CIPAC

COLLABORATIVE INTERNATIONAL PESTICIDES ANALYTICAL COUNCIL LIMITED

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

Minutes of the 58th Annual meeting

The 58th meeting was held on Wednesday 25th June 2014 in Hotel Crowne Plaza, Liège

Those attending

- Items 1 to 6 on 25th June: members, correspondents, observers and expert witnesses.
- Items 7 to 14 on 25th 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 Hänel, opened the 58th CIPAC meeting, and welcomed all the participants. He remarked that there had again been some difficulties during the year in sending out samples for the collaborative trials due to customs and courier restrictions in certain countries. He thanked the trial organisers and participants for their patience and understanding with these issues and reminded participants that samples should be declared correctly to customs officials to avoid any legal problems.

2. Apologies

Apologies were received from:
Mr A. W. Burns, Mr J. Foltýn, Mrs L. Janeš, Mrs A. Kashouli-Kouppari, Mr A. Martijn, Mr A Ramesh, Mr F Sánchez-Rasero and Mrs J. Schlosserova.

3. Adoption of the agenda

The following amendments were made to the Agenda:

Items 4.1 and 4.5 were presented together as they had the same presenter.
New item 5.8: Use of nitrogen as carrier gas for GC

4. Reports of expert witnesses

4.1 Alpha-cypermethrin by Mr Ramanathan Natarajan (4938, 4939)

Mr Natarajan presented the results of a study showing the applicability of method CIPAC/454/LN/M for the determination of alpha-cypermethrin in the product "Veeralin" (alpha-cypermethrin and PBO incorporated LN):

- The nominal concentration of the new formulation falls within the range of the existing method
- The retention times of alpha-cypermethrin and dioctyl phthalate (internal standard) in the sample solutions and calibration solutions did not deviate by more than 0.5% from that in calibration solutions
- Analysis of blanks, calibration solutions, spiked blank formulation, and "Veeralin" sample solutions showed the absence of compound interference

- Accuracy (recovery) data were generated at two laboratories using a blank formulation and gave acceptable results
- Precision (repeatability) data were generated at two laboratories and gave RSD of 0.7% and 0.4% (Acceptable Horwitz value = 2.91%)
- The results demonstrated applicability and validity of method CIPAC 454/LN/M/2.1 & 3.2 (GC-FID) for the determination of alpha-cypermethrin content in the presence of piperonyl butoxide in Veeralin LN.

Mr Natarajan proposed that the extension of the method is accepted.

The following comments were received from the meeting:

- No comments

4.2 Brodifacoum by Mrs Susanne De Benedictis (4942, 4943)

Mrs De Benedictis presented the results of a **full scale** collaborative study on the determination of brodifacoum in technical product (TC) and ready to use bait (RB) formulation using HPLC-UV, with a C18 column (temperature = 50°C), detection at 266 nm and external standard calibration. Brodifacoum consists of cis /trans isomers in the range 50:50 / 80:20. The content of brodifacoum is defined as the sum of both diastereomers; however the cis /trans ratio can be determined simultaneously with the determination of the content if necessary.
Two samples of TC and three samples of RB were provided. 18 laboratories offered to participate however due to the issues discussed below, results and data were received from 12 laboratories.
There were challenges for the collaborative study due to the toxicity of the active substance. These included difficulties in shipping samples. Logistic issues led to a delay of between 4 weeks (easy destinations) and up to 3.5 months. Air transportation of compounds with high inhalation tox is very challenging and so unfortunately shipment was not possible at all for some destinations (China, Panama, Ukraine and Romania)
To ensure the safety of participants and to prevent any misuse during transport

- Each participant was sent clear safety instructions
- The amount of tech. AI and internal standard shipped was reduced to the absolute minimum

As it was the aim to minimise the amount of toxic material sent around the globe, the exact weighing was provided in a small vial. This approach would have required a quantitative transfer from the shipment container in a volumetric flask, leading to:

- Higher exposure risk for the operator (contamination during quantitative transfer from vial to volumetric flask)
- High dependence of the result on the quantitative transfer (which is not part of the method)

Hence it was decided to add an internal standard (same IS as for RB formulation analysis). TC samples were provided in pre-weighed vials already including the internal standard
Ms De Benedictis emphasised that the use of an internal standard for the analysis of technical brodifacoum and the use of pre-weighed technical samples and reference standards were only for safety reasons and have no beneficial impact on the performance of the method. The absence of a weighing error is compensated by the dispensing error during preparation of the pre-weighed vials.
The sample preparation and the extraction procedure for the RB samples are essential to give reliable results.
The single block of RB (20 g) needs to be grated and extracted (90 min, stirring) using 95 ml of an extraction solvent (acetonitrile: water: acetic acid 80:18:2), heptane (200 ml) and internal standard solution (5.0 ml).
The use of a chemically similar substance as internal standard (difenacoum) is recommended to

compensate for any adhesion effects to paraffin or minor losses in the heptane layer.
The statistical evaluation was carried out according to the CIPAC guidelines and showed the following outliers and stragglers:

For TC1 Lab 8 was identified as a Cochran's straggler
For TC2 Lab 8 was identified as a Cochran's outlier and Lab 9 as a Grubb's outlier
For RB1 Lab 5 was identified as a Grubb's straggler and as a Cochran's straggler
For RB2 Lab 5 was identified as a Cochran's outlier
For RB3 there were no outliers or stragglers identified

Lab 5 reported problems on day 1 with the quantitative transfer of the internal standard during analysis of the RB formulation samples. No data were excluded from the initial evaluation. When all the data were included the Horwitz criteria were met in all cases. It was also shown that the values obtained for the cis/trans ratio for all labs showed good agreement.

Ms De Benedictis concluded that the method is suitable and proposed the method be adopted by CIPAC.

The following comments were received from the meeting:

- No comments were received**.**

4.3 Fenazaquin by Mr Rene Cochran (4975, 4976)

No information was received or presented at the meeting.

4.4 Hexazinone by Ms Yue Wang (4952, 4953)

Ms Wang presented the results of an applicability study of CIPAC Method 374/WG/M for the determination of hexazinone in Nutrichem WG.
The nominal concentration of the new formulation falls within the range of the existing method; however there were issues observed with the peak shape for hexazinone, as the concentration of the test solutions overloaded the detector leading to peak flattening. An additional dilution step was therefore included in the sample preparation of the WG.
Accuracy (recovery) data were generated at two laboratories using a blank formulation and gave acceptable results
Precision (repeatability) data were generated at two laboratories and gave RSD of 0.16% and 0.17% (Acceptable Horwitz value = 1.40%)
The results demonstrated applicability and validity of method 374/WG/M for the determination of hexazinone in Nutrichem WG.

Ms Wang proposed that the extension of the method is accepted.

The following comments were received from the meeting:

- You have proposed to grind the granules before extraction – is this really necessary? Have you tried to extract the granule without the milling procedure? Ms Wang replied that the current CIPAC method indicates that samples should be milled or ground so they have followed the original CIPAC method exactly.
- Hexazinone has a relevant impurity and your company has already developed a method for determination of this impurity in the TC. Would this method also be applicable to your WG? Ms Wang replied that they already validated the method in-house and they are preparing to conduct a small scale validation of this method using 3 labs.

4.5 PBO by Mr Ramanathan Natarajan (4940, 4941)

Mr Natarajan presented the results of a method extension of CIPAC/33/LN/M for the determination of piperonyl butoxide (PBO) in the product "Veeralin" (alpha-cypermethrin and PBO incorporated LN):

- Nominal concentration of PBO in the new LN is 2 g/kg which is at the lower limit of acceptability of the current method (2 g/kg to 334 g/kg). Minor modifications were therefore proposed:
  -In the existing CIPAC method stock calibration solution of piperonyl butoxide (PBO) is prepared by dissolving 250 mg in 50 mL xylene. **Use 50 mg instead of 250 mg.**
  -LN sample of 0.5 g is digested with 23mL xylene + 2 mL octadecane internal standard solution.**Use 1 g LN sample for digestion instead of 0.5 g.**
- Linearity of the detector response in the concentration range 20 mgL^{-1} to 160 mgL^{-1} is linear with $r^2 \geq 0.99$.
- The retention times of the piperonyl butoxide and octadecane (internal standard) peaks in the sample solutions do not deviate by more than 0.5% from that of the calibration solutions.
- Analysis of blanks, calibration solutions, spiked blank formulation and VEERALIN sample solutions showed the absence of compound interference
- Accuracy (recovery) data were generated at two laboratories using a blank formulation and gave acceptable results
- Precision (repeatability) data were generated at two laboratories and gave RSD of 0.8% and 0.5% (Acceptable Horwitz value = 3.41%)
- The results demonstrated applicability and validity of method CIPAC 33/LN/M/ 3 (GC-FID) for the determination of piperonyl butoxide content in the presence of alpha-cypermethrin in Veeralin LN.

Mr Natarajan proposed that the extension of the method is accepted, with the modifications suggested

The following comments were received from the meeting:

- No comments

4.6 Pyraoxystrobin by Ms Haixia Wang (4936, 4937)

Ms Wang presented the results of a **full scale** collaborative study on the determination of pyraoxystrobin in technical material (TC) and suspension concentrate (SC) using HPLC-UV, with a C18 column (temperature = 30°C), detection at 280 nm and external standard calibration. Two samples of TC and three samples of SC were provided. 26 laboratories offered to participate and data were received from all 26 laboratories.
15 different brands of HPLC column were used across the laboratories however these were mostly comparable to the column suggested in the method. Some laboratories conducted the HPLC analysis at 25 °C or ambient temperature rather than the proposed 30°C.

The following remarks were also received from the participating laboratories:

- We recommend choosing a wavelength equal to 254 nm;
- It is possible to use approximately 5 minutes instead of the recommended 15 minutes to dissolve the sample in an ultrasonic bath.
- It would be recommended to emulsify the SC samples with 10% water and then to dissolve in acetonitrile.
- It would be recommended to quantify the samples using a calibration curve.
- It would be better to increase the temperature by 5 ℃ or 10 ℃.

The statistical evaluation was carried out according to the CIPAC guidelines. In Lab 4, the response factor for the calibration solution B differed much more than 1.0% from that for the calibration solution A, which did not comply with the procedure of HPLC method of pyraoxystrobin for CIPAC full scale collaborative trial. So the data of the Lab 4 was invalid and excluded from the statistical evaluation.
The following outliers and stragglers were identified:

For TC1 Labs 13 and 17 were identified as Cochran's outliers and Lab 16 as a Grubb's outlier
For TC2 Labs 12 and 17 were identified as Cochran's outliers and Lab 16 as a Grubb's outlier
For SC1 Lab 9 was identified as a Dixon's outlier, Lab 23 as Cochran's outlier.
The results from Lab 16 were considered an outlier due to issues with overlapping peaks.
For SC2 Lab 15 was identified as a Grubb's outlier and Lab 16 as a Cochran's outlier
For SC3 Labs 2 and 23 were identified as Cochran's outliers, Labs 9 and 15 as Grubb's outliers.

All results, apart from Lab 4, were initially included in the evaluation. In the initial evaluation the Horwitz criteria were met for TC 1 and TC 2. For the SC samples (SC1, SC2 and SC3) the Horwitz criteria were met after the removal of stragglers and outliers

Ms Wang concluded that the method is suitable and proposed the method be adopted as provisional by CIPAC.

The following comments were received from the meeting:

- In my experience for SC formulations it is better and faster if the sample is dissolved in a small amount of water before adding the acetonitrile, that way you need have less time in the ultrasonic bath. Did you try this?
- Two other laboratories also commented that they would recommend the addition of some water to the SC samples and also a reduction of the time in the ultrasonic bath.
  Ms Wang replied that similar comments were received last year after the small scale trial so they had tried the addition of water. They believed it made no difference to the method.
- It was noted that two labs measured a pyraoxystrobin content of 108% in the TC. These labs should check their data more thoroughly and perhaps adjust the conditions of measurement because it is very strange to measure 108% for a TC.
- Why did you use the wavelength 280 nm instead of the absorbance maxima of 254 nm?
  Ms Wang replied if the absorption maxima were used then there was a risk of detector saturation and all the sample sizes would need to be reduced to avoid this.

4.7 Quaternary ammonium compounds by Ms Diane Rains (4965, 4966)

Ms Rains presented the results of a **full scale** collaborative study on the determination of quaternary ammonium compounds by titration using an ionic surfactant electrode.
Quaternary ammonium compounds (quats) is the general term used for compounds that consist of saturated alkyl groups attached to a nitrogen atom associated with an anionic species (e.g., chloride or bromide). They are used in many disinfectant products. Originally a collaborative study was designed to be conducted within AOAC International; however due to changes in the structure of AOAC International the study was moved to CIPAC.
The method measures the quaternary ammonium compounds as total quaternaries and is suitable for concentrated and ready-to-use (RTU) disinfectant formulations. The method is not suitable for products containing large amounts of alcohol (methanol, ethanol, isopropanol, etc.) and/or hydrochloric acid.
A potentiometric titration, utilising an ionic surfactant electrode and a titrant of sodium lauryl sulfate, is used to determine the amount of quaternary nitrogen in the sample. As the method uses a specific electrode, these were supplied to the laboratories.
19 laboratories offered to participate in the collaborative study and samples were shipped to 14 laboratories. There were issues with sending samples to Romania and China. 12 laboratories returned a full set of results within the deadline for submission. 7 samples of detergents were sent to participants. These covered a range of concentrations and active substances (different quats). One laboratory reported some precipitate for one sample and another sample appeared to be cloudy/hazy. The precipitate was mixed before sub-sampling. The cloudy sample was analysed

using a smaller sample size which reduced the initial "bumpiness" observed in the early titration curve.
One laboratory recommended more conditioning of the electrode prior to use. It was recommended to include three "throw away" titrations for a new electrode and for electrodes that had not been used in more than a month. Unconditioned electrodes will give higher RSDs (>5%) indicating the need to condition further
The statistical evaluation was carried out according to the CIPAC guidelines. For Sample C lab 6 was identified as a Grubb's outlier.
No other outliers were identified. All results were initially included in the evaluation.
In the initial evaluation the Horwitz criteria were met for all samples.

Ms Rains concluded that the method is suitable and proposed the method be adopted as provisional by CIPAC

The following comments were received from the meeting:

- There were no comments.

4.8 Silthiofam by Mr Wim Van Thuyne (4959, 4960)

Mr Van Thuyne presented the results of a **small scale** collaborative study on the determination of silthiofam in technical material (TC) and flowable concentrate for seed treatment (FS) using reverse phase-HPLC-UV, with a C18 column, detection at 260 nm with internal standard calibration. The study was conducted in collaboration with ESPAC.
One sample of TC and one sample of FS were provided. 8 laboratories participated in the small scale study.
The following deviations from the method protocol were noted:

- Different column vendors + dimensions (comparable stationery phases used)
- Different mobile phase composition
- Different flow rate
- Different mode of addition of internal standard: Volumetric addition of a stock solution
- Different sample preparation for FS due to the formation of precipitation

The statistical evaluation was carried out according to the CIPAC guidelines. Lab 6 reported a possible bad injection on the 2nd injection of the first preparation; however the data point was not removed as final result identical to 1st injection.
All results were initially included in the evaluation. In the initial evaluation the Horwitz criteria were met for all samples when the internal standard was used.
When the results were calculated without the internal standard the interpretation of the available data showed multiple possible outliers. 3 options were evaluated:

- All results were initially included in the evaluation. In this instance the Horwitz criteria were met for the TC but failed (just) for the FS.
- Removal of Lab 1&2 + 2 data points of Lab 6 at each level. In this instance the Horwitz criteria were met for the TC and the FS.
- Selected removal of data points of Lab 1, 2 &6. In this instance the Horwitz criteria were met for the TC and the FS.

Mr Van Thuyne concluded that the method is suitable and proposed that a full scale trial is conducted using the internal standard.

The following comments were received from the meeting:

- Why did you use an HPLC column with a particle size of 10 µm? Mr Van Thuyne replied that this was the most commonly used column in his lab. He noted that other labs had used either a 10 µm or 5µm column, that there was no significant interference from the matrix and the retention time of the internal standard and active ingredient were separated

by 3.5 min for the 10µm column. From this he surmised that the particle size would not influence the results significantly.

- What temperature should be used for the HPLC column? This wasn't included in the method so different participants may have used different temperatures. Mr Van Thuyne replied that this information had not been included in the method in error and that this may explain some of the differences seen in results. He proposed that a temperature of 40°C will be added to the method.
- For sample preparation for TC why did you need to place the sample in an ultrasonic bath for 15 min? The TC dissolved very easily? Mr Van Thuyne replied that this was done to make the sample preparation the same for the TC and FS. This step is needed for the FS; however the method can be updated to reflect that less time is needed for the TC.

4.9 Trifloxystrobin by Mr Michael Haustein (4954, 4955)

Mr Haustein presented the results of a **full scale** collaborative study on the determination of trifloxystrobin in technical material (TC), emulsifiable concentrate (EC), flowable concentrate for seed treatment (FS), suspension concentrate (SC), water dispersible granules (WG) and ready to use liquids (AL) using HPLC-UV, with a C18 column (temperature = 50°C), detection at 280 nm and external standard calibration.
Two samples of TC, 1 sample of AL, 1 sample of EC, 1 sample of FS, 1 sample of WG and 1 sample of SC were provided. 33 laboratories offered to participate, however the trial was limited to 24 participants due to the availability of samples for the study. The first 24 respondents were therefore chosen. Data were received from 22 laboratories within the requested timeframe.
The results of one participant were rejected as a number of major changes to the method were introduced:

- Use of a non-equivalent separation column
- Change of column-dimensions
- Change of flow-rate
- Change of injection volume

As a result retention time and peak-width changed significantly. Moreover, the laboratory remarked on additional retention time variation
The statistical evaluation was carried out according to the CIPAC guidelines. The following outliers and stragglers were identified: For the FS Lab 20 was identified as a Grubb's straggler No other statistical outliers were identified. All results were initially included in the evaluation. In the initial evaluation the Horwitz criteria were met for all samples.

Mr Haustein concluded that the method is suitable and proposed the method be adopted as provisional by CIPAC.

The following comments were received from the meeting:

- Do you need to place the standard in an ultrasonic bath for 15 min to dissolve it? In our experience this is not necessary. Mr Haustein replied that this was to ensure that the sample was homogenous but agreed that it was not necessary.
- Why did you choose an injection volume of 3 µl – this may be too small for some laboratories? Mr Haustein replied that good repeatability can be achieved with a 3 µl injection volume without causing column saturation He also noted that some of the labs that participated had used 5 µl injection with no problems.
- Why did you choose detection at 280 nm when the absorbance maximum is approx. 250 nm? Particularly for the AL formulation this lead to a small peak as it was a much lower concentration than the other samples. Mr Haustein replied the wavelength had been chosen to avoid saturation of the detector, and that even at the low concentration of the AL formulation the results gave good repeatability.

- The retention time of the active ingredient is quite early; within 1-3 min. Mr Haustein replied that this was intentional to give a fast method.
- It was further commented that not all labs will use the exact same column and may have problems with this early elution. Mr Haustein replied that some laboratories in the study had used a double length column and this gave a longer retention time. The results were still acceptable with the longer column.
- It would have been be useful if participants could have received the report before the meeting so they would have the chance to look at the data in detail. Mr Haustein apologised and replied that the report will be sent out soon.
- It was noted that you used an EC formulation in the collaborative study. There used to be a trifloxystrobin DC formulation. Did you reformulate? Mr Haustein replied that he didn't know but remarked that EC was now a common formulation type.
- Is it necessary to change the flow rate of the HPLC pump for the column-flush phase of the method? Mr Haustein replied that this was done to make the method quicker and that it is not mandatory to have the flow rate change.

5. Reports of expert witnesses on other matters

5.1 Release/retention rate for pyriproxyfen matrix release formulation by Ms Yumiko Kozuki and Makiko Mukumoto (4950)

Ms Kozuki presented a brief introduction to a proposed new formulation type (matrix release formulation).
Ms Mukumoto presented information on a proposed method for determining the release rate or retention rate for the new formulation type.
The method needs to be

- Product specific
- Simple and informative method to describe release properties
- Able to distinguish a good product from a bad one

Ms Mukumoto outlined some of the method development already undertaken and proposed two possible methods (a replenishment method and a non-replenishment method) to take forward for further development and collaborative studies.

- To evaluate AI movement of MR immersed into water in short period, testing systems using shaking in 50% ethanol/water is most appropriate.
- Two testing systems, using non-replenishment and replenishment methods, are able to distinguish good MR from a bad one
- Non-replenishment method is simpler but longer, and replenishment method is shorter but requires more steps

Ms Kozuki and Ms Mukumoto proposed that following any opinions and suggestions obtained from CIPAC, the method will be modified and then a collaborative study will be conducted.

The following comments were received from the meeting:

- Can you clarify the type of shaking that is needed if any at all? Ms Mukumoto replied that they had used horizontal shaking not rotary shaking.

5.2 Permethrin enantioselective identity test by Mr Gerhard Krautstrunk (4946, 4947)

Mr Krautstrunk presented the results of a **peer validation** study for an enantioselective identity test for permethrin in technical material (TC) and EW formulation.
Permethrin 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 331/TC/M/- determines the *cis*- and *trans*- isomers together. An analytical method allowing the determination of the enantiomeric ratio of the four permethrin

isomers was therefore developed to be used in combination with the chemical purity determined using CIPAC331/TC/M/-.
The method uses a Phenomenex LUX Cellulose-3 column; 3 µm; 250 mm x 4.6 mm with hexane/*iso*-propanol = 95/5 (v/v) mobile phase, including a small amount of formic acid to prolong the life of the column. Detection is at 235 nm.
Two laboratories took part in the peer validation for the TC using two different TC samples

- The method separates all four permethrin isomers and allows quantification of all four permethrin isomers in TCs.
- The identity check was done successfully using certified reference standards for all four permethrin 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.

Analysis of a representative EW formulation proved to be more complex as the formulation contains another active ingredient (also consisting of several isomers) and a synergist. Two laboratories took part in the peer validation for the EW.

- Slight interferences (caused by additional active substances) are found under the peaks corresponding to 1*S*, *cis* permethrin and 1*S*, *trans* permethrin.
- A negative peak was observed and indicated to be caused by different refraction index of the sample solvents (can be easily eliminated).
- The column is very sensitive regarding the water content in the eluent which may effect the robustness of the method.
- The identity check was done successfully using certified reference standards for all four permethrin isomers.
- The method separates all four permethrin isomers and allows to quantify all four permethrin isomers in formulation in combination with (CIPAC331/TC/m/-)
- The method showed to be suitable for use as an enforcement method for determination of the permethrin enantiomer ratio in formulation.
- The validation showed statistically acceptable agreement between the measurements from the two participating laboratories.

Mr Krautstrunk considered that the method is suitable and proposed it to be accepted as a new CIPAC method for the determination of the permethrin enantiomer ratio. He proposed to use the new chiral analytical method for permethrin technical materials in combination with CIPAC331/TC/m/- for the quantification of all four permethrin isomers in technical materials.

The following comments were received from the meeting:

- None

5.3 Transfluthrin enantioselective identity test by Mr Gerhard Krautstrunk (4948, 4949)

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.

5.4 d-tetramethrin by Ms Chen Yuanyan (4967)

Ms Yuanyan presented identity tests and a test for determining the enantiomeric purity of d-tetramethin

- The identity tests consisted of normal phase HPLC and IR spectra
- The d-tetramethrin content was determined by GC-FID and internal standardisation
- The method for the determination of d-tetramethrin content was validated with respect to linearity of response, precision and accuracy. The validation data were within acceptable criteria.
- The isomer ratio of the enantiomer is determined by normal phase HPLC using a CHIRALPAK® AY-H, 250 mm × 4.6 mm (i.d.), 5 µm chiral column with detection at 230 nm.
- Example chromatograms were presented demonstrating separation of the four isomers.

The following comments were received from the meeting:

- None

5.5 Toluene-relevant impurity in formulations by Mr Robert Kettner (4944,4945)

Mr Kettner presented the results of a **full scale** collaborative study on the determination of toluene in formulations by headspace GC with FID or MS detection. The study was conducted in collaboration with DAPA.
Two samples of EC, 1 sample of FS, 1 sample of WG and 1 sample of SC were provided. Each formulation contained different active ingredients and was therefore predicted to contain a different level of toluene. 13 laboratories participated in the trial.

The following remarks were received from the laboratories:

- Lab 4: Nitrogen instead of helium used as carrier gas. Recommendation to extend the time of the temperature program (formulation EC2)

- Lab 5: Injection volume 500 µl instead of 1000 µl; chromatography shortened due to MS detection, toluene-d8 used as internal standard.
- The data were also evaluated by external calibration (using the internal standard D_8-toluene). The results generated were comparable to those obtained by standard addition. Column: DB5, 30 m, 0.32 mm, film thickness 0.25 µm – temp program adjusted.
- Lab 6: Column: ZB-624, 60 m, 0.32 mm, film thickness 1.8 µm; Split ratio: 15:1
- Lab 8: Carrier gas: hydrogen, shaking time: 12 s, split ratio 5:1
- Lab 9: Analysis also performed with MS detection
- Lab 10: Column: BGB 5, 30 m, 0.32 mm, film thickness 0.25 µm - temp program adjusted. Split ratio: 50:1
- Lab 12: Column: DB-624, 30 m, 0.25 mm, film thickness 1.4 µm
- Lab 13: Hold time of final column temperature increased.

A mixture of fixed transfer line (5 labs) and gas syringe (8 labs) auto samplers and FID (9 labs) or MS (4 labs) detection were used.

The statistical evaluation was carried out according to the CIPAC guidelines. The following outliers and stragglers were identified:

For the EC1 Lab 7 was identified as a Mandel's k-straggler
For the EC2 Lab 6 and Lab 12 were identified as Mandel's k-stragglers
For the FS Lab 5, Lab 9 and Lab 12 were identified as Mandel's k-stragglers
For the SC Lab 12 was identified as a Mandel's k-outlier
For the WG Lab 6 was identified as a Mandel's k-straggler

All results were initially included in the evaluation. In the initial evaluation the Horwitz criteria were not met for any samples. When the outliers were removed from the statistical calculations the Horwitz criteria were met for the FS, SC and WG sample. The % RSD_R for both EC-formulations tested was slightly above the Horwitz value after elimination of stragglers/outliers. Mr Kettner proposed that due to the universal applicability of the method (all formulation types), the use of different sampling devices for the headspace-technique (fixed transfer line or gastight syringe) and the use of different detectors (FID or MS), a slightly higher coefficient of variation in this collaborative trial is acceptable.

Based on the results of this CIPAC collaborative study, DAPA consider this method to be fit for use and recommend that it be accepted as a provisional CIPAC MT-method for the determination of toluene as relevant impurity of the active ingredient at low levels in solid formulated products and in aqueous and organic solvent based liquid formulated products

The following comments were received from the meeting:

- Why do you recommend that labs use heavy toluene as an internal standard instead of ethylbenzene which is cheaper? Mr Kettner replied that it is only a recommendation for labs to use this if it is available
- It would be preferred if you do not mention "relevant" impurity in the title of the method. It is outside of the remit of CIPAC to address whether an impurity is relevant or not, CIPAC's role is to develop and collaboratively test methods.
- You mention that for one a.s there is a limit of maximum 0.5% toluene. This seems odd to me. Mr Kettner replied that the limits are set as part of the regulatory process in the EU.
- On the basis of all the results using either GC-FID or GC-MS could you see any significant difference between the two detection techniques? Mr Kettner replied that there was no significant difference and that if laboratories had both detection systems either would be suitable to use.

5.6 Extension of MT 46.3 to LN by Mr Olivier Pigeon (4956, 4957)

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 <u>once</u> 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.

5.7 Equivalence of CIPAC MT Methods by Mr Markus Müller (4961)

Mr Müller on behalf of DAPF presented a brief discussion on the impact of the review of MT methods and the replacement of some older methods with newer versions.
Revisions of CIPAC Methods

- Fundamentally positive: to meet new development in technology and to better characterize formulations
- Downside: might cause problems in the acceptability of a physical-chemical data package by some registration authorities still requiring test being done with previous MT method versions.
  Some examples of revised MT methods:
- MT 47.2 (persistent foam) replaced by MT 47.3
- MT 75.2 (pH of aqueous dispersions) replaced by 75.3 (determination of pH values)
- MT 159 (pour and tap) replaced by MT 186 (bulk density)
- and many more...!

Do different versions of a physical-chemical test method lead to similar results?

- Answer: it depends... – need to check!
- Possible sources of information: CIPAC Decisions, Minutes of CIPAC TC, "Bedside Book", Minutes of DAPF Meetings (German Speaking Formulation Panel), expert knowledge...

Is information on equivalence of MT Methods accessible to the outside world?

- Yes, rather limited: decisions, "review of MT Methods"
- No: Minutes of TC, Bedside-book, DAPF Minutes...

Proposal/Recommendation

- An Excel synopsis table on equivalence/non-equivalence of CIPAC MT Method versions be drafted by DAPF and presented at 59th CIPAC Meeting in Athens
- If CIPAC agree and take note of the table, it could be published on CIPAC.org
- This would facilitate easy access to information re equivalence/non-equivalence of CIPAC MT methods

The following comments were received from the meeting:

- The differences between MT 47.2 and 47.3 for persistent foam, besides the cylinder there is a change in temperature so these methods would not be considered equivalent. Mr

Müller replied that there are many revisions underway including considering harmonising the temperature at the moment. For this example there are bridging studies to show that persistent foam gives the same results under both tests.

- I'm not sure I see the benefit of this list. If a CIPAC MT method has been replaced then there has generally been data presented to CIPAC to demonstrate that the new method gives similar result to the old method, otherwise the method will not have been replaced. So why do we need a guide? Mr Müller replied that this consideration had been driven by the Regulatory Authorities asking for data using a method that is marked as "obsolete" on the CIPAC website. Regulatory Authorities have the right to ask for whatever data they need to address their own requirements; however this guide could serve a purpose to aid the interpretation of data packages.
- In the case of persistent foam MT47.2 is not obsolete and can still be used. Mr Müller replied that the issue was that if there is a new method published this will not immediately show up in data packages and a data package with an older version of the method may be sent to Regulatory Authorities. The Regulatory Authority would then require bridging data to be submitted until a data package using the new method is provided. A summary of the equivalence or non-equivalence of methods would be a pragmatic solution to this problem.
- One member commented that their National standard is the CIPAC method but when a newer method is published it is not clear how this should be dealt with. It is not clear sometime when a new extension is proposed whether the newer or older version will still be acceptable.
- For SC suspensibility the CIPAC method gives the choice of determination either by a.s content or by gravimetric method. Which should registrants or authorities use?
- It is up the individual authorities or registrants to choose which version of a test method is used. It is not the responsibility of CIPAC to dictate that.

5.8 Use of Nitrogen as a carrier gas

After clarification with colleagues from JAPAC it was agreed that as this issue is related to point 6.2: Update of guidance documents and would therefore be discussed under that agenda item.

6. Replacement of obsolete methods

6.1 Comments on existing methods

MT 172 by Mr Alain Dubois (4962)

Mr Dubois remarked that during the last proficiency test organised by FASFC it was noted that some participants had problem with this method - in particular which temperature should be used. In the published method, part of the sentence is missing so it's not clear what should be done to report the results.

The Chairman remarked that CIPAC will make an amendment under the errata on the website and that this will also be taken up during the review of MT methods.

CIPAC/239 pirimiphos-methyl by Mrs Susanne De Benedictis (4963)

Mrs De Benedictis presented some information about issue that had been found with the CIPAC methods for the determination of pirimiphos-methyl in formulations (specifically EC and CS formulations). Extensive investigations and round robin studies have been performed to better understand the issues and to be able to propose changes to the current CIPAC method that improve clarity and minimize the potential for incorrect analyses.

In one case, when analysing samples of formulated products, the results obtained for the AI content were significantly higher (5 % – 10%) than the nominal content.

- A root cause analysis showed that overdosing could be ruled out. The most like cause was

that the purity of the reference substance used was significantly lower than the purity indicated on the label.
- Inappropriate shipping and handling of the material could cause degradation of the AI. This is a known phenomenon for organophosphates

Thus, a statement has been added in the method that describes how the reference substance should be treated. As the same holds also for the reference substances of the impurities, a similar statement was added in the respective paragraph.
When analysing samples of the same batch of the CS formulation, the results for the total AI content in some of the labs was lower than in other labs.
- The investigations revealed that the labs with the lower results had an ultrasonic bath with low power. Further tests also showed that the results were even lower if too many bottles have been placed into the ultrasonic bath at the same time.

Thus, a sentence has been added in the CIPAC method informing the reader of the consequence of a low power bath for CS formulations. In addition a statement has been added to limit the number of bottles simultaneously in the ultrasonic bath to three.
In one of the labs the low injector temperature (170 °C) led to peak tailing after multiple injections.
- As a consequence the variations of the response factor increased.
- This phenomenon could be reduced by increasing the injection temperature.
- However care must be taken to not increase the temperature too much. Otherwise decomposition of the AI may take place.

Thus, it is proposed to introduce a comment in the method that the temperature may be increased slightly if it's ensured that this does not lead to decomposition of the AI.
Further work on **CS formulations** led to the conclusion that the AI may not be completely extracted after 15 minutes sonication (in particular when the power of the ultrasonic bath is near the lower limit of what is stated in the method).
- Tests have shown that **60 minutes** sonication gives higher results. This does not lead to a significant decomposition of the AI.
- The possibility to improve the consistency of the sample preparation for CS formulations was also considered by adding a bit of water (2 ml) prior to sonication and discarding the first ml when filtering proved useful.

Thus, it is proposed to change the sonication time from 15 min to 60 min and change the sample preparation.

Determination of the isomer of pirimiphos-methyl, which is a relevant impurity:
- The original method applied the sample preparation as for the CS formulations. However, we are now proposing to increase the sonication time to 60 minutes.
- But this time period is not suitable for the determination of the isomer because this can lead to extended isomerisation (CH_3O-P=S and CH_3S-P=O). As a consequence the measured amount of the isomer would be too high.
- Thus, we propose to use the sample preparation conditions of the TC to determine this relevant impurity in TC and EC.
- For the CS formulations a statement has been added that the sonication time for the determination of the isomer is 15 min rather than 60 min.
- To compensate for the possibly incomplete extraction of both components from the capsules, the content of the AI and the isomer in the same sample are analysed.

A similar approach is proposed for the other four relevant impurities. They are being determined by GC/MS:
- For CS formulations the sonication time is fixed to 15 minutes to avoid degradation and isomerisation of the relevant impurities. And to compensate for the possibly incomplete extraction of the impurities as well as the AI from the capsules, the same sample is used

to determine the content of the impurities with GC/MS and to determine the content of the AI with the standard GC method (CIPAC method 239/TC/M/3).

Mrs De Benedictis concluded that although several changes to the existing CIPAC method 239 have been proposed, these changes are not considered to be fundamental changes. Rather they are primarily clarifications that should enable the experimentalist to generate valid results without the need for conditioning and intense pre-testing. They should not adversely affect the results of the collaborative trials done in the past.

Mrs De Benedictis proposed to accept these changes without the need for further collaborative testing and to include them into the methods prior to publication.

The following comments were received from the meeting:

- None

MT 190.2 pirimiphos-methyl by Mrs Susanne De Benedictis (4964)

Mrs De Benedictis presented some information about issues that had been found with the CIPAC MT method for the determination of the release rate of pirimiphos-methyl

Analysis of the same batches in different labs led to different release rates. Two factors were considered as potential causes:

- Type of roller (smoothness of the rolling motion / vibrations)
- Temperature during rolling

Tests have been done to prove / disprove these hypotheses

Two different types of rollers compared.

- Same bottle dimensions and rolling speed as described in the method
- Conclusion: The type of roller does not have a significant influence
- However, if a different roller is used than the two here, there may be more significant differences

In order to test the hypothesis that the temperature during rolling is the primary cause of the differences, a preliminary test at different temperatures was performed (all other parameters were kept the same):

- Release rate after 15 minutes is quite independent of the temperature
- Experiments were conducted with the same batch at different temperatures.
    - Release rate after 15 minutes is quite independent of the temperature

Propose to only determine the release rate after 15 minutes and to change the specification accordingly:

- This value gives sufficient evidence that the AI is released slowly from the capsules.
- From the analytical point of view there is no need to be able to control the temperature of the bottle on the roller.
- Some labs may have difficulties to keep such equipment between 20 °C and 25 °C.
- As a consequence, the method has been changed to only refer to a rolling time of 15 minutes

Mrs De Benedictis concluded that the next steps were to

- Firstly decide whether or not to change the published specification accordingly.
- If the change is being adopted, CIPAC method 190.2 would have to be changed as described.

The following comments were received from the meeting:

- None

6.2 Revision/Update of guidance documents

JAPAC are considering whether to substitute helium carrier gas with nitrogen in GC methods and they have presented a poster during the CIPAC symposium showing the comparison of some of the methods using different carrier gases. When the CIPAC guidance for the scope of

extensions to a method is used this could be considered a major/minor change or a change to chromatographic conditions. JAPAC would be interested to know members views on this proposal. In particular what would the status of the method be if the carrier gas is changed? Should this be a guidance issue? It was noted that nitrogen is not given as a carrier gas in the current guidance for CIPAC methods.

The following comments were received from the meeting:

- I am against replacing helium with nitrogen as carrier gas. If you have had the chance to compare the performance of the separation using helium with that using nitrogen in my view the resolution is lower and retention times increase when you use nitrogen. It is well known that good quality helium gas to use for GC is expensive.
- In my experience I would recommend hydrogen rather than nitrogen if you are looking purely to lower costs. Hydrogen gives better performance than nitrogen and is more akin to helium.

These comments indicate that a revision or update of our CIPAC guidance is needed. This has been mentioned briefly at a previous meeting but unfortunately CIPAC have not had the opportunity to provide an updated draft. The Chairman and Secretary will begin work on a draft revision and send round for comments.

Closing remarks

The Chairman requested a call for comments on the following:

- Template for submission of National Control analysis data: please send any comments/issues with these to the Chairman and Secretary. Comments will be discussed with Mr Jim Garvey with the aim of a revised version being sent out at the end of 2014 for further comments.
- Review of Handbooks G & H. ESPAC has completed the work. A draft proposal will be placed on the CIPAC website shortly for comments.

The Chairman, Mr Hänel, thanked all the presenters, all participants of the collaborative studies and all meeting participants for their comments. He remarked that CIPAC are always willing to listen to proposals on how to improve the system.

Mr Hänel declared the open meeting closed.

7. Minutes of the 57th meeting (4933/P)

The minutes were circulated to members by e-mail. No corrections or comments were received therefore the minutes were accepted.

8. Secretary's report (4934/P)

Mr László Bura presented the Secretary's report for the period from the 57th CIPAC meeting held in Kyiv, Ukraine, 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.

9. Discussion of individual compounds

789: Amisulbrom

At the 57th meeting, 2013 in Kyiv the method was adopted as provisional. No further comments were received.

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

333: Deltamethrin (LN, incorporated, ext.)

At the 57th meeting, 2013 in Kyiv it was concluded that extension of the scope of CIPAC method 333 (CIPAC/4673) for the determination of the total content of deltamethrin in incorporated PE LN formulations remains as a **provisional** CIPAC method as the wash method was not finalised. As the wash method has been now been finalised this method can be promoted to a **full CIPAC method**.

709: Nicosulfuron

At the 57th meeting, 2013 in Kyiv it was agreed that pending the comparison of extraction solvents and provision of the additional information the extension can be adopted as provisional. No further comments were received.

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

715: pyriproxyfen

At the 57th meeting, 2013 in Kyiv the method extension for pyriproxyfen was accepted as a provisional CIPAC method. No further comments were received.

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

MT 179 Degree of dissolution and solution stability

At the 57th meeting, 2013 in Kyiv it was agreed that the extension could be accepted as provisional, becoming MT 179.1 No further comments were received.

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

MT 197 Disintegration of tablets

At the 57th meeting, 2013 in Kyiv it was agreed that the method could be accepted as provisional. No further comments were received.

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

Alpha-cypermethrin

The meeting considered that sufficient information had been provided to demonstrate the applicability of the method.

It was confirmed that the existing method for the determination of alpha-cypermethrin incorporated into filaments is applicable for VEERALIN, a new LN containing alpha-cypermethrin and piperonyl butoxide.

Brodifacoum

The meeting discussed the comments received during the open meeting.
It was agreed that although the approach of providing pre-weighed standards was unusual it was understandable. The issue was that the organiser could not send out sufficient analytical standard on its own as this would not have been able to pass through customs so they used the pre-weighed samples as a solution to send out less material. This is unusual but given the toxic nature of brodifacoum acceptable.
The way the method was written was slightly confusing given that pre-weighed samples and standards were provided. This will be relayed back to the company so that the method description is clearer.

The meeting agreed that pending this clarification the method can be adopted **as provisional**.

Hexazinone

The meeting discussed the comments received during the open meeting.
It was noted that although data for the method for hexazinone were provided, no data had yet been provided for the method for the relevant impurity.

It was confirmed that the existing method for the determination of hexazinone in WG formulations is applicable for Hexazinone WG manufactured by SHANGYU NUTRICHEM CO., LTD. with a modification in standard and sample preparation, consisting of a twofold dilution

PBO

The meeting considered that sufficient information had been provided to demonstrate the method extension was acceptable.

It was confirmed that the existing method for the determination of PBO content in polyethylene LN (incorporated into filaments) is applicable for VEERALIN, a new LN containing alpha-cypermethrin and piperonyl butoxide with a modification in the standard weight in the stock calibration solution and sample weight.

Pyraoxystrobin

The meeting discussed the comments received during the open meeting.
The meeting considered that the proposed sonication time of 15 minutes was too long and it was agreed that the description for the sample preparation should be amended to clarify that this time is only needed if there is an issue with dissolution of the SC samples
The meeting also reconsidered whether the addition of a small amount of water would be helpful to aid dissolution. The trial was conducted without this step included in the method so it was questioned whether the method should be amended seeing as it has not been tested.
The trial organisers have said that after they had received the comments on the addition of water they did try this and it made no significant difference. The meeting was reminded that this issue was also discussed last year during the small scale trial. It was agreed that this would be clarified with the trial organiser.

The meeting agreed that pending these clarifications the method can be adopted **as provisional**.

Quaternary ammonium compounds

The meeting considered that sufficient information had been provided to demonstrate the method was acceptable

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

Silthiofam

The meeting discussed the comments received during the open meeting.
The main issue was whether or not an internal standard was really needed for the method. According to the presentation of results given to the open meeting an internal standard was necessary.
One member commented that during the trial they had issues with the instrument and that the internal standard had meant that their results were still accepted so there may be some advantages to using an internal standard.
The meeting considered that if the full scale trial was conducted with the internal standard then it will be possible to consider the data both with and without the internal standard. A decision can then be made after the full scale trial as to whether the internal standard is really necessary.

The meeting agreed that a **full scale trial should be conducted with the internal standard.**

Trifloxystrobin

The meeting discussed the comments received during the open meeting.
The meeting considered that the proposed sonication time of 15 minutes was too long and it was agreed that the description for the sample preparation should be amended to clarify that this time is only needed if there is an issue with dissolution of the samples.
The meeting also discussed whether the proposed injection volume of 3 µl was acceptable. It was noted that no remarks from the laboratories were presented to the open meeting so it was not clear if other laboratories had had issues with the smaller injection volume. From the response from the company it appears that some laboratories did use 5 µl. The meeting agreed that as the method states to use 3 µl this should remain but a footnote could be included to indicate that injection volumes up to 5 µl are also appropriate.
The meeting agreed that a clarification in the method about the short retention time would also be useful.

The meeting agreed that pending these clarifications the method can be adopted **as provisional**.

Release/retention rate for pyriproxyfen matrix release formulation

The meeting discussed the presentation given during the open meeting and the comments received
The meeting considered that the first step would be to get confirmation from WHOPES as to whether they need release rate in the specification for the new formulation. It was noted that currently there is no specification template for matrix release formulation as it is a novel formulation. The draft specification is currently under development however it is expected that the JMPS will ask for data on release rate for this product.
The meeting was reminded of the issues with LN methods and washing methods that meant it was many years before suitable methods were available. Is the use of ethanol/water designed to be a model to mimic what would happen in the water bottles to allow a specification that can be tested quickly?
It was noted that in the presentation it was shown that the active ingredient content slowly decreases over 6 months and that the company are trying to model a test to cover this. It was questioned whether this is really determining the release rate or just the amount of active ingredient that is retained in the product over time?
The WHO explained their understanding is that once the water jug containing the formulation is emptied completely, if you add more water to the container, through the process of diffusion the active ingredient content will increase and then becomes effective again. The 6 month period is the period of efficacy that the company is claiming but this has not yet been tested by WHOPES
It was agreed that there are two ways to measure the release index you can either measure what is retained in the formulation after time or what is in the mixture (i.e. the treated water). Perhaps retention index might be a better way to refer to this test.
The company had data that showed the tests could distinguish between a good and bad product, but it's not clear what a bad product is. Does a bad product not release active ingredient rapidly into water? Or does it not contain enough active ingredient to be effective? The time taken to reach an effective concentration in the water will depend on the volume of water (i.e. 1 L will reach saturation quicker than 10 L).
The rate of release has to be controlled. It cannot be too fast or too slow. The correct amount needs to be correlated with WHOPES trials to see what is good or bad product in the field.
Once this has been resolved then this product should be modelled to develop a CIPAC method.
Critical factors that need to be considered when developing this method:

- The product is intended to be used in potable water so how much of the insecticide is

available is a critical factor as you cannot exceed risk assessment values.
- How fast the product is releasing active ingredient as the water is replenished.
- How can we prove the long lasting 6 month effect? This is the most challenging. This is not a "fast kill" product it's designed to regulate the growth of new larvae. All this will become clearer as WHOPES develop their testing.
- All these details need to be worked out.

The meeting noted that the presentation was a first proposal and that two different protocols were suggested. The company will need to choose which model will be best for a small scale trial.
The meeting agreed to **feedback to the company that the concept seems reasonable, however there are many issues to be resolved and for next steps there is a need for a close co-operation with WHOPES to ensure the method is reasonable and applicable.**

Permethrin- enantioselective identity test

The meeting considered that sufficient information had been provided to demonstrate the method was acceptable

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

Transfluthrin - enantioselective identity test

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.

d-tetramethrin

The meeting discussed the presentation given during the open meeting and the comments received
It was noted that the company were presenting a method for comments and wanted to know whether they can conduct collaborative trials through CIPAC.

The meeting agreed to propose to the company **to conduct a small scale trial** in the first instance. The company should also **apply for an ISO common name** for their pesticide

Toluene-relevant impurity in formulations

The meeting discussed the comments received during the open meeting.
It was agreed that CIPAC should not state that the method is for a relevant impurity in the title as whether or not a compound is a relevant impurity is for regulatory authorities to decide and not CIPAC. It was agreed that the method will be published as an MT method for the determination of toluene in certain formulation types.

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

Extension of MT 46.3 to LN

At the 55th meeting, 2011 in China the method was adopted as tentative with some further work on validating the method required.

At the 57th meeting, 2013 in Kyiv it was discussed that no validation data has been received as the focus for the "LN group" had been on finalising and collaboratively testing the washing method for LNs. Now that the washing method has been finalised work to validate this method further is on-going. The method remained tentative.
The meeting considered the new collaborative study presented at this years meeting.

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

Equivalence of CIPAC MT Methods

It was not clear why CIPAC should get involved with this issue. It is a problem that the Industry and National Regulatory Authorities need to resolve amongst themselves.
CIPAC already have a statement on the website to clarify that methods considered obsolete or no longer supported can be accepted by National Regulatory Authorities. Should we strengthen the wording on the CIPAC website?
This could be a tool to help to try to determine the equivalence of methods. For e.g. when FAO/WHO consider a revision of specification we need to update the methods and ensure that the products can still comply with the same clauses once the method has been updated.

The meeting agreed to send a **message to DAPF to ask them to explain further** what the benefits of this will be for CIPAC.

10. Matters related to FAO and WHO specifications
There were no issues.

11. Any other business

It was noted that several MT methods have recently been revised and updated to change the temperature at which the test is conducted from 30 °C to 25 °C. Is it planned to revise all the MT methods? The meeting were informed that DAPF are proposing to do exactly this. They are currently gathering data and they will present at the next CIPAC meeting.

There is a growing interest in developing multi pesticide methods. How will CIPAC deal with this as we do not have procedures to allow multi-residue methods except in exceptional cases? It was noted that 10 or 15 years ago the same question was asked. Whilst a multi-pesticide approach would be of great use to the national control laboratories, it is unlikely that multi-pesticide methods will be proposed to CIPAC as the methods are proposed by industry and there may be no benefit to Industry to propose these methods. In terms of CIPAC methods the process would be the same if the method is able to determine 1 or 25 pesticides. However, we need someone to propose the trial.

It was noted that, again, reports are either received too late or not at all before the meeting. This does not allow for careful consideration of the methodology in advance. This subject has been discussed previously and CIPAC made it clear that information should be submitted 2 weeks before the meeting. If it is later than that we cannot guarantee that the method will be discussed. The meeting were reminded that CIPAC members have the opportunity to refuse to discuss something if it is received too late.

12. Closure

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

Sonia Tessier	László Bura
Assist. Secretary	Secretary