MAH RESPONSABILITIES

TAKING INTO ACCOUNT THEIR KNOWLEDGE OF THE MANUFACTURING PROCESSES AS WELL AS THE POTENTIAL SOURCES OF NITROSAMINE IMPURITIES, MAHs SHOULD WORK WITH MANUFACTURERS OF API AND FINISHED PRODUCTS IN ORDER TO REVIEW THE API AND FINISHED PRODUCT MANUFACTURING PROCESSES WITH RESPECT TO THE ARRANGEMENTS FOR PREVENTING NITROSAMINE FORMATION AS WELL AS CONTAMINATION OR CROSS-CONTAMINATION.

**STEP 1 RISK EVALUATION:** MAHs should perform risk evaluation of their medicinal products containing chemically synthesised API.

**STEP 2 CONFIRMATORY TESTING:** In the event that a risk of presence of nitrosamines is identified as a result of the risk evaluation, confirmatory testing should be carried out using appropriately validated and sensitive methods in accordance with the prioritisation deriving from the risk evaluation conducted in step 1.

**STEP 3 CHANGES TO THE MARKETING AUTHORISATION:** MAHs should apply for a variation in a timely manner to introduce any required changes, such as amendment of the manufacturing process or changes to product specifications.
An electronic form was developed using SMUH-ALTER (national application for submission of Variation), where the MAH directly submits the results of its analysis and nitrosamine risk.

SMUH-ALTER – HOW TO USE THE SUBMISSION FORM?
TO START THE REGISTRATION CLICK ON THE BUTTON “NITROSAMINE RISK ASSESSMENT”
TO SUBMIT THE RISK ANALYSIS, CLICK ON THE BUTTON “SUBMIT NITROSAMINE ANALYSIS RISK”
IF YOU WANT TO SUBMIT RISK ANALYSIS TO “NO”

1. Click on “NO"

2. It is always necessary to include a search criteria

Then click on “Search”
IF YOU WANT TO SUBMIT RISK ANALYSIS TO "NO"

3. After the search, click on the button “Submit” in the line corresponding to the medicinal product for which the risk analysis is to be submitted.
IF YOU WANT TO SUBMIT RISK ANALYSIS TO “YES”

1. Click on “YES”

2. Then click the button “Edit” to have access to the medicinal product sheet
In the field “Analysis Scheduled Date” the proposed time for carrying out the confirmatory test must be selected. Click on “Submit”.

In the field “Analysis Result” select the final result after the confirmatory test. Click on “Submit”
CHANGE THE RISK ANALYSIS FROM “NO” TO “YES”

1. Click on “YES” and insert a search criteria for the medicinal product that is necessary to change the risk. Then click on “Search”.

2. Click on “Edit” in the line of the medicinal product to be changed and you will have access to the medicinal product sheet.

3. In the field “Analysis Scheduled Date” the proposed time for carrying out the confirmatory test must be selected. Click on “Submit”.

The risk will become YES.
RISK ANALYSIS “NO” BECAUSE THE MEDICINAL PRODUCT IS NOT MARKETED

Submit the risk “NO”. Then access the medicinal product sheet as if it were a submission “YES” and in the field “DESCRIPTION” write “NOT MARKETED”.

![Image of medicinal product sheet with focus on the Description field, indicating where to enter the text NOT MARKETED.]
THANKS