

## Managing nitrosamine levels using EUDRAGIT® polymers



With their inherently low nitrite content, EUDRAGIT® polymers are a reliable choice for minimizing the risk of nitrosamine formation in oral drug products, and simplifying compliance with evolving nitrosamine regulations.

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- 1 Low nitrite content of EUDRAGIT® polymers
- 2 Reduced nitrosamine risk
- 3 Regulatory support

## Why nitrosamines are problematic

Nitrosamines such as N-Nitrosodimethylamine (NDMA) are classified as probable human carcinogens. Nitrosamines are formed by the reaction of vulnerable amines and a nitrosating agent, such as nitrite. This can occur during API synthesis, drug product manufacturing or storage. Nitrosamine Drug Substance Related Impurities (NDSRIs) can also originate from APIs or impurities containing vulnerable amines. Nitrosamines have been identified in a wide range of pharmaceuticals, highlighting the need for proactive risk management across the industry.

## Mitigating the risk of nitrosamines

Prolonged exposure with trace levels of nitrosamines above acceptable limits can increase cancer risk, which is influenced by factors such as daily dosage, duration of use, and the specific nitrosamine involved. To ensure patient safety and regulatory compliance, pharmaceutical companies must conduct thorough nitrosamine risk assessments. EUDRAGIT® polymers help offer a proactive solution for managing nitrosamine formation thanks to their consistently low nitrite levels.

## Our Method for Detecting and Quantifying Nitrites

Detecting trace levels of nitrites in pharmaceutical excipients—especially at parts-per-billion (ppb) levels—requires highly sensitive and validated analytical methods. Here's how we ensure accurate and reliable detection of nitrites in EUDRAGIT® polymers.

### ANALYTICAL TECHNIQUE

- **Method used:** HPLC-UV/PDA with Ion Pair Chromatography
- **Detection Limit:** Established Limit of Detection (LOD): 5 ppb  
LOD is the lowest amount of analyte that can be detected but not necessarily quantified as an exact value.
- **Sensitivity:** Limit of Quantitation (LOQ): 10 ppb  
LOQ is the lowest concentration that can be determined with acceptable accuracy and precision.
- **Validation Standards:**
  - Lhasa Ltd. guidance on *Analytical Nitrite Methods*
  - IQ Consortium's *Nitrosamine Risk Assessment—Excipients and Nitrites Group*
  - ICH Guideline: *Validation of Analytical Procedures; Text and Methodology Q2 (R2)*

### RESULTS

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|--|----------------------------|------------------------------|
| ▪ Nitrite levels in tested EUDRAGIT® polymers were below the detection limit | ▪ EUDRAGIT® L 100-55 < LOD | ▪ EUDRAGIT® E 100 < LOD      |
| ▪ EUDRAGIT® L 30 D-55 < LOD  | ▪ EUDRAGIT® L 100 < LOD    | ▪ EUDRAGIT® S 100 < LOD      |
|  | ▪ EUDRAGIT® NE 30 D < LOD  | ▪ EUDRAGIT® FL 30 D-55 < LOD |
|  | ▪ EUDRAGIT® E PO < LOD     | ▪ EUDRAGIT® NM 30 D < LOD    |

## Risk Mitigation Through Low-Nitrite EUDRAGIT® Polymers

- Nitrite levels detected in tested EUDRAGIT® products were found to be very low, falling below the established limit of detection (LOD).
- No need to qualify a low-nitrite or controlled grade
- No need for reformulation efforts

Questions? Want to learn more about the analytical method? Get in touch with our team.

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