BASF
We create chemistry

Control nitrosamines with low nitrite excipients from BASF

More than 80 years ago, BASF invented PVPs, and we fully understand their chemistry. We have excipients with low nitrites, particularly povidones (PVPs), copovidones and crospovidones.

Our povidones, copovidones and crospovidones have always been low nitrite grades with high lot-to-lot consistency.

You can continue using BASF excipients as-is.

- ✓ **No efforts or costs in qualifying a new "low nitrite" or "controlled nitrite" grade.**
- ✓ **Assured supply chain resiliency since you can order povidone with low nitrites from any of our 3 global sites: USA, Germany and China.**
- ✓ **No need for costly reformulations.**

We have measured, and not detected nitrites in our products. Our LOQ and LODs are:

Povidones Kollidon® 30, 12 PF & 17 PF
LOQ = 0.1 ppm; Ion Chromatography

High molecular weight povidone Kollidon® 90 Evo, copovidones (Kollidon® VA 64 & VA 64 Fine) and crospovidone Kollidon® CL grades
LOQ = 2 ppm and LOD < 0.7 ppm; Ion Chromatography

ABOUT NITROSAMINES

In pharma, nitrosamines are formed from the reaction of secondary or tertiary amines (usually from the API) with nitrites (from excipients or process impurities). There are two categories of nitrosamine impurities:

1 Nitrosamine Drug Substance-Related Impurities (NDSRIs) = formed from the API and its process impurities. Regulatory agencies have established acceptable intake (AI) limits for these. [1,2]

2 Nitrosamines from the formulation and drug product manufacturing process (impacted by water quality, high heat and humid processes, etc).

- Up to 40% of common APIs and 30% of API impurities can form NDSRIs. [3]
- Nitrites in excipients can lead to both types of nitrosamine impurities.
- As of 2023, the average nitrite content in excipients is 0.83 ppm. [4]

Published articles have consistently demonstrated that BASF excipients have the lowest nitrite values and are seen as best-in-class by our customers.

For crospovidones [5]

NDMA formation due to active ingredient degradation and nitrite traces in drug product

For povidones [6]

Avoiding N-nitrosodimethylamine formation in metformin pharmaceuticals by limiting dimethylamine and nitrite

Table 1. Nitrites in crospovidone from different suppliers

ISP Chemicals [6]	Supplier A [7]	Supplier B [7]	BASF [7]
11.3 ppm	9.3 ppm	0.83 ppm	< LOQ (0.5 ppm)

We are transparent with our nitrite values, share risk assessments and the validated analytical method we use for testing.

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Understanding nitrite analytical results

Limit of Quantitation (LOQ)

The lowest amount of nitrite we can see and reliably measure

Limit of Detection (LOD)

The lowest amount of nitrite we can see

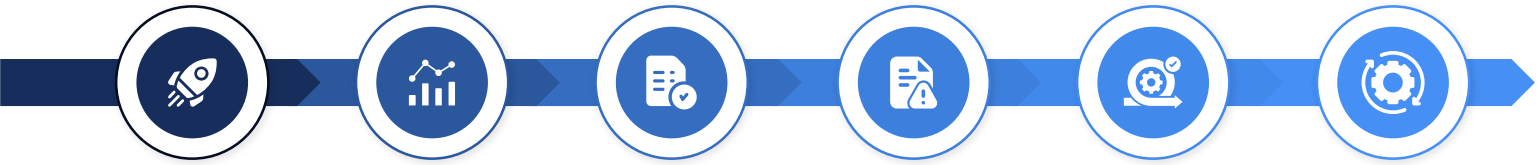
What we provide

Nitrosamine risk assessments with average nitrite values and LOQ of our analytical methods

Our validated analytical methods so you can confidently measure nitrites at your site

Technical guidance on formulation strategies for nitrosamine reduction (antioxidants, ZoomLab®)

We listen to our customers and are continuously improving our LOQs to detect as low as possible. Our journey is ongoing.



Nitrosamine topic started

BASF developed analytical methods LOQ 2ppm LOD 0.7pppm

We tested our products (n=5 batches, at least)

Nitrosamine risk assessments with LOD and average values per product

New methods targeting lower LOQ/LOD

Updated risk assessments for PVPs and crospovidones

For more information, contact your BASF representative or contact us via our website: pharma.basf.com/speak-with-an-expert

[1] Recommended Acceptable Intake Limits for Nitrosamine Drug Substance-Related Impurities (NDSRIs): Guidance for Industry, FDA, August 2023.
[2] ICH M7(R2) Guideline on assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk, EMA, July 2023.
[3] Nudelman, et al. Organic Process Research & Development, 2023 27 (10), 1719-1735. https://doi.org/10.1021/acs.oprd.3c00100
[4] Knocks, G. (2024, March 21). The Nitrite Database - what do we know so far about the risk of excipients? [Presentation]. Lhasa Limited nitrites in exicipients collaborative meeting. Leeds City Centre, UK. https://www.lhasalimited.org/events/lhasa-limited-nitrites-in-excipients-collaborative-meeting/
[5] Golob, et al. Journal of Pharmaceutical Sciences, 2023 112 (5), 1277–1286. DOI: 10.1016/j.xphs.2023.03.007
[6] Schlingemann, et al. Int J Pharm, 2022 620. DOI: 10.1016/j.ijpharm.2022.121740
[7] Boetzel, et al. Journal of Pharmaceutical Sciences, 2023 112(6), 1615-1624. DOI: 10.1016/j.xphs.2022.04.016

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