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FOLLOW UP TO ENVIRONMENTAL IMPACT ASSESSMENT (EIA) TRAINING
https://vichsec.org/en/training/module-4.html

QUESTIONS AND ANSWERS ARISING FROM THE TRAINING PRESENTATIONS
FEBRUARY 2022

Question 1: What types of analyses would be expected for a Tier C evaluation?

The question relates to VICHGL 38 – Phase II guidance. The guideline provides a tiered approach to the EIA, with the first tier (Tier A) using simpler, less expensive studies and conservative assessment factors to perform a conservative assessment of risk. If Tier A analysis leads to a prediction of unacceptable risk, the applicant will need to progress to a Tier B analysis. The aim of Tier B analysis is to refine the EIA by conducting ecotoxicity studies using more sensitive endpoints and longer exposure durations. Tier B studies reduce uncertainty allowing for lower assessment factors to be used in predicting risk. A trade-off is that these studies are more resource intensive.

In some cases the outcome of a Tier B analysis may still be a prediction of unacceptable risk. In these cases, the assessment will need to progress to Tier C. The types of studies that are needed for Tier C will be determined on a case-by-case basis, taking into account the specificities of the chemical substance/product under investigation and the environmental compartment or organisms that are of highest potential risk. Tier C studies would be aimed at either refining the effects assessment or the exposure assessment. For example, Tier C studies or analyses could include a species sensitivity distribution analysis, a targeted monitoring study, or generating modelling data.

As Tier C studies and analyses are substance/product specific, and specific to the environmental compartment or organism at risk, there needs to be some interaction between the applicant and the regulatory authority in order to determine the type of studies that may be needed.

Question 2: There are Organization for Economic Cooperation and Development (OECD) guidelines that relate to Tier A and B testing. In contrast, there is no internationally recognised guidance on Tier C studies. Are there any plans to develop relevant guidance?

As highlighted in the response to Q1, Tier C studies tend to be substance/product specific and specific to the environmental compartment or organism at risk, and consequently development of general guidance would be difficult. However, on a case-by-case basis, authorities might make use of guidance developed by other national or foreign regulatory authorities. For example, the United States (US) Environmental Protection Agency (EPA) has guidance on conducting a species sensitivity distribution analysis, and the US Food and Drug Administration (FDA) may make use of these.

In general, a guideline would only be developed if an area of concern was seen repeatedly. In the European Union (EU) there is some Tier C guidance available on toxicity to terrestrial plants (Plant testing strategy in the risk assessment for veterinary medicinal products | European Medicines Agency (europa.eu)). Several antibiotics were observed to cause toxicity to plants and thus it was considered beneficial to develop guidance on the topic. A Reflection Paper relating to the effects of parasiticidal products on dung fauna has

also been developed (Higher tier testing to investigate the effects of parasiticidal veterinary medicinal products on dung fauna | European Medicines Agency (europa.eu)).

Question 3. The presentation on the requirements of the EIA in Japan indicates that an environmental risk assessment is not part of the legal requirements in Japan but the guidelines have been adopted by the industrial associations. Is an EIA required in Japan?

The EIA is not a legislative requirement in Japan. It is an area in which the industry self regulates. Veterinary Medicinal Product (VMP) applications include the EIA in the technical dossier and this is assessed by the regulatory authorities. Where appropriate, a Tier B analysis should be provided and the regulatory authority may suggest further studies, as necessary.

It is not possible to refuse an authorisation based solely on the results of the EIA. Consequently, where other assessment areas conclude positively for a product, the regulatory authorities work with the applicant to try to find a way to minimise environmental impact, particularly by agreeing on appropriate risk mitigation measures to include in the product information.

Question 4: What type of risk mitigation measures might be implemented in relation to EIA?

Relevant mitigation measures might include reducing the dose to a level that is still effective but results in less environmental risk, or restricting the use (and hence environmental exposure) to certain animal classes or to only in animals of lower body weight.

It may be possible to work with other regulatory authorities on mitigations. For example, the US FDA has derived water quality benchmarks for some aquaculture drugs that can be used by the US EPA to mitigate potential environmental impacts through the US EPAs permitting authority.

In Japan the relevant part of the Product Information would be expanded to emphasise relevant concerns, highlighting uses that pose a particular risk. In some cases the most risky uses may be eliminated from the licence.

Question 5: To what extent is disposal considered in the evaluation. For example, might the impact of disposal of unused product by incineration be considered?

In the EU the evaluation focuses on the intended use of the product without specific consideration of disposal of unused product. The environmental impact resulting from improper disposal of materials from manufacturing sites is also not part of the evaluation[1].

There was a comment that, in Japan, there had been concern about inappropriate disposal of medicines (human and veterinary) twenty years ago. However, in general exposure has been shown to be very low with no conclusion reached on the environmental impact.

There was a comment that, in India, which has an active manufacturing industry for active pharmaceutical ingredients, each state has an Emissions Control Board, which is responsible for granting disposal permissions.

As an aside it was mentioned that gases/ash produced from incineration at temperatures over 800ºC are generally not considered to represent a risk[2]. Therefore, only improper disposal (e.g. through the drains) or disposal in landfills could imply a risk for the environment.

[1] Post meeting note: In the EU, while disposal is not considered as part of the EIA, the legislation requires that EU countries have appropriate systems in place for the collection and disposal of waste VMPs.
[2] For more information see the WHO Guidelines for safe disposal of unwanted pharmaceuticals in and after emergencies, available at https://apps.who.int/iris/handle/10665/42238