CIPAC

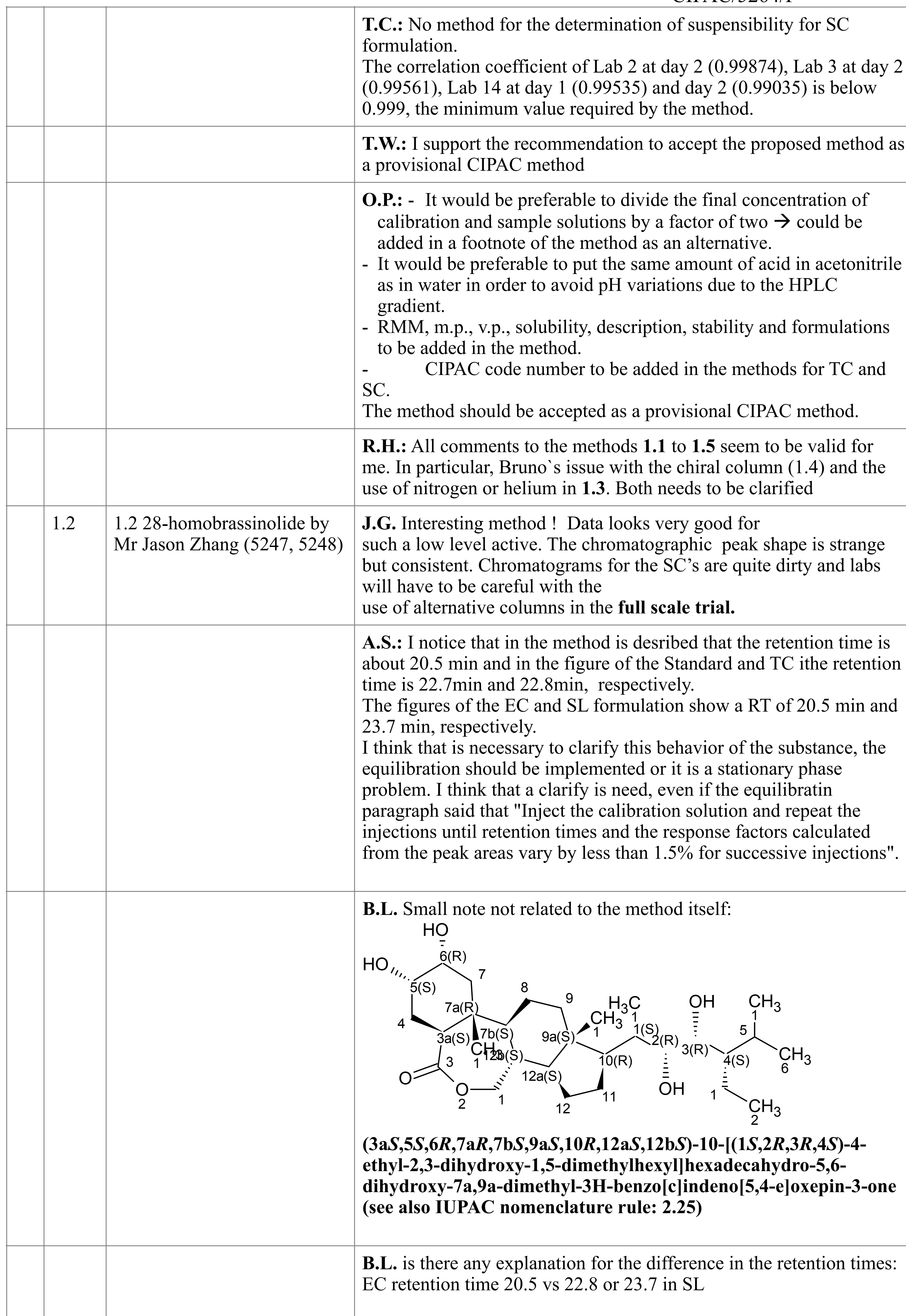
COLLABORATIVE INTERNATIONAL PESTICIDES ANALYTICAL COUNCIL LIMITED

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

MINUTES OF THE 64th ANNUAL MEETING

The 64th virtual meeting hold by correspondence.

		Reports	Comments
1	1.1	florasulam by Mr Eric Zhao (5257, 5258)	**J.G. No issues,** seems like a robust method. There is a wide variation in the retention time between columns but the chromatograms look very clean so I don't see any selectivity problems.
			B.L. In the description of the method: „Typically, the correlation coefficient should be 0.999 or better. If not, repeat the calibration" Did laboratories 3 and 14 report the reason why their calibration lines didn't meet the requirements set by the method? lab 3 day 2 calibration r<0.999 lab 14 day 1, lab 14 day 2
			From last year's minutes: ➢ Mrs Nováková asked whether the addition of a small amount of water, prior to the addition of acetonitrile was tried to enhance solubilisation of florasulam. Mr Zhao replied that this was not tried as there were no problems in the analysis of the samples. **Comment from Lab. 7:** The SC samplescannot be dissolved completely in pure ACN with ultra sonification.After adding mobile Phase A and approx. 60 minutes ultra sonification they are dissolved completely. I prepared every sample in the same way: **B.L.** Would this addition of water/mobile phase be necessary for the sample preparation?
			CZ: Laboratory 13 changed chromatographic conditions (= temperature, flow rate, inject volume, no gradient). **This data should be excluded from the statistical evaluation**. According to AM preparation of florasulam in SC formulation is: Add 40mL ACN in the flask, place flask in the ultrasonic water bath… There is not mention time of sonification. One remark from participant (lab. 7, remarks 4) was that time of sonification is 60min! My proposal is to add to the method time of sonification /or better the addition of a small amount of water, prior to the addition of acetonitrile. It can reduce the time of sonification.
			T.R.: Table 2 Two HorRat values <0.30, an explanation is missing In TC-2 one Grubbs outlier was identified but was still incorporated in the dataset. No statistical evaluation of the same dataset with the outlier removed
			B.P.: Remark: Please inform the company to send the participant her individual results. Actually, we missed this information.



			T.C.: No method for the determination of suspensibility for SC formulation. The correlation coefficient of Lab 2 at day 2 (0.99874), Lab 3 at day 2 (0.99561), Lab 14 at day 1 (0.99535) and day 2 (0.99035) is below 0.999, the minimum value required by the method.
			T.W.: I support the recommendation to accept the proposed method as a provisional CIPAC method
			O.P.: - It would be preferable to divide the final concentration of calibration and sample solutions by a factor of two → could be added in a footnote of the method as an alternative. - It would be preferable to put the same amount of acid in acetonitrile as in water in order to avoid pH variations due to the HPLC gradient. - RMM, m.p., v.p., solubility, description, stability and formulations to be added in the method. - CIPAC code number to be added in the methods for TC and SC. The method should be accepted as a provisional CIPAC method.
			R.H.: All comments to the methods **1.1** to **1.5** seem to be valid for me. In particular, Bruno`s issue with the chiral column (1.4) and the use of nitrogen or helium in **1.3**. Both needs to be clarified
	1.2	1.2 28-homobrassinolide by Mr Jason Zhang (5247, 5248)	**J.G.** Interesting method ! Data looks very good for such a low level active. The chromatographic peak shape is strange but consistent. Chromatograms for the SC's are quite dirty and labs will have to be careful with the use of alternative columns in the **full scale trial.**
			A.S.: I notice that in the method is desribed that the retention time is about 20.5 min and in the figure of the Standard and TC ithe retention time is 22.7min and 22.8min, respectively. The figures of the EC and SL formulation show a RT of 20.5 min and 23.7 min, respectively. I think that is necessary to clarify this behavior of the substance, the equilibration should be implemented or it is a stationary phase problem. I think that a clarify is need, even if the equilibratin paragraph said that "Inject the calibration solution and repeat the injections until retention times and the response factors calculated from the peak areas vary by less than 1.5% for successive injections".
			B.L. Small note not related to the method itself: **(3a*S*,5*S*,6*R*,7a*R*,7b*S*,9a*S*,10*R*,12a*S*,12b*S*)-10-[(1*S*,2*R*,3*R*,4*S*)-4-ethyl-2,3-dihydroxy-1,5-dimethylhexyl]hexadecahydro-5,6-dihydroxy-7a,9a-dimethyl-3H-benzo[c]indeno[5,4-e]oxepin-3-one (see also IUPAC nomenclature rule: 2.25)**
			B.L. is there any explanation for the difference in the retention times: EC retention time 20.5 vs 22.8 or 23.7 in SL

			B.L. it is not clear why Automatic sampler: 50µL is mentioned when 10 ul is injected? react 30min in calorstat at 50°C. probably a different description would be more convenient
			CZ: Why did laboratory 5 change column temperature and injection volume? Retention time of 28-Homobrassinolide according to analytical method is approx. 20,5min. Retention time of 28-Homobrassinolide on the chromatograms in AM are: 22,7 min for ST, 22,8 min for TC, 20,5min for EC sample and 23,75min for SL sample. Are the chromatograms from one sequence of measuring?
			T.R.: Slide 4-6 Seven HorRat values <<0.30, explanation? Method Example chromatograms show differences in retention time?
			B.P.: Particle size column 5 µm?, not so clear based on method and partly information from participants - Question/investigation? Why lab 3 have some stragglers, outliners - Examples of chromatograms SL, EC from participants (different column, equipment). Based of the example chromatograms from the method it seems not so easy to integrate the peaks correctly. Second Differences of the chromatograms between participants based on "type" of column? - Retention times in method, examples chromatograms quite different, 20.5 min method, examples 20.5, 22.8, 23.7 min. - Results look so far fine
			T.C.: The compound is synthesized using plant extracts as raw material, with 6 chiral centres in the molecular structure, and a derivative is formed and analyzed by HPLC. Considering the complexity of the matrix, it is suggested that a full validation report of the method be required to show the appropriate specificity, linearity, accuracy and precision. The difference of retention time between EC (20.515), SL (23.750) and Standard (22.712) from attached figures, exceeds 1.5% as the method requires.

			T.W.: (1) Common name I would like to point out that “28-Homobrassinolide” is not a common name of ISO. According to the information on the Alanwood home page, “homobrassinolide” has been used in the literature without official status in ISO, while the name of “brassinolide-ethyl” is approved only in China. (2) Retention time The peaks of 28-Homobrassinolide are shown in Fig. 2 – Fig. 5 in the document (5247) of analytical method. The retention times of this compound found in the chromatograms of Fig. 2 to 5 are significantly different. I suspect that these results are derived from several laboratories employing different equipment and conditions. Should they be from a single laboratory under the same condition, the variations in relative retention time are more than 1.5%, which is the upper limit for identity tests as described in paragraph 2.1of the document. It is recommended to pick chromatograms from trials employing the same equipment and conditions, make sure that the variations in retention time are within acceptable ranges and replace Fig. 2 to 5 with these newly picked chromatograms.
			O.P.: Why is it necessary to derive 28-homobrassinolide with phenylboronic acid before HPLC determination ? - Method : (c) Preparation of standard and sample solutions → is a standard / sample weighing of 15 mg sufficient to ensure an acceptable uncertainty of measurement of the analytical method and the representativeness of the laboratory sample ? - The calorstat at 50°C should be described in the section Apparatus of the method. - On the chromatograms, the 28-homobrassinolide peak area in the TC sample solution is different from the peak area in the calibration solution despite the amount of 28-homobrassinolide is the same. Subject to the reply to questions and some clarifications, the method should be proposed to a large-scale collaborative trial.
	1.3	metribuzin by Mr Michael Haustein (5253, 5254)	**J.G.** Issues with the use of nitrogen and hydrogen as mobile phases. Might be worth putting in a note to say these are not recommended. **Otherwise data very good.**
			B.L. SC formulation, calculation Flame-ionization detection detects the amount of carbon in a sample, the total amount of ions is directly proportional to the amount of carbon in the sample. If we add 0.5 ml water in plus, and inject the same amount as for the standard, the amount of the IS injected is different and leads to a slight overestimation of the result. This is rather an academic discussion, however for corretness the mode of calculation or the mode of preparation should be updated.
			B.L. it is not clear why Automatic sampler: 100µL is mentioned when 1.5 ul is injected? Can the injection volume be changed according to some of the proposals in the comments?
			CZ: Method is O.K. and works well. Because of the statistical evaluation my proposal is to add to the method option for carrier gas: Helium or Nitrogen or Hydrogen.

			B.P.: For statistical evaluation, use all results. Carrier gas differences not so important in this case. Carrier gas has effect of the quality of separation, but based of the example chromatograms, this is in this case not necessary/relevant. - We had a quite strong fronting (participant) by this trial. The results was good, but was this an exception in our case or observed by other participant too? Summary: Fine for me → go to provisional
			T.C.: Replace R or R' with Hs or Hw in the Calculation equation. No method for the determination of Suspensibility for SC formulation. The identity test of WG ,WP and SC (2.2 UV spectrometry) is not used for TC.
			T.W.: I support the recommendation to accept the proposed method as a provisional CIPAC method.
			O.P.: It should have been useful to do the statistics with the 11 laboratories that used helium and the 4 laboratories that used hydrogen to see if hydrogen can also be used as carrier gas in the method. RSD_R < RSD_R(Hor) for 2 TC, 1 WG, 2 WP and 2 SC, RSDR > RSDR(Hor) for 1 WG and 1 SC. - 0.3 ≤ HorRat ≤ 1 without elimination of outlier / straggler, except for WG-1 and SC-3. RSD_R < RSD_R(Hor) for 2 TC, 2 WG, 2 WP and 3 SC with elimination of labs using nitrogen and hydrogen as carrier gas. - 0.3 ≤ HorRat ≤ 1 without elimination of outlier / straggler with elimination of labs using nitrogen and hydrogen as carrier gas. The method should be accepted as provisional CIPAC method, with recommendation to use helium as carrier gas
	1.4	quizalofop-P-ethyl by Mr Jason Zhang (5255, 5256)	**Data is good.** The stats are good without the elimination of outliers or stragglers and therfore **I don't see any issues.**
			CZ: 17 laboratories took part in the collaborative study of Quizalofop-P-ethyl by HPLC. Results of 16 laboratories were statistical evaluated. Data of one laboratory (Lab. 6) was not usable because the chromatographic column was change to Daicel ODH and enantiomers were not separated completely. In the report there is not more details about this column, but I noticed that the same or similar column were used also by laboratory No. 3 and No. 8. Laboratory No. 3 changed the ratio of mobile phase and injection volume. If you focus on remarks of the participant, only seven laboratories tested the method without changes (one of them only extended run time). 8 laboratories changed the method, mostly injection volume and/or ratio of mobile phase, lab. 16 changed also reagents in mobile phase. I would like to see statistical evaluation only from results which follow strictly the original method without changes.
			T.R.: Slide 12 Data of lab 6 not usable. Not clear why, explain. Slide 20-21 Sample A: RSDR without outliers (0.779) worse than with outliers (0.765)? Slide 23-27 All figures: what do all the coloured lines mean? All figures: the "L" is missing in the title of the graph: Quizalofop-P-ethy

			B.P.: Chiral HPLC, I'm not happy to mix here different columns, Chiralpak AD-H, Phenomenex Lux Chiralpak OD-H and Chiralpak AY-H. In these cases, you have to optimize the mobile phase to have a sufficient separation. Here I recommend using only the results with the correct column. Otherwise, we need a proposal from the organizer how we have to formulate the different columns in the method. I think in this case you cannot this formulate like colum XXX … or equivalent. However, the method looks fine and can promoted to provisional with this clarification
			T.C.: Regarding the Identity tests, since the active ingredient is the R-isomer only, and IR could not tell whether it is R, S or R/S, additional identity test may be required.
			T.W.: I support the recommendation to accept the proposed method as a provisional CIPAC method
			O.P.: The CIPAC method is not available in the CIPAC Members Area. - What are the changes from the last year chiral HPLC method ? It was recommended last year to replace hexane by heptane for safety reasons. Is a standard / sample weighing of 10 mg sufficient to ensure an acceptable uncertainty of measurement of the analytical method and the representativeness of the laboratory sample ? RSD_R < RSD_R(Hor) for 2 TC and 3 EC without elimination of outlier / straggler - 0.3 ≤ HorRat ≤ 1 without elimination of outlier / straggler Subject to the providing of the method and the reply to questions, the method should be accepted as a provisional CIPAC method
	1.5	spinetoram by Ms Jennifer Jones (5249, 5250)	**J.G.:** There seems to be a problem with the calculation of the HorRat ratio here. The values are not calculated using the RSD_R values quoted in the report. If they were all but SC2 and WG would be above 1 and DT would be above 2. **The company needs to be asked to check their calculations.**
			CZ: *From Report Minutes of the 63rd Annual meeting 2019, Braunschweig:* *As laboratory three was the only laboratory that consequently reported low results and used a reversed phase C18 HPLC column, the recommendation was made to only use a C8 column in the analysis of spinetoram TC and SC formulations.* 2020 results from coll. test: *7 laboratories used C8 column, 4 laboratories C18 column. Explanation of organizer: Based on statistical analysis, the modification of the column had no significant impact on the result.* I think that this method is O.K. also if C18 column is used. But we must comment original method. In this case I also prefer split statistical results for original method with C8 HPLC column without modification and for all results (C8 and C18 HPLC column). The same was done by Currenta for metribuzin (Carrier gas He and N2 or H2) see common comment to item 1.1-1.5:

			B.P.: Results look fine for me. The higher HorRat value by the DT formulation is acceptable for me (lower content an typically higher inhomogeneity by this formulation type). Clear, the sample for the trial was grinded, but anyway for me this result is typically and ok. - I'm unhappy with the different column types C18 instead C8 of this trial (for mit not equivalent). However, this seems the reality and the results are good. I prefer only differences inside the same phase e.g. C8. Different dimension are then ok, because in this cases you are quite sure that the separation is more or less the same (sequence of peaks). Anyway, the method looks fine and robust and can promoted to provisional. (it's not possible to delete all C18 participant (4) because the you have not enough results)
			T.C.: No identity tests in the method. The method is not drafted according to the template according to CIPAC guideline. For TC1, TC2, SC1 and DT, RSD_R is above RSD_R (hor). No method for the determination of Suspensibility for SC formulation.
			T.W.: I support the recommendation to accept the proposed method as a provisional CIPAC method
			O.P.: The information on spinetotoram should be added in the method. - Representative chromatograms for the calibration solution and TC, SC, WG and DT sample solutions should be added in the method. - The HorRat value should be added in the table of Appendix I. - It seems there is a confusion between %RSD and RSD_R RSD_R and HorRat values should be clarified before taking a decision on the acceptability of the method.

		General comments	**CZ: Common comment to item 1.1-1.5:** In all collaborative tests one or more participant (laboratories) changed chromatographic conditions and did not tested original method. In my opinion data from non-original method must be exclude from the main statistical evaluation. In the case of changes in original method, the statistical evaluation would be: **a) only for results made by original method** **b) for all results** The evaluation of results from collaborative test of metribuzin is very good example. If participant plan to change something in method e.g. chromatographic column it must be agreed by organizer of collaborative trial that the column is equivalent to original before the beginning of trial. It means at the same time when the laboratory registers for the trial. I know that usually the organizer of collaborative trial does not know in advance who from participants will change something in method and who will follow strictly original method. Organizer can receive more results from "modified" AM then from original AM. I think that nowadays there are a lot of participants who are willy to take part in collaborative trial. I suggest creating a list of participants who did not follow the original method. This list will be available for next organizer of collaborative trial and participants on the list will not take part in other trials for e.g. one year or more. (They will be able to take part in collaborative trial only in the case of lack another participant.) The list will be available e.g. at assistant of CIPAC who will send the list to organizer of coll. trial in advance or on the web side. The goal of this list is to reduce number of participants who change/modify original method.
			B.L.: The relative retention time of XY in the sample solution should not deviate by more than 1.5% (1, 2???) from that of calibration solution B.L.: We have these options in the methods, shouldn't we unify?
			B.L.: Equilibration of the system Pump sufficient eluent through the column to equilibrate the system. Inject 10µL portions of the calibration solution C1 and repeat the injections until retention times and peak areas vary by less than ±0.5% of the mean for three successive injections. Here we also have variations. The same question as before.
2	2.1	prothioconazole-desthio in prothioconazole by Mr Friedhelm Schulz (5251, 5252)	**J.G. No issues, this method is fine.** We've used it in our lab without problems.
			CZ: No comments. Very good method and evaluation!
			T.R.: Prothioconazole EC 250 HorRat <0.30 (three times) explanation?
			T.W.: I support the conclusion to accept the proposed method as suitable method for the determination of this impurity.

3	3.1	Validation of analytical methods by Ms Angela Santilio (5259) (draft guidance)	**J.G.:Seems OK to me.** The requirement for recovery experiments means that blank formulations will be required which in turn means that these methods can only be validated in this way by companies. **CZ**: **Line 103, 104, 105: there is link to Appendix 2 but in the text, there is not any Appendix** **T.R**.: Good starting point but should be further discussed **B.P.: -** No comment yet. What is the goal of the document? Guidance for analytical labs as in the introduction for CIPAC analytical methods? - In this case the guidance is for me too detailed. Example for a control lab it's nearly impossible to receive a specific blank formulation for a sample. **H.K.:** I think that it is well written, however I have two comments. See my comments on the document. It is not clear to me if the intention of providing such a document is for manufacturers or for official labs. If I remember well, this document should be useful (and be applied) by official labs. If it is correct then it should be revised accordingly. In any other case I think that it is OK.

T.W.: Specificity

In order to make sure that the effects of co-formulants are considered in evaluating the specificity of the MT method, for which the test samples are derived from formulations, line 61 should be changed as follows:

Interferences from impurities and co-formulants in the product should not contribute more than 3% to the total peak area measured for the target analyte.

Recovery (accuracy)

Because test samples of analytical MT methods are not necessarily plant production products themselves and include preparations derived from them, line 88~89 should be changed as follows:

The recovery of the method should be reported as mean recovery of the pure active substance in the test sample and relative standard deviation when applicable (n > 2).

Precision (repeatability)

For the same reason, line 98-99 should be changed as follows:

The precision (repeatability) of the method is required for the a.s. in the technical active substance and in the test sample.

Editorial comments:

Numbering is irregular, such as (i) Specificity, a) Linearity, b) Recovery, c) Precision and d) LOQ.

Ref 9 and ref 10, which appear in line 160 of the document, are not listed under the References (p. 5). On the other hand, ref 1 listed under the References, is not referred to in the body of the text.

O.P.: This draft guideline is a copy past of some paragraphs of the EU document SANCO/3030/99 rev.5. I am a little bit confused as at the CIPAC Managementy Comittee Meeting of last year, we decided to draft a guidance document setting up minimum requirements for validation of analytical methods used in MT methods. This new guideline may be redundant with the actual CIPAC guidelines on method validation to be performed in support of analytical methods for agrochemical formulations.
This should be further discussed next year

R.H.: Angela's proposal as a starting point is good. However, there is some need for clarification.
First of all, I think that the aim of this document should be more specific, i.e. criteria for analytical methods used in MT methods to determine ai / impurities by chromatographic techniques (or a better wording, just to make the propose very clear).
I agree that the document need further discussion. Maybe we can, after some amendments, distribute it very soon to the CIPAC community for comments. So that we will be hopefully able to finalise at next year's meeting.

4	4.1	Comments regarding the method mancozeb by Ms Claudia Vinke 34/TC/M and 34/WP/M	**C.V.:** As the new CIPAC method for Mancozeb could save time compared to the titration method we performed some studies with HPLC. Unfortunately, in Germany there is no WP product available so we used standard material from Dr. Ehrenstorfer, which is stable until March 2022. We were faced some problems: It was not possible to solve the standard according to the method description using ultrasonic only. After 65 min still some solid particles were visible. A complete dissolution was possible by manually shaking the standard solution for 2.5 min. Using a horizontal shaker with about 100 rpm dissolution was completed after 13 min. According to the method you need a minimum of 60 min to check the stability of standard solution C1 and additional a minimum of 30 min to check the quality of C2 compared to C1. We checked the stability by injecting C1 20 times in a row. The first 2 injections were outliers according to Dean&Dixon and had to be discarded. Therefore, we needed 90 min for checking the C1 stability. With an overall stability of 4 h for the standard solutions and sample solutions there are maximum 3 h left, realistically only 2.5 h for analysing samples. In a row, you can only analyse maximum 4 samples. Regarding our intra-lab requirements on method validation we are not able to validate the method in one sequence with repeatability, linearity and recovery. The method gives no information regarding the differences in the peak areas of C2. In one measurement we found a difference of 1.19 % between injection 1 and injection 2. Is this acceptable? For the measurement we used an Eclipse Plus C18 column (4.6 x 50 mm, 1.8 µm) instead of an Agilent Extent C18 (4.6 X 150 mm, 5 µm). This results in a retention time of approximately 3.1 min instead of approximately 7.5 min. In the method it is mentioned that also an equivalent column can be used. From the column material the column we used is equivalent. But we were faced a shift in the retention time during the measurement. In the stability test for C1 we observed a shift in the retention time. Taking the Dean&Dixon outlier into account the shift compared to the 1. Injection was higher than the given 0.5 % after 12 injections. Discarding these outliers, the shift was higher than 0.5 % after 13 injections. We also measured a sample from 2018 (WG formulation) and in this sequence we found a shift in the retention time for C1, too. This shift was higher than 0.5 % after 5 injections. But the method allows a shift of 1.5 %, so everything is okay. Regarding the sample from 2018 (a WG formulation) the HPLC method gave a concentration of Mancozeb of 595 g/kg, which is out of specification as the content should be 680 g/kg. The titration method performed in February 2019 gave a concentration of 692 g/kg. A repetition of the titration method is still pending but it seems unlikely that the degradation of Mancozeb in a formulation is 14 % in 15 months. We can report the results of the titration after we repeated the study. It is a pity that there are no WP formulation on the German market, otherwise we would do some further studies. If there is a possibility to get a WP formulation I would be happy to get a sample to perform some further studies with the method. I have one additional remark regarding the values for the repeatability r and the reproducibility R given in the method. The values are given in g/kg and not in %. Calculating the relative values for the TC with 850 g/kg r is between 1.06 % and 2.24 % and R is between 1.76 % and 2.82 %. Calculation of the Horwitz value for this concentration gives a Horwitz-RSDr of 1.37 % and a Horwitz-RSDR of 2.05 %. That means that r and R is partly higher than given by Horwitz. For the WP formulation with 830 g/kg the situation is even worse. I wonder whether this is acceptable for a CIPAC method as according

			J.G: We haven't used this method yet so my comments on Claudia's are purely theoretical. 1. **Paragraph 1&2 (Claudia)** If there are problems with the standard preparation then we are in trouble already. 2.**Paragraph 3 (Claudia)** On page 3 the method give a value of 1% for the acceptable variability of C2 or am I reading this incorrectly? 3. **Paragraph 3, last section (Claudia)** The discrepency between the results of the two methods is worrying ! 4. **Paragraph 5 (Claudia)** R value slightly higher than the Horowitz value gives a HorRat of just over 1.0 which puts it in the **"acceptable but requiring explanation"** zone. Given that problems have been identified with the method I would be reluctant to promote it to full method. **CZ**.: We noticed that in the HPLC mancozeb method is not enough specified compound EDTA. EDTA is an acid with very low solubility in water (0,2 g/L) and alone will not react with mancozeb. Different behavior has disodium salt Na2H2EDTA and tetra sodium salt Na4EDTA. These salts have very good solubility in water and can convert mancozeb to disodium salt nabam which is finally analyzed. In the method should be specified CAS No of EDTA to know which compound is really used. **Question for Claudia: Which compound of EDTA did she use?** According to AM calibration solution (and sample) in flask is placed in an ultrasonic bath until the sample has been dissolved completely (about 5 min, keep bath temperature not higher than 15°C). Environmental temperature must be below 20°C. **Did Claudia keep these conditions of temperature?** Temperature is critical step for reaction of mancozeb with EDTA to complete conversion of mancozeb into nabam. It seems that the conversion was not completed. **Solution B: Why sodium sulphite is used? And why is used in so high concentration (3g/1L)?** The first question was asked in Tokyo and question was not answered.
			T.R.: Mancozeb is not soluble in whatever solvent might be used. What is happening is that mancozeb disintegrates in EBDC (and other ions). Of course EBDC is not stable either. As a result mancozeb is not determined but the EBCD-ion is chromatographed and determined. Substances present in the formulation might influence the degradation process and therefore the HPLC method is only applicable to straight mancozeb based formulations. The remark about the validation parameters RSDr and RSDR is correct.

			H.K.: Last December we analyzed two 80WP samples containing mancozeb and we did not faced such problems during the analysis. Of course the method is a time consuming one, but the last version provides acceptable results. We used analytical standard from Sigma Aldrich with purity 97.5% and was dissolved very well according to the proposed procedures**.**
			● **T.C.:** Normally, the ultrasonic treatment is able to control the dissolution process in a more accurate and efficient way while achieving the equivalent result compared to hand shaking. That is why most CIPAC methods use ultrasonic instead of hand shaking. ● A shorter column with smaller particle size (1.8um) was used, which can cause a shorter retention time. ● The current method does not cover WG formulation. ● For r and R issue, I think there is a misunderstanding here. According to CIPAC guideline, r and R indicated at the end of the method is not used to compare with HorwitzRSDr or HorwitzRSDR to determine the acceptability of method validation. The RSDr and RSDR obtained from the statistical results of the collaborative trials do.
			T.W.: Our laboratory has a guideline that "equivalent columns" should be same in length, inner diameter, packing material and particle size. The column used by Claudia has shorter length and smaller particle size than those designated in the method, which could be the reasons for the shorter retention time and larger RSD. In order to decide whether the reported poor performance of this method is caused either by the analytical method itself or by the use of a column which is not equivalent with the one designated in the method, it is necessary to measure the retention time or RSD using a column of same length or exactly equivalent column if available. Alternatively, it may be useful to review the results of large scale study in order to see the effect of different types of columns on analytical results. In these considerations, it is important to compare the values obtained by the HPLC method with a true value (titration method). The CIPAC method should be enough validated because it is used for judgement of meet to specification. In case it is found that the use of columns with particular specifications is critical for the satisfactory performance of this method, it should be clearly indicated when the method is finalized.
			O.P.: The CIPAC TC Meeting of last year concluded that HorRat values should be calculated If $1 < HorRat \leq 2$, the method should be promoted to full CIPAC method for such a complex fungicide and because the HPLC method is really an improvement compared to the titration method

			R.H.: The issue here is for my understanding the lack of experiences using this method. Where is the misunderstanding concerning the validation parameters RSD_r and RSD_R. Claudia/Theo or Tim? I do not think that it is at the end of the day a helpful approach to argue that the HPLC method is easier than the titration method and therefore it should be accepted What is your opinion?
	4.2	Summary of New & Revised CIPAC MT methods (DAPF)	**J.G.: Seems OK to me.** The requirement for recovery experiments means that blank formulations will be required which in turn means that these methods can only be validated in this way by companies. **CZ**.: In the DAPF Document there is a wrong citation of CIPAC MT 30.5 (Handbook H). **Correct citation is CIPAC MT 30.5 (Handbook J).** R.H.: Let us create a disclaimer and afterwards we will publish it on our web site as a DAPF document (as already discussed). I will try to make a first proposal
	4.3	4.3 Revision of MT 190 Lambda-cyhalothrin slow-release CS (5260.5261)	**J.G**.: I don't know what the question is here, we have no proposal !! **B.P**.: Belonging the argumentation by Syngenta. Here, WHO has to decide, if this modified method makes sense for them and the WHO specification. From the technical and analytical point, more or less nothing change (only the calculation), so it's ok for me. Formal point: now method MT 190.1? , superseded method MT 190?. To discuss and decide by CIPAC **O.P.:** The code number of the revised method MT 190 should be changed to MT 190.1 - A paragraph describing the reason for revision as actually done for all revised MT methods should be added in the method. The revised method should be accepted as provisional CIPAC method
5		Minutes of the 63rd meeting (5244/P)	
6		Secretary's report (5187/P)	
7	338	acephate	Apart from collaborative trial we have not used this method. No products registered on the Irish market.
	454 + 570	Alpha-cypermethrin + chlorfenapyr	Apart from collaborative trial we have not used this method. Not much call for LN products in Ireland.
	91	atrazine	Apart from collaborative trial we have not used this method. No atrazine products registered on the Irish market.
	994	broflanilide	Apart from collaborative trial we have not used this method. No broflanilide products registered on the Irish market.
	997	"etpyrafen"	Apart from collaborative trial we have not used this method. No " etpyrafen" products registered on the Irish market. T.W.: *1 Could be accepted as a full method for "cyetpyrafen", instead of "etpyrafen", which is the provisionally approved ISC common name for this compound.
	465	hexaconazole	Apart from collaborative trial we have not used this method. No hexaconazole products registered on the Irish market.
	34	mancozeb	Not used, yet.
	737	spirodiclofen	Apart from collaborative trial we have not used this method. No spirodiclofen products registered on the Irish market.
		MT46.4	Not used, yet

R.H.: **7.** I agree that all can be promoted to full except the manoceb method. As mentioned above, more practical experiences are needed.

Limin's respons

Comments regarding the method mancozeb by Ms Claudia Vinke 34/TC/M and 34/WP/M	C.V.: As the new CIPAC method for Mancozeb could save time compared to the titration method we performed some studies with HPLC. Unfortunately, in Germany there is no WP product available so we used standard material from Dr. Ehrenstorfer, which is stable until March 2022. We were faced some problems: It was not possible to solve the standard according to the method description using ultrasonic only. After 65 min still some solid particles were visible. A complete dissolution was possible by manually shaking the standard solution for 2.5 min. Using a horizontal shaker with about 100 rpm dissolution was completed after 13 min. It is a pity that there are no WP formulation on the German market, otherwise we would do some further studies. If there is a possibility to get a WP formulation I would be happy to get a sample to perform some further studies with the method.	In my lab, powder sample is completely dissolved at pH 11 EDTA 20mmol solution under 40 kHz ultrasonic water bath within 5 minutes. If necessary, we would like to provide a video to show the whole process.
	CZ.: We noticed that in the HPLC mancozeb method is not enough specified compound EDTA. EDTA is an acid with very low solubility in water (0,2 g/L) and alone will not react with mancozeb. Different behavior has disodium salt Na2H2EDTA and tetra sodium salt Na4EDTA. These salts have very good solubility in water and can convert mancozeb to disodium salt nabam which is finally analyzed. In the method should be specified CAS No of EDTA to know which compound is really used. Solution B: Why is used? And why is used in so high concentration (3g/1L)? The first question was asked in Tokyo and question was not answered.	disodium salt EDTA-2Na is used with the CAS No: 6381-92-6. 3.72 g EDTA is used in the method and the molecular weight of EDTA-2Na is 372. sodium sulphite is added as antioxidant

metribuzin: Michael: after discussion of the below-mentioned comments from the virtual meeting with the colleagues from Bayer and Jiangsu Sevencontinent I would like to give the
following response from our side:

1. Carrier gas
   We would like to leave the method text unchanged with respect to carrier gas as the recommendations given below are completely opposite: one gives the advice to add the carrier gas option Nitrogen/Hydrogen, another recommends to state that the use of Helium is mandatory.

2. SC formulation, calculation
   A valid hint also given from the one or other participants. Therefore we decided that for determination of SC samples the respective calibration solution has to be prepared identically, that means also with pre-suspension with 0.5 mL of water.
   Will be presented in the revision of document 5253

3. We could not follow the comment given with respect to the autosampler and injection volume, respectively, as the method only describes the injection volume of 0.2 mueL and I could not verify this issue from the comments of the individual participants. Therefore, we would like not to take this remark into further account.

4. Apart from this remarks, the colleagues from Seven Continent found some issues in the method text which should be adapted for harmonization purposes. Therefore, we will add an additional section “suspensibility” for the SC sample. Moreover, we found that there is an inconsistency between the identity test for the TG (GC-MS) and the formulation types (UV).
   This failures also will be corrected in the revised document.