To whom it might concern

Modifications to be applied to the Swissmedic GC-MS/MS method for Nitrosamines to test Metformin batches (API and PF).

Berne, 20.02.2020

The Swissmedic OMCL is providing to all interested MAH, some additional information related to the already published "*31_PV_171_Nitrosamine_by_GC_MS_MS_V01 EN_Final*" method published on both Swissmedic and EDQM homepages.

In order to use the method for testing Metformin HCl API and FP, the user has to apply the following modifications (See red text for changes):

6.5 Solutions

- Replacement of the "1M NaOH solution (ACN/ISTD)" with "Milli-Q solution (ISTD)":

Milli-Q solution (ISTD)	100 µL ISTD-dil solution is diluted to 1 L with H2O MilliQ.	14 days / 25°C

7.1 Sample preparation

A representative sample is prepared from about 10 ground tablets. The quantity of mixed tablet powder is weighed into a 15 mL centrifuge tube, which corresponds to an amount of active ingredient of approx. 250 mg, paying attention to not exceed 1.5 g of total mass. For API samples, 250 mg of active ingredient are weighed in each case.
This sample powder is mixed with 10 mL Milli-Q Solution, vortexed briefly and then shaken well for at least 5 minutes. 2.0 mL of dichloromethane are added to this suspension, vortexed briefly and then shaken well for at least 5 minutes. The suspension is then centrifuged at about 10'000 g for at least 5 min. The upper aqueous phase is gently removed, so that the lower organic phase can be withdrawn more easily.

These adaptations will allow the user to test correctly Metformin HCl samples.

Please be reminded that the method needs to be fully validated prior to use.

Best regards
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