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**A Low Nitrite
Microcrystalline Cellulose**

AVICEL® PH LN

Pharma Solutions at IFF provides you access to one of the broadest microcrystalline cellulose (MCC) portfolios in the industry. Backed by decades of innovation, and expertise, Avicel® PH offers a long history of manufacturing the highest-quality pharmaceutical grade MCC.

Our deep polymer understanding has allowed for continuous improvement, portfolio expansion, and sustained innovation in this space. We are committed to the excipient industry and our strategic intent is to continuously invest in our brands. As a testament to this, we have added a new line of low nitrite grades to our proven Avicel® cellulose portfolio.

Avicel® PH Low Nitrite (LN) grades offer the performance and reliability you have come to know from the Avicel® brand. Avicel® PH LN with low nitrite level is the preferred solution for pharmaceutical companies with a need to reduce the risk of N-nitrosamine formation in oral solid dose formulations containing MCC.

Nitrosamine impurity gaining relevance

- N-nitrosamines (commonly called nitrosamines) are considered probable or possible carcinogens according to the International Agency for Research on Cancer, an agency within the World Health Organization

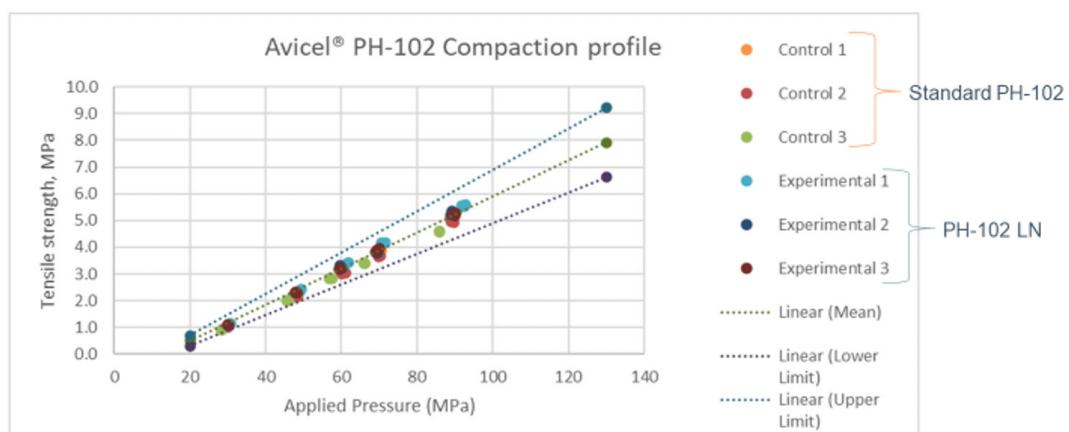
- Since 2018, nitrosamines have been found in several drug products including angiotensin II receptor blockers (ARB), Metformin and Ranitidine. Regulatory bodies across the world have requested that pharmaceutical companies evaluate, investigate, and control the formation of nitrosamines in their drug products.
- Nitrosamine formation involves the reaction of secondary or tertiary amines (present as functional groups in Active Pharmaceutical Ingredients [API], as a reaction by-product or as impurities) with a nitrosating agent like nitrous anhydride. Nitrous anhydride can form from the protonation of nitrite (via nitrous acid) under acidic conditions. Nitrites are found in many excipients, food products, plants, and water.
- Many pharmaceutical customers are looking for excipients that contain no nitrites or low levels of nitrites as part of their nitrosamine risk mitigation plans.

Delivering Avicel® low nitrite strategy

Customers are looking for the highest quality and performance in their oral dosage forms. Our experts aim to provide them with excipients that meet the core needs for reliability, sustainability, quality, and predictable performance standards to develop and produce robust formulations. To ensure this, all Avicel® grades, including Avicel® PH LN are produced using a qualified and validated process. Standard Avicel® grades and Avicel® PH LN are equivalent with respect to product specifications and formulation performance (Table 1). Avicel® PH LN has a nitrite specification and test result on the certificate of analysis (specification of no more than 200 ppb). Pharma Solutions at IFF has developed a specific analytical methodology to measure nitrite in MCC.

Table 1: Compaction Profile

A comparison report about performance of Standard Avicel® PH-102 and Avicel® PH-102 LN suggests they have equivalent profiles



Features & Benefits

Avicel® MCC is commonly used for improving the physical formulation properties of tablets and enabling easier processing of more robust dosage forms.

With the development of differentiated grades, Avicel® PH LN grades distinguish themselves as indispensable

tools for developing oral solid dose formulations while mitigating the potential formation of N-nitrosamines in finished drug products. Their versatile functionality brings many benefits to the formulation of APIs with Nitrosamines formation risk, including:

- Lower risk of nitrosamine formation
- Nitrite specification on COA

- Batch to batch consistency regarding nitrite content
- First choice of binder and compression aid for direct compression and dry granulation
- Improved powder flow and tablet content uniformity
- Improved tablet compactibility

AVICEL® PH MCC LN grade	Applications Dosage forms	Specification
AVICEL® PH-101 LN	<ul style="list-style-type: none"> • High shear wet granulation • Extrusion spheronization 	<ul style="list-style-type: none"> • Nitrite level, µg/kg ≤ 200 • Nominal Particle Size, µm 50 • Moisture, % 3.0 to 5.0 • Loose Bulk Density, g/cc 0.26 – 0.31
AVICEL® PH-102 LN	<ul style="list-style-type: none"> • Direct compression • Dry granulation 	<ul style="list-style-type: none"> • Nitrite level µg/kg ≤ 200 • Nominal Particle Size, µm 100 • Moisture, % 3.0 to 5.0 • Loose Bulk Density, g/cc 0.28 – 0.33
AVICEL® PH-112 LN	Low moisture grade for <ul style="list-style-type: none"> • Direct compression • Dry granulation 	<ul style="list-style-type: none"> • Nitrite level, µg/kg ≤ 200 • Nominal Particle Size, µm 100 • Moisture, % NMT 1.5 • Loose Bulk Density, g/cc 0.28 – 0.34
AVICEL® PH-200 LN	<ul style="list-style-type: none"> • Direct compression • Dry granulation 	<ul style="list-style-type: none"> • Nitrite level µg/kg ≤ 200 • Nominal Particle Size, µm 200 • Moisture, % 2.0 to 5.0 • Loose Bulk Density, g/cc 0.29 – 0.36
AVICEL® PH-200 LM LN	Low moisture grade for <ul style="list-style-type: none"> • Direct compression • MADG process (Moisture Activated Dry Granulation) 	<ul style="list-style-type: none"> • Nitrite level µg/kg ≤ 200 • Nominal Particle Size, µm 200 • Moisture, % NMT 1.5 • Loose Bulk Density, g/cc 0.30 – 0.38

*The COA and performance data can be provided in a report upon request.





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