January 2021

Implementation of the REACH Action Plan for Review/Improvement of Registration Dossiers

= Summary report of the pilot project =

1. Introduction

On 26 June 2019, Cefic launched an unprecedented action aimed at proactively and systematically reviewing and improving, if needed, the data previously submitted in REACH registration dossiers. The Cefic multi-annual Action Plan provides a framework for REACH registrants to evaluate the safety data in a stepwise manner. Within the framework of this Action Plan, a Cooperation Agreement has been established with ECHA. More information is available on Cefic's website[1].

The Cooperation Agreement with ECHA foresees that Cefic and ECHA run a pilot project. With the active participation of a small set of volunteer companies and ECHA, the objective of the work was to select substance case studies and to explore different read-across approaches and respective testing strategies, with a view to generate data to improve compliance of registrations under REACH, and for industry to better understand ECHA's expectations. The learnings from this pilot are intended to inform the broad community of companies having committed to the Cefic Action Plan about steps to consider when reviewing and improving the content of their dossiers.

2. Pilot project – approach taken

The pilot project ran from December 2019 until October 2020 and was designed as follows:

1. Volunteer companies and ECHA agree on the (group of) substances, within the companies' portfolio (in one case, one substance triggered work on a whole category covered by a consortium), that could merit an improvement of the data in their dossiers;
2. Volunteer companies /consortium establish a testing strategy that would allow for the improvement of the data in the selected dossiers;
3. ECHA provides their feedback on the company's / consortium's proposed testing strategy;
4. One meeting between all parties is organised to discuss the arguments presented and to agree on the best way forward;

[1] https://cefic.org/our-industry/reach-dossier-improvement-action-plan/

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5. Companies demonstrate the commitment to the agreed way forward by submitting their testing strategy in their dossier updates, testing proposals and confirmation of CRO (Contract Research Organisation) for commissioned lower tier studies.

The pilot project consisted of four case studies, involving groups of substances registered by the three volunteer companies. Each case study is described below and some final considerations on the process followed are also presented. The volunteer companies worked in collaboration with their respective consortium, where necessary.

In each step, Cefic was present to facilitate interactions between all the participants involved in the project and ensure compliance with competition law. Lessons with wider application to all registrants have been collected and described in a detailed report that has been made available to the signatory companies. In addition a workshop was organised in October 2020 with signatories to the Cefic Action Plan to explain the learnings (with almost 200 participants).

3. Summary of the learnings

ECHA clarified at an early stage that, when preparing a testing strategy based on grouping and read-across, the following information prepared by the registrant should be provided:

- *Well-defined category of substances, with clear boundaries;*
- *Unambiguous SIP (Substance Identity Profile), adequate information on registered substances and proposed test materials;*
- *Read across hypothesis;*
- *Complete Annex VII/VIII data, considering adaptation possibilities, and/or other supporting data to support the read across hypothesis (e.g. toxicokinetics);*
- *Documentation of the testing strategy and its timeline;*
- *For a category of mainly Annex IX/X substances, experience shows that 30-50% higher tier studies with data from the registered substances is needed to support the read across hypothesis. Deviations to these percentages are possible with the proper justification (e.g. worst case, very similar compositions);*
- *Timely updates and provision of final read-across justification document, data and adaptations.*
- *Testing proposals (TP) only for the sub-set of substances which require testing in line with the strategy, should be submitted at early stage.*
    - *e.g. To generate standard information for Human Health endpoints at Annex X this requires TPs for 90-day repeated dose toxicity (RDT) and 1st/2nd species prenatal developmental toxicity (PNDT), extended one-generation reproductive toxicity study (EOGRTS); TP for EOGRT only examined after 90-day study available.*

The final review and endorsement of the category approach is possible only when all the higher tier studies, any needed supporting data and updated registrations have been provided.

Some of the key findings from the pilot project:

- All parties involved in the project acknowledged the good work, collaboration and relevant scientific discussions on the pilot testing strategies. A significant amount of work was carried out leading to useful learnings on both ECHA and industry sides. The projects have provided a significant opportunity for the companies involved to improve the information in their registration dossiers and to successfully implement grouping and read-across approaches.

- Overall, it was concluded that since each case that was discussed is complex and needs specific considerations and approach, the development of more generic guidance may not be particularly helpful. More examples and sharing results of actual case studies is expected to be more appropriate. This could be the subject of future workshops.
- Registrants should consider updating their dossiers before establishing a testing strategy to further improve the data quality of the dossier. Any considerations made by ECHA on the proposed strategy are developed on the basis of the existing information in the registration dossier.
- The discussions on the four case studies clearly have provided more clarity on the 'conditions' that testing strategies should fulfil (using the Read-Across Assessment Framework as a basis) and clarified that a science-based category justification needs to be supported by a significant amount of data (lower tier (Annex VII/VIII) bridging studies and/or toxicokinetic information).
- Clear and unambiguous substance identity of the registered substances and the proposed test materials is of critical importance.
- In all four cases, testing strategies were developed that include the need for more testing for a subset of substances in the category. Overall, provided that the category is scientifically acceptable, this would lead to less testing than if testing would be required on each single substance (which would be the case if a dossier does not pass the Compliance Check).

It was concluded that if registrants demonstrate a clear commitment towards their proposed testing strategy and defined timelines (e.g. via Testing Proposals), this can be taken into account in ECHA's further evaluation planning.

4. Concluding remarks and next steps

This pilot project has helped industry reach a better understanding of ECHA's expectations for a compliant read-across approach based on four diverse and complex case studies. While every case is different and needs specific considerations, many learnings can be re-applied, in particular:

- Science-based read-across adaptation needs to be supported by a justification and a significant amount of data;
- All cases led to more testing to justify the read-across approach, but ultimately, if the read across holds this leads to less testing than if the Compliance Check fails and testing is required on each single substance;
- The practical organisation (consortia management) can be challenging, in particular for bringing in new group members (e.g. due to including additional substances in the category);
- Some concerns were also raised concerning the timely availability of laboratory capacity; and
- ECHA can provide feedback, but responsibility remains with the registrants to make the case.

Moving forward, ECHA intends to further cooperate with companies/consortia that are willing to proactively submit testing strategies covering groups of substances, within the limits of its resources.

The experience gained with the pilot projects has been used to propose a process outlining future interaction of ECHA with companies within the framework of this Action Plan: companies have the possibility to inform ECHA of their review/update intentions and whether a testing strategy would be submitted to ECHA for feedback. ECHA foresees that it can handle interaction with industry on at least six testing strategies in 2021, provided these strategies are submitted in a staggered manner over time. In case a higher number of groups are proposed, ECHA will clarify which ones can be taken on board, based on its own planning.

HOW TO BECOME A SIGNATORY COMPANY: All material and explanations are provided on the Cefic website: https://cefic.org/our-industry/reach-dossier-improvement-action-plan/

Disclaimer: *it is for each individual company to ensure compliance with the duties and obligations arising from the REACH Regulation. The present document intends to capture the content of this pilot project. This report is to be relied upon at the user's own risk. No liability will be accepted for damages of any nature whatsoever resulting from the use or reliance on the information contained in this report.*