Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423)

Volume 4 Issue 6 June 2020

Perspective

Nitrosamine Impurities in Pharmaceutical Drugs

Tabrez Shaikh*

Lab Manager at Indoco Research Centre, Navimumbai, Maharashtra, India

***Corresponding Author:** Tabrez Shaikh, Lab Manager at Indoco Research Centre, Navimumbai, Maharashtra, India.

Received: January 28, 2020

Published: June 01, 2020

© All rights are reserved by **Tabrez Shaikh.**

FDA and EMA in mid of June 2018 became aware of the presence of Nitrosamine impurity in generic drug substances and drug product, valsartan an angiotensin II receptor blockers (ARBs) or 'Sartans' class medicines which is used to treat patients with hypertension (high blood pressure) and heart. Later, various Nitrosamine impurities were detected in other sartan and non-sartan drug substances and drug products. This announcement leads to voluntarily recall hundreds of batches of these generic versions by pharmaceutical distributor worldwide.

Nitrosamine impurities are known to be mutagenic and carcinogenic, very small exposure of these impurities can lead to cancer. These impurities may be formed and get incorporated into a drug substance or drug product through reagent, catalyst, solvent or raw materials used in the process of manufacturing.

Nitrosamine impurities impact the genetic material by means of mutations through chromosomal breaks, rearrangements, covalent binding or insertion into the DNA during replication. These changes in the genetic material, caused by the exposure to very low levels of Nitrosamine impurities, can lead to cancer.

The various regulatory authority has published the press release or notice regarding the control of these impurities with the interim limit. Food and drug administration (FDA) and European Medicines Agency (EMA) in July 2018. Therapeutic Goods Administration (TGA) of Australia made advice in a public notice introduced requirements for sponsors of 'sartan' blood pressure medicines to take measures to avoid the presence of Nitrosamine impurities.

Nitrosamine impurities are limited to acceptable excess risk in drug substance and drug product by well accepted ICH M7 (R1) guideline where for the calculation of its limit, the median toxic dose TD50 (Shows toxicity in 50% cases) is used. The TD50 is the well-accepted by ICH M7 (R1) for the calculation of the acceptable excess risk to calculate acceptable intake (AI) for mutagenic and carcinogenic impurities and it is a well-recognized international standard. The extrapolation to the excess risk level for cancer is calculated by linear back extrapolation to the dose theoretically causing a 1:100,000 risk by dividing the TD50 by 50,000 (50% or 0.5 x 100,000).

All amine along with nitrosating agents are considered to be antecedent in the generation of Nitrosamines impurities in the drug substance or drug products. Thus avoiding the use of these nitrosating reagents and amine can prevent Nitrosamine impurity formation. Reuse of solvent and catalyst increase the chance of reintroduction of nitrosamine impurities hence recovered solvent and recovered catalyst should be avoided in the manufacturing process.

The development of analytical methods to determine Nitrosamines impurities is the challenging task due to very low levels of impurities present in the complex matrices. The developed methods also need to be validated to conform to GMP requirements. Several methods have been published by the FDA to cover NDMA and NDEA in different 'sartans'. The EMA has indicated the extension of measures to include more Nitrosamines.

Other regulatory authorities (Canada, Switzerland and Singapore) have adopted their own measures and published analytical methods. Most of the methods used for testing of Nitrosamines in drug substance and drug product utilize the chromatographic techniques such as reversed-phase liquid chromatography (LC) or gas chromatography (GC) combined with various detectors such as mass spectrometry (MS), Ultraviolet spectrophotometry (UV) or nitrogen chemiluminescence (NCD).

Assets from publication with us

- Prompt Acknowledgement after receiving the article
- Thorough Double blinded peer review
- Rapid Publication
- Issue of Publication Certificate
- High visibility of your Published work

Website: www.actascientific.com/

Submit Article: www.actascientific.com/submission.php

Email us: editor@actascientific.com

Contact us: +91 9182824667