Coordination Group (CG) e-consultation on storage stability and simplified authorisations

CONCLUSION FROM CG-30 (3 July 2018)

A CG member introduced the conclusions of an e-consultation related to data requirements for setting the shelf life of a product following a simplified product authorisation procedure at CG-30 (CG-29-2018-03) – please see Annex I of this document. The consultation was on whether it was possible to submit efficacy data to set the shelf life for a simplified authorisation instead of submitting long term and accelerated storage stability data.

At CG-30, CG members agreed the following in the case of a simplified authorisation in relation to storage stability (point (p) of Article 22(2) of the BPR):

- The shelf life of a product could be set based on either efficacy data OR long-term chemical storage stability data. The eCA is required to confirm the option chosen and summarise why it is appropriate for that case in the PAR.

- Accelerated storage stability data would not be needed in the case of the shelf life being supported by efficacy data.

- In all cases the analytical methods for analysing the concentration of active substance would need to be validated.

- Given that the active substances are included on Annex I and so already deemed to be intrinsically 'low risk', a case can be made by the eCA that an assessment of degradation products is not required when data shows an active content change of >10% and acceptable aged bait efficacy data are available.

- Applicants may provide storage stability data in addition to the above on a voluntary basis.

ANNEX I. SUMMARY OF DISCUSSIONS

1. Initial question from the UK – 21 May 2018

Background
The UK has a simplified authorisation question on which we would welcome Member States views.

An applicant does not currently have a complete and robust storage stability chemistry package and would need to conduct both long term and accelerated storage stability tests, and provide validation data and methods of analysis for each of the actives in the product. As an alternative, they would prefer to produce long term efficacy data to support the proposed shelf life of the product.

With the above in mind, we believe that the following points are relevant based on the BPR and previous CG/CA discussions on storage stability data for simplified authorisations:

1. Article 20(1)(b) of the BPR dictates what information should be submitted by an applicant in support of a simplified application. This includes an SPC containing information required in point (p) of Article 22(2), i.e. conditions of storage and shelf-life of the BP under normal conditions of storage. However, Article 20(1)(b) does not request a product dossier satisfying the requirements of Annex III which we would judge the core set (whereas this is a requirement for non-simplified products – Article 20(1)(a)(i)).

2. The CA paper on this subject (CA-May14-Doc.5.5 – Final) confirms point 1 above. However, the unclear part is the text in para (6) '*The Commission services consider that data on storage stability, stability and shelf life as requested in point 3.4 of Annex III of the BPR shall also be included in applications submitted…through the simplified procedure*' as they directly affect the efficacy of the product. Whilst we can agree that the shelf life links back to the efficacy requirement in Article 25, we are not clear why 3.4 of Annex III is quoted since Article 20(1)(b) of the BPR does not require it.

   CA-May14-Doc.5.5 – Final further states that '*Stability data could be waived where the applicant demonstrates that the product is efficacious by the end of the proposed shelf-life (i.e. data from efficacy tests using aged/stored product)*', which suggests that as long as the product is determined to still be efficacious for the proposed shelf life, efficacy data alone would be sufficient and chemistry data would not be required.

3. An additional CA paper (CA-March16-Doc.4.6 – Final.rev1), Q&A (4) in Annex I, also does not indicate the storage stability (chemistry) as a core requirement to support simplified applications.

Question
Are chemistry data on storage stability still required since a reference to 3.4 of Annex III is quoted in CA-May14-Doc.5.5 – Final, even where alternative efficacy data are available?

The UK CA believes that because Article 20(1)(b) does not require a dossier in accordance with Annex III for a simplified application, whereas other product application types do (Article 20(1)(a)(i)), that a chemistry stability study would not be defined as a core data requirement for simplified applications and efficacy data could be used instead to support Article 22(2)(p).

As such, for this application our view is that point (p) of Article 22(2) could be supported by efficacy data alone.

2. Update summary from the UK following initial 3-week e-consultation period – 21 June 2018

Summary of comments received
The UK received 4 responses from MS.

(i) One MS supported the UK view that as a full product dossier in accordance with Annex III is not required under Article 20(1)(b) of the BPR, and given the information in CA-May14-Doc.5.5 – Final that '*stability data could be waived where the applicant demonstrates that the product is efficacious by the end of the proposed shelf life'*, that efficacy data are sufficient to support the proposed shelf life and a storage stability study is not a core requirement for simplified authorisations.

(ii) One MS was in general regulatory agreement with the UK that data on storage stability were not obligatory for simplified applications. However, they judged that certain key parameters not provided via efficacy testing were important to support shelf life, such as visual observation of commercial packaging, colour changes and a loss of homogeneity, and also case-by-case other relevant changes such as pH if outside pH 4-10, suggesting that a general description of the product prior to and after storage should be provided.

(iii) One MS believed that storage stability testing and validation of analytical methods are required, judging, however, that long term data could be waived if an accelerated study plus efficacy data on stored product demonstrating the product effective at the end of the shelf life were provided. They also felt that flexibility options such as efficacy data were useful for when storage stability testing is not possible.

(iv) One MS was not in favour of general waiving of storage stability testing or replacing this with efficacy data. They judged the efficacy option in CA-May14-Doc.5.5 – Final as secondary data applicable only in either supporting cases (difficult to conclude from storage stability data alone, degradation products mentioned) or exceptional cases, also citing the general physchem guidance that storage stability studies are a primary requirement. In addition, the MS believed that validation data and methods of analysis for each of the actives are always necessary.

Conclusion and proposed way forward

Two MS judged that efficacy data alone can be used to support shelf life for simplified authorisations. Three MS judged that storage stability data are required but had differing views on how these data should be presented, i.e.

- A general description of the product prior to and after storage is required to include, for example, visual observation of commercial packaging, colour changes and a loss of homogeneity, and also case-by-case relevant changes such as pH if outside pH 4-10.

- Long term data could be waived if an accelerated study plus efficacy data on stored product are available demonstrating the product effective at the end of the shelf life. Validation of analytical methods also required.

- Storage stability testing and validation of analytical methods are required. Efficacy, together with degradation products information, viewed as supporting data where applicable.

MS recognised that flexibility is useful in certain circumstances, such as when chemistry stability testing is not possible.

Against this background no consensus was reached and so the UK propose further discussion at CG-30 to gain additional MS input. To facilitate this process and based on the comments received to date, we propose the following points for discussion:

- Given that the data requirements for Annex III are not required in Article 20(1)(b) of the BPR, is there a legal basis to request a core accelerated or long-term storage stability study in support of a simplified authorisation application when other data are available that support the shelf life, e.g. aged bait efficacy?

- In the absence of a core accelerated or long-term stability test, what are the key physchem parameters required to support Article 22(2) point (p) and Article 25 in cases where other data are available that support the shelf life (such as aged bait efficacy), e.g. validation of analytical methods?

- In the presence of a core accelerated or long-term stability test, are there any additional physchem parameters required to support Article 22(2) point (p) and Article 25, e.g. validation of analytical methods?

- If a long-term storage stability study shows an active content change of >10%, if acceptable aged bait efficacy data are also available would an assessment of degradation products be required, given that the actives are included on Annex I and so already deemed to be intrinsically ‘low risk’?