

Nitrosamine contamination policy for FPP applications (an update)

N-Nitrosamines are a class of substances of concern to international regulators and the pharmaceutical industry. This is because many nitrosamines are highly potent mutagenic agents that have been classified as probable human carcinogens.

For this reason, in April 2020 PQT/MED, in line with other international regulators, called for manufacturers to undertake a risk evaluation of all API and FPP manufacturers currently submitted to PQT/MED (please refer to <https://extranet.who.int/pqweb/news/manufacturers-conduct-risk-assessments>).

In line with international practice this approach involves a three-step process.

- Step 1: Risk Evaluation for the potential presence of nitrosamines.
- Step 2: Confirmatory Testing if a potential risk is identified.
- Step 3: Updates to the relevant authority regarding mitigation strategy, if the presence is confirmed.

For all new applications submitted since 1 January 2021, a risk assessment must have been completed before submission and the application should include a declaration indicating the outcome of the risk assessment. The risk assessment report is to be submitted on request.

PQT/MED has issued additional guidance regarding submission of variation applications for changes to specifications, processes or controls that may be proposed as part of the step 3 mitigation strategies.

In addition, since changes to the FPP manufacturing process, sources of raw materials, packaging, and storage may affect the potential for the presence of nitrosamines in the FPP, PQT/MED also expects that manufacturers have considered what effect the changes proposed may have on the potential for nitrosamine contamination. In this respect, the variation application form for FPPs has been revised to include the necessary declaration. Further information can be referred to [FAQ: variation document](#).

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