking in sample extraction? Especially thinking of heat build-up during prolonged sonication. It was tested by a participant of the meeting and did not result in any deviations.

The report was not available, but will be made available to the participants shortly after the CIPAC meeting.

5. Reports of expert witnesses on other matters

5.1 Retention properties of pyriproxyfen matrix release formulation by Mrs M. Mukumoto (4999, 5000)

Mrs Mukumoto presented a **small scale** collaborative trial of retention properties in pyriproxyfen MR. The long lasting effectiveness of release/retention properties of MR products is important for the quality of MR products and should be controlled. The procedure should be specific, simple and informative, and be able to distinguish a good from a bad product. The proposed method can be divided into two procedures: one in which half of the extracting solvent was replaced and replenished by fresh solvent and one in which the solvent was not replaced. The latter procedure is more comparable to the daily situation in which an MR product will be used and was therefore selected. Also shaking during sampling was abandoned as this is not common during application of the MR product.
Three different MRs were investigated: MR-G, MR-R and MR-W. The pyriproxyfen content of all three products proved to be identical and uniformly dispatched. The products were investigated by removing one quarter of the product at 0 hr and after 1, 2, and 4 hrs after the start of the experiment and analysing them for pyriproxyfen content. The analytical procedure was based on ethyl acetate extraction, reversed phase C18 HPLC, UV-detection at 254 nm and internal standard based quantification. Four laboratories took part in the small scale collaborative trial. After data processing repeatability, ranging from 0.48% to 1.22%, and reproducibility, ranging from 0.87% to 1.49%, were calculated (two Cochran's outliers). The proposed method is considered appropriate for the determination of release/retention properties of pyriproxyfen MR.
JAPAC proposed the method to be accepted as a provisional CIPAC method.

The following comments were received from the meeting:
- Three laboratories changed the flow rate, why? Mrs Mukumoto replied that this was performed for adjusting the retention time of pyriproxyfen as requested by the method description, as a consequence, the method has been followed.
- Three different time points were analysed: 1, 2, and 4 hrs. Is this appropriate? Have you tried 8 or 16 hours? Mrs Mukumoto replied that less points were not adequate and more time points would make the procedure unnecessary long and complex.
- The product is going to be used in plain water. Why was 50% ethanol/water used as

solvent? Mrs Mukumoto explained that the study was continued up to 6 months, when the a.s content was still 1.6%. With the accelerated system with water 1.6% was reached after 8 weeks, with ethanol/water 1.6% was reached in 4 hours. This was the reason for selecting 50% ethanol/water as the solvent system.

5.2 Revision of MT 171.1- dustiness by Mr B. Wiese (5003)

Mr Wiese, on behalf of DAPF, presented the revision of MT 171.1 – dustiness. In this method dustiness is defined as the property of a granular product to release dust into the air when handled under specified conditions. The aim of testing dustiness according to FAO/WHO Manual, chapter 4.5.34, is to restrict the dustiness of granular formulations, which may liberate dust into the air when handled and applied, and hence the risks to users. Therefore granular products must be at least "essentially non dusty". The method is applicable to GR, WG, EG and SG type products.
The reason for revision (besides editorial) was that major changes have occurred in

- removal of obsolete references
  Note 4 (related to a dust measuring apparatus from Hoechst) is obsolete
- up-date description of equipment
  Note 4 should be replaced by references to modern commercial suppliers
- sampling
  Reference is made to MT166. It is appropriate to describe that a representative sample must be used.
- error correction in result table
  The result table (Category 2) of the original MT 171 method contained errors and was re-placed by a new table.
- definition of range for sample weight
  Precise sample weight is impossible to meet for larger granules like GR unless granules are intentionally broken which is not allowed by method and may create false results. Accurate weighing (30.0 ± 0.5g, weighed with an accuracy of 0.1 g) is therefore entered in MT171.

Mr Wiese finalised his presentation with some recommendations:

- to make changes in revised CIPAC MTs more visible to users
- to introduce "Reason for revision"
- to introduce the reference that changes from MT 171 to MT 171.1 do not influence test results.

The following comments were received from the meeting:

- Which of both procedures (gravimetric based or optical based) is preferable? Mr Wiese answered that the gravimetric method should be the method of choice.
- Method revision can be editorial or related to the content of the method, or both. As these are strictly separated items they should be addressed separately. Mr Wiese answered that this also relates to the decision whether to revise or replace MTs, which is a subject of much discussion. Nevertheless it is important to keep track of document changes.

5.3 Proposal for using the HorRat value for the evaluation of the precision in collaborative trials by Mr M. Haustein (5002)

Mr Haustein presented a proposal from DAPA for using the HorRat value as an extended criterion for the assessment of the reproducibility in collaborative trials.
After a short introduction about the background of the HorRat value he proposed to draw conclusions from the actual calculated HorRat value, and therefore suggested that the HorRat value should be divided in three categories:

- $0.3 \leq \text{HorRat} \leq 1$ Fully acceptable, recommended range

- HorRat < 0.3 or 1 < HorRat ≤ 2 Acceptable, however explanation required
- HorRat > 2 Not acceptable

The following comments were received from the meeting:

- The lower HorRat value of 0.3 was discussed as being too high or even not necessary at all. Also the higher HorRat value of 2.0 was mentioned as being too high.
- It was not clear whether outliers or stragglers were included or excluded in the criteria setting of the DAPA proposal. This should be made clear.
- Was the proposal tested with existing collaborative trials?
- This was not the intention of DAPA as it was a proposal intended for discussion.
- DAPA will compile all comments and come with a final proposal. This proposal will also be brought forward in the update process of SANCO/3030/99 rev.4.

After acceptance of the final proposal the meeting recommended to test the outcome of previous collaborative trials against the proposed categories.

5.4 Equivalence of CIPAC MT Methods by DAPF

No progress was made from the last year proposal.

6. Revision/update of CIPAC guidelines

The Chairman remarked that the process of revising or updating of our CIPAC guidance has started. The meeting is requested to send in comments on all guidelines available on the website. Proposals for fundamental changes are welcome but it should be recognised that the goal is revising/updating and not completely rewriting the CIPAC guidelines.

7. Replacement of obsolete methods, comments to existing methods

7.1 Comments to existing methods

MT 18.5

Mrs Y. Kozuki remarked that two different methods were designated as 18.5 (Handbook F, p.67 and Handbook H, p.302). One of them has to be changed to 18.6.

CIPAC/600 cyproconazole

CIPAC got a question from a user whether the elution order in the published cyproconazole method is correct. With the help of the company conducting the trial it was clarified that the published CIPAC/600 cyproconazole method is correct.

MT 188, 189, 190

The Chairman remarked that necessary editorial changes will be picked up by Mr Hänel and Mr Bura.

7.2 Revision of MT methods

The Chairman remarked that revision of MT methods (new Handbook F) unfortunately has a low priority.

8. National reports

The following country reports, including any collaborative studies in which they participated, were presented: Belgium (2 reports: for agriculture and public health), China, Czech Republic, Denmark, El Salvador, France, Germany, Greece, Hungary, Ireland, Italy, Japan, Netherlands, Panama, Romania, Slovenia, South Africa, Spain, Switzerland, Thailand, Ukraine and the United Kingdom.

National reports that were provided electronically are available on the CIPAC website.

Several comments were given by the meeting about the Excel template of the report, especially calculation errors were mentioned. Nevertheless it was acknowledged that the use of such a template would

- Result in standardization
- Make evaluation possible
- Make drawing of meaningful conclusions possible
- Make building of a reliable database possible

Other comments were related to the wish to add a visual feature like a bar-chart, to identify (and unify) the reporting period, and to have the possibility of adding relevant impurities. Also it was not clear what the meaning was of the worksheets [others included] and [others not included]. Mr Garvey explained that the worksheet [others included] should contain all results obtained in a certain period and that the worksheet [others not included] should contain the results from the official monitoring. It was proposed not to include the registration samples as the title refers to QC data. It was also proposed not to include the suspicious samples as agricultural samples as this may lead to erroneous conclusions.

The Chairman, Mr Hänel, thanked all presenters, all participants of the collaborative studies and all meeting participants for their extensive comments.
Mr Hänel declared the open meeting closed.

9. Minutes of the 58th meeting (4992/P)

The minutes were circulated to members by e-mail. Comments were received concerning the enantio-selective identity test for permethrin, where the permethrin enantiomer ratio in the active ingredient as well as in a complex EW formulation was presented, but missing from the report. As a consequence, the minutes and the decisions should be modified accordingly. After these corrections the minutes were accepted.

10. Secretary's report (4993/P)

Mr Bura presented the Secretary's report for the period from the 58th CIPAC meeting held in Liège, Belgium, covering the attendance, number of trials conducted, the decisions taken concerning the methods and the election of correspondents and members of CIPAC. The report had been previously circulated to members by e-mail. No comments were received.

11. Discussion of individual compounds

370: Brodifacoum

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

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

964: Pyraoxystrobin

At the 58th meeting, 2014 in Liège the method was accepted as provisional CIPAC method with the need for clarifications relating to the sonication time and adding water to aid dissolution. After full clarification has been presented, this method can be promoted to a **full CIPAC method**. Mr Bura will advise editorial remarks with Mrs M. Mukumoto.

MT 199 Quaternary ammonium compounds

At the 58th meeting, 2014 in Liège the method was accepted as provisional. No further comments were received. The final MT number will follow in due time.

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

617: Trifloxystrobin

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

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

331: Permethrin

At the 58th meeting, 2014 in Liège the enantio-selective method was adopted as an enantioselective identity test. At last year's CIPAC meeting the peer validation work for the new chiral permethrin method (CIPAC Doc 4946) for the permethrin enantiomer ratio in the active ingredient as well as in a complex EW formulation was presented. The peer validations were successful for both matrices and proposed the new chiral method to be accepted as the new CIPAC method for determining the enantiomer ratio both in the a.s. as well as in the formulation. By mistake the EW formulation was not mentioned neither in the minutes, nor in the decisions.

741: Transfluthrin

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.

MT 198 Toluene

At the 58th meeting, 2014 in Liège the method was adopted as provisional. Mr Hänel remarked that the method target is not residue or impurity testing. No further comments were received.

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

MT 46.3 Accelerated storage procedure of the LN formulations

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

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

794 Chlorantraniliprole

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.

693 Fenazaquin

The meeting discussed the comments received during the open meeting.

The need for the normal phase HPLC method was regarded questionable, as it proved to result in non-reproducible retention times. Both the technical and the EC and SC products should preferably be analysed with one method, preferably using the reversed phase HPLC column. Therefore a **small scale trial** was strongly recommended. This advice will be forwarded through ESPAC (Mr Garvey).

635 Silthiofam

The meeting discussed the comments received during the open meeting.

Remarks were made by the meeting about the use of an internal standard which should be kept in the method, and that gravimetrical addition of the internal standard is preferred compared to volumetric addition of the internal standard. However both the gravimetric and the volumetric procedures will lead to acceptable results and both ways can be used.

The meeting agreed that with the addition of a note that the addition of the internal standard can be done also volumetrically, the method can be accepted **as provisional**.

715 Pyriproxyfen, matrix release formulation

The meeting discussed the comments received during the open meeting.

The two compared extraction procedures were discussed (extraction for 4 hrs at 40°C or for 24 hrs at room temperature). The meeting had a preference for the room temperature procedure as it would not involve thermostatic equipment, therefore easier to perform.

The meeting agreed that the method can be accepted **as provisional**.

715 Pyriproxyfen, retention properties

The meeting discussed the comments received during the open meeting.

The meeting discussed about the possibility of using this method also for MR formulations. This was not known and Mr Hänel and Mr Bura will contact Mrs Mukumoto for further information.

Taking the special situation of the MR formulation into account, it is possible to adopt the method with the current validation data as tentative method with the need for further work on validation the method. It is not necessary to conduct a full trial, but rather to provide more validation data from additional laboratories to prove that the method works. These additional data could be presented at a CIPAC meeting and CIPAC could then promote the method as full (or first as provisional and the year later as full). The proposal was that at least four sets of acceptable validation data are needed to fulfill the requirement of at least eight labs for a full trial.
The method for the determination of retention properties of pyriproxyfen matrix release formulations (CIPAC/4999) was accepted as a **tentative** CIPAC MT method with the request of additional validation data.

Revision of MT 171.1- dustiness

The meeting discussed the comments received during the open meeting.

The proposals to make changes in the method for the determination of the dustiness of granular products MT 171 (CIPAC/5003) were **accepted** with the proposal to include the reason of the revision.

Proposal for using the HorRat value for the evaluation of the precision in collaborative trials

It was agreed to ask for comments concerning the proposal of using the HorRat value and also to send comments concerning the improvement of the guidelines, including the outlier treatment.

767 1-methylcyclopropene

Mr Hänel reported that the data set of GC method (CIPAC/4669) for the determination of 1-methylcyclopropene in the SmartFresh 3.3% vapour-releasing product contained faulty calculations. After recalculation, the RSD_R values were slightly above the Horwitz values, and it was discussed and concluded that this can be regarded as acceptable in this particular case. As a consequence, the method can be accepted as **full** CIPAC method.

12. Matters related to FAO and WHO specifications

There were no issues.

13. Any other business

In revising Handbook G and H a problem will arise with the FAO if obsolete CIPAC methods will be removed. WHO will encounter no problems as there are no links for the obsolete methods to WHO.

14. Closure

The Chairman thanked the organising team and the participants for their contribution to the success of the meeting and closed the meeting.

Theo de Rijk	László Bura
Assist. Secretary	Secretary
(August 2015)	