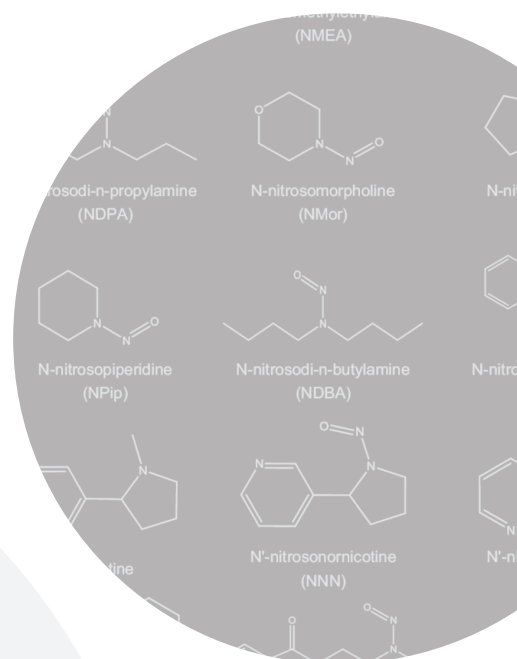


KYMOS

Nitrosamine Impurities Analysis

- Compliance with EMA and FDA guidelines and LOQs
- Screening for target Nitrosamines with LC-MS/MS or HS-GC-MS
- Quantitative method validation for specific N-nitrosamines



KYMOS
PHARMA SERVICES, S.L.

www.kyimos.com
Kyimos Pharma Services S.L.
Parc Tecnològic del Vallès
Ronda Can Fatjó, 7B
08290 Cerdanyola del Vallès
Barcelona, Spain

Phone (+34) 93 548 18 48
Fax: (+34) 93 170 29 99
info@kyimos.com



PHARMAPROGRESS
a KYMOS company

www.pharmaprogress.com
Pharmaprogress S.r.l.
Via Alessandro Volta 12
60020 Camerata Picena
Ancona, Italy

Phone (+39) (0) 71 749 99 19
Fax (+39) (0) 71 749 63 41
info@pharmaprogress.com

REGULATORY FRAMEWORK

Nitrosamine compounds are potent genotoxic carcinogens in several non-human species and are classified as probable human carcinogens by the International Agency for Research on Cancer (IARC). Since June 2018, several N-nitrosamines have been detected in batches of multiple drug substances. Health agencies require pharmaceutical companies to carry out risk assessments to produce a list of all N-nitrosamines likely to be present in their APIs and/or drug products, and experimentally demonstrate their absence.

STRATEGIC APPROACH

Kymos proposes an approach compliant with regulatory requirements and consisting of three steps:

- Risk assessment according to regulatory guidelines in collaboration with our partner Azierta.
- Screening for target N-Nitrosamines at a default limit of 0.03 ppm (or higher upon client request).
- Development and validation of a quantitative method for nitrosamines exceeding established limits.

VALIDATION	PARAMETERS
Method for validation and quantification purposes	<ul style="list-style-type: none">▪ Specificity▪ Linearity▪ Accuracy▪ Precision (repeatability and intermediate precision)▪ Detection limit▪ Limit of quantification▪ Range▪ Stability▪ Robustness (upon request)

N-NITROSAMINE ANALYSIS

We offer our experience in testing for N-nitrosamine impurities in APIs and drug products using HS-GC-MS and LC-MS/MS. The list below shows nitrosamines currently available, but new ones can be added upon client request:

- NDMA: N-Nitrosodimethylamine
- NDEA: N-Nitrosodiethylamine
- NDIPA: N-Nitrosodiisopropylamine
- NEIPA: N-Nitrosoethylisopropylamine
- NDBA: N-Nitrosodibutylamine
- NMEA: N-nitrosomethylethylamine
- NDPA: N-Nitrosodipropylamine
- NMBA: N-Nitroso-N-methyl-4-aminobutyric acid
- NPYR: N-Nitrosopyrrolidine
- NPIP: N-Nitrosopiperidine
- NMOR: N-Nitrosomorpholine
- NDELA: N-Nitrosodiethanolamine
- MNPZ: mono-N-Nitrosopiperazine
- DNPZ: di-N-Nitrosopiperazine
- NDPhA: N-Nitrosodiphenylamine

HIGH ANALYTICAL CAPACITY

KYMOS offers quick turnaround at competitive prices owing to its dedicated team, significant sample analysis capabilities and two back-up methods available:

- Liquid chromatography-mass spectrometry (LC-MS/MS) Agilent 6490 Triple Quadrupole
- Headspace Gas Chromatography (HS-GC-MS) Agilent 7890 with a 5977 Single Quadrupole limits.

