Forum Newsletter: October 2022
Nitrosamine Update (EU)

Updates for Nitrosamines (EU)

Summary
Extension of deadline for step 3 and updated step 2 template for downgrading risks.

Are you aware of the latest deadlines on Nitrosamines and your new possibilities?
As you might know all Marketing Authorisation Holders (MAHs) were requested in 2019 to review the potential risks of their products with respect to Nitrosamines. First, only drug products containing drug substances produced by chemical synthesis were included in this exercise, later also biologics.

Background

The process consists of 3 steps:

- **Step 1: Risk evaluation**
- **Step 2: Confirmatory testing** (if a risk is identified in step 1)
- **Step 3: Submission of the variation/Update of the MAA** (e.g. changes in the manufacturing process)

Templates were provided for reporting the outcome of step 1 and step 2. If you have identified a risk, you had to move into confirmatory testing, which needed sufficiently sensitive and validated methods. As of step 2, this caused additional costs for you. The intended deadlines for step 1 (31 March 21 for chemically defined drug substances and 1 July 21 for biologics) as well step 2 (26 Sept. 22) have already passed.

Extension of Deadline for Step 3

You are now focusing on step 3 for the submission of variations, depending on the outcome of step 2.
Please submit your variation by

- **1 October 2023** for chemical medicinal products **(New deadline)**
- **1 July 2023** for biological medicinal products

EDQM also just now extended the deadline for CEP-holders to submit their step 3 revisions by 1 October 2023.

New Possibility to correct Step 1 Assessment

A matter of constant discussion in industry was that timelines for step 1 assessments were too short and thus lead sometimes to inadequate information due to missing data. So, potential

risk was noted on the template and automatically moved the drug product to step 2 (confirmatory testing). This created additional costs for the MAH.

However, now you have the chance for corrections as the step 2 template was updated recently. You can **downgrade your previously submitted Step 1 assessment from "risk" to "no risk" in specific cases**, i.e. if data, once missing, are now available.

If you want to do so, please use the **updated Step 2 template (no nitrosamine detected response template)** and mark the corresponding tick-box. This means you can modify your previously submitted step 1 outcome to „**no risk“** based on new/additional information received from e.g. the API or excipient manufacturer, if you consider all root causes and published guidances. This could save you time and money.

Further Information

Please have a look into the **updated Q&A document from EMA (Rev. 11)**, considering risk factors, confirmatory testing, and submission of information to Authorities.

Please feel free to contact us, if you would like to know more about nitrosamines and if you need support on these activities to cover regulatory expectations. We know the details and guide you through the process.

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