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**Rationale and Explanations for the Proposed Changes to the CIPAC Method 239 for Pirimiphos-Methyl**

In recent months Syngenta got aware of some issues related to the use of the CIPAC methods for the determination of this AI in formulations (specifically EC and CS formulations). Extended investigations and round robin studies have been performed to better understand the issue and to be able to propose changes to the current CIPAC method that improve clarity and minimize the potential for incorrect analyses.

The following issues have been observed:

1. When analyzing samples of formulated products, the results obtained for the AI content were significantly higher 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, we have added a statement in the method (on page 2) 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 on page 8.
2. When analyzing samples of the CS formulations, 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, we have added a sentence on page 3 informing the reader of the consequence of a low power bath for CS formulations. In addition on page 6 a statement has been added to limit the number of bottles simultaneously in the ultrasonic bath to three.
3. 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.
Thus, we propose to introduce a comment on page 3 of the method that the temperature may be increased slightly if it’s ensured that this does not lead to decomposition of the AI.
4. 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 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.
Thus, on page 6 we propose to change the sonication time from 15 to 60 minutes.
5. All these investigations also revealed the following possibilities to improve the consistency of the sample preparation for CS formulations: Adding a bit of water (2 ml) prior to sonication and discarding the first ml when filtering proved useful.
Thus, these changes have been introduced on page 6 as well.
6. 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 (see point 4 above). But this time period is not suitable for the determination of the isomer because this can lead to extended isomerization (CH3O-P=S and CH3S-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 (page 6). And for the CS formulations a statement has been added on page 7 that the sonication time for the determination of the isomer is 15 rather than 60 minutes. And 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.
7. 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 isomerization 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).

We are confident that all these changes improve clarity and will help the analysts to produce reliable results.

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