May 17th, 2014

**Rationale and Explanations for the Proposed Changes to the CIPAC Method MT 190.2 (Determination of Release Properties of Pirimiphos-Methyl CS Formulations)**

During the scale-up of the production of the CS formulation Syngenta got aware of some issues related to the use of this CIPAC method. Extended investigations and round robin studies have been performed to better understand the issues and to be able to propose changes to the current method that improve clarity and to improve reproducibility.

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. The same change has been proposed to the CIPAC method 239/TC/M.
2. When analyzing samples of the CS formulations in several labs, the release rate of the same batch showed fairly large variation. Closer investigation led to the assumption that the temperature during the rolling of the bottles may be a key contributing factor. To test this hypothesis, a preliminary test at different temperatures was performed. The following results were generated:

As can be seen in this graph the release rate after 15 minutes is quite independent of the temperature, whereas the release rate after 180 minutes varied substantially. The value for the low temperature experiment was indeed below the specification limit. To provide further evidence of the importance of the temperature during rolling, experiments were conducted with the same batch at different temperatures. The resulting data further support the hypothesis:

Again, the lower the temperature the lower the release rate after 60 and 180 minutes whereas the value after 15 minutes stays quite constant.
This information was shared with Markus Mueller and Olivier Pigeon beginning of May. Based on this discussion we now propose to only determine the release rate after 15 minutes. This value gives sufficient evidence that the AI is released slowly from the capsules. And 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 control to keep such equipment between 20 and 25°C.
Thus, we have modified the method to only refer to a rolling time of 15 minutes (on pages 1, 2 and 4).

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