**SUMMARY DOCUMENT**

**Step 2 submission – Article 5(3) referral regarding risk of nitrosamine impurities in medicinal products containing chemically synthesised active pharmaceutical ingredients**

**Administrative details**

|  |  |
| --- | --- |
| **Product name in the MS** |  |
| **Drug substance(s)** |  |
| **PL number** |  |
| **DCP/MRP procedure number** (if applicable)**\*** |  |
| **Information is also submitted to the following EU MS\*** |  |
| **UK MAH** |  |
| **Drug substance source:** | CEP – CEP number(s)  ASMF – UK ASMF number(s)  Full 3.2.S |
| **Marketed status** | Marketed  Not marketed |

\*for tracking purposes please provide this information also for submission made from 1.1.2021 onwards

**Summary of analytical method information & nitrosamine limit**

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| --- | --- | --- | --- |
| **Nitrosamine tested for** | **LOD (ppm)** | **LOQ (ppm)** | **Limit applied (ppm)** |
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**Summary of batch data**

| **Nitrosamine tested for** | **Drug substance** | | **Finished product** | | |
| --- | --- | --- | --- | --- | --- |
| **Batches found with levels > LOQ\*** | **Batches found with levels > limit\*** | **Batches found with levels > LOQ\*** | **Batches found with levels > limit\*** | **Number of marketed batches\*\*** |
|  | Yes  No#  No | Yes  No#  No | Yes  No#  No | Yes  No#  No | >LOQ:  >Limit: |
|  | Yes  No#  No | Yes  No#  No | Yes  No#  No | Yes  No#  No | >LOQ:  >Limit: |
|  | Yes  No#  No | Yes  No#  No | Yes  No#  No | Yes  No#  No | >LOQ:  >Limit: |
|  | Yes  No#  No | Yes  No#  No | Yes  No#  No | Yes  No#  No | >LOQ:  >Limit: |
|  | Yes  No#  No | Yes  No#  No | Yes  No#  No | Yes  No#  No | >LOQ:  >Limit: |
|  | Yes  No#  No | Yes  No#  No | Yes  No#  No | Yes  No#  No | >LOQ:  >Limit: |
|  | Yes  No#  No | Yes  No#  No | Yes  No#  No | Yes  No#  No | >LOQ:  >Limit: |

\*if yes, please state number (No#) of batches affected

\*\* If contamination above the LOQ/Limit is detected, please state the number of these batches that are on the market at the time of submission

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Nitrosamine tested for** | **Drug substance** | | **Finished product** | |
| **Number of batches tested** | **Average (min-max) detected (ppm)** | **Number of batches tested** | **Average (min-max) detected (ppm)** |
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**Submission checklist**

|  |  |  |  |
| --- | --- | --- | --- |
| **Document / Content** | **Document name**  *(please provide the name of the document as submitted; if all documents are collated into one pdf, please ensure this is bookmarked and has a table of contents)* | **Included in submission** | |
| Summary document |  | Yes | No |
| Step 1- Risk Evaluation documents |  | Yes | No |
| CMDh templates |  | Yes | No |
| Risk assessment summary |  | Yes | No |
| Calculation of limit applied |  | Yes | No |
| Justification of sampling plan |  | Yes | No |
| Batch data in tabulated form (Excel spreadsheet) |  | Yes | No |
| Description of the analytical method\*\*\* |  | Yes | No |
| Validation of the analytical method\*\*\* |  | Yes | No |
| Stage 3 submission plan \*\*\*\* |  | Yes | No |

\*\*\*Where required to be included for each method used

\*\*\*\*Please indicate where not applicable based on stage 2 testing and risk assessment

**Guidance**

Please refer to the relevant guidance on the CMDh website under <https://www.hma.eu/620.html> (see Q&A document).

***Calculation of limit applied***

Please detail how the limit applied has been derived for the specific product.

***Justification of sampling plan***

Please justify briefly the sampling plan. This should follow recognised sampling practice and should be representative

* of the supply chain if multiple alternative sites or suppliers (e.g. starting materials, excipients) may be used.
* across the age of batches in the supply chain (i.e. batches at/near shelf-life should be included)
* of all packaging options.

***OMCL testing of samples***

Please be prepared to ship upon request from the MHRA samples of finished product batches and samples of the drug substance used for their production to the MHRA Laboratory.