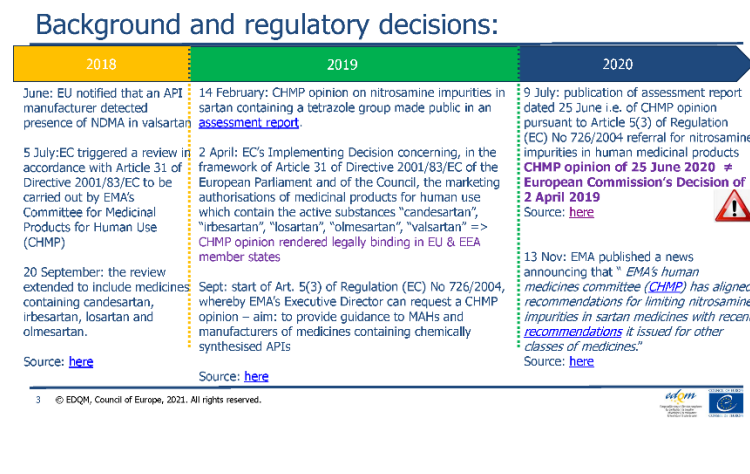


EDQM Webinar on N-Nitrosamines Impurities (21/01/2021)

N-nitrosamine impurities in medicinal products, Presentation by Cathie Vielle

Background & Regulatory Decisions - Useful information & urls links:



2018 Source: https://www.ema.europa.eu/en/documents/variation-report/sartans-article-31-referral-chmp-assessment-report_en.pdf

Assessment Report: https://www.ema.europa.eu/en/documents/variation-report/sartans-article-31-referral-chmp-assessment-report_en.pdf

2019 Source: https://ec.europa.eu/health/documents/community-register/2019/20190402144194/dec_144194_en.pdf

2020 Source: https://www.ema.europa.eu/en/documents/referral/nitrosamines-emea-h-a53-1490-assessment-report_en.pdf

Recommendations: https://www.ema.europa.eu/en/documents/referral/nitrosamine-impurities-final-outcome-art-53_en.pdf

2020 Source: <https://www.ema.europa.eu/en/news/nitrosamines-ema-aligns-recommendations-sartans-those-other-medicines>

Regulatory decisions - ctd:

2020

9 July: publication of assessment report dated 25 June i.e. of CHMP opinion pursuant to Article 5(3) of Regulation (EC) No 726/2004 referral for nitrosamine impurities in human medicinal products finalised. The Art. 5(3) had been triggered by the EMA Director in Sept. 2019.

These recommendations **apply to all medicines**. They include:

- developing additional guidance on:
 - the roles and responsibilities of companies involved in the manufacture of medicines;
 - controlling impurities;
 - [good manufacturing practice \(GMP\)](#);
 - sampling and testing.
- improving communication with patients and healthcare professionals;
- expanding cooperation with international partners;
- further developing information technology systems.
- ✓ **the control of the presence and risk of nitrosamine impurities shall be done at the level of the medicinal product**

Publication of the outcome of a lessons learned exercise - *not entirely aligned with art. 5(3) opinion - (also triggered by the Art. 31 referral)* on the presence of nitrosamines in sartan medicines by the European medicines regulatory network: [Lessons learnt from presence of N-nitrosamine impurities in sartan medicines](#).

Lessons Learnt Publication: https://www.ema.europa.eu/documents/report/lessons-learnt-presence-n-nitrosamine-impurities-sartan-medicines_en.pdf

N-nitrosamine impurities: CEP applications, Presentation by Ekaterina Nagdiyev

CHMP opinion on Article 5(3)

- Opinion published in June 2020, available on EMA website:
https://www.ema.europa.eu/documents/referral/nitrosamines-emea-h-a53-1490-assessment-report_en.pdf
- EMA Q&As updated accordingly: [EMA Q&As](#)
- Risk of nitrosamine impurities:
 - Extended to biological products due to common risk factors (chemical reagents, packaging)
 - Exceptions for products indicated for advanced cancer (ICH S9 scope)
 - Deadlines for step 1 postponed
 - Root causes for the presence of nitrosamines:
 - APIs (route of synthesis, raw materials, degradation)
 - Interactions with finished product components (excipients, packaging)
 - GMP related aspects (cross-contaminations, recovered materials, etc)

EMA Q&As: https://www.ema.europa.eu/en/documents/referral/nitrosamines-emea-h-a53-1490-questions-answers-marketing-authorisation-holders/applicants-chmp-opinion-article-53-regulation-ec-no-726/2004-referral-nitrosamine-impurities-human-medicinal-products_en.pdf