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PRESS RELEASE

Dipharma publishes a peer-reviewed study in Organic Process Research & Development: a novel approach to detect and characterize nitrosamine formation in APIs

The pioneer method combines the nitrosation assay procedure (NAP) with ^{15}N-enriched nitrosating reagents and ^{15}N NMR spectroscopy for a safer Active Pharmaceutical Ingredients manufacturing process

Milan, Italy - Dipharma Francis S.r.l. (Dipharma), a leading Contract Development and Manufacturing Organization (CDMO) and a global manufacturer of Active Pharmaceutical Ingredients (APIs) and advanced intermediates, **proudly announces the publication of the open-access article titled: "*Hunt for NDSRIs: Unveiling Hidden Threats with the Novel ^{15}N-Enriched NAP Test*" in the scientific journal Organic Process Research & Development (OPR&D).**

The work outlines a novel and insightful approach developed by Dipharma to detect nitrosamine impurities, particularly nitrosamine drug-substance-related impurities (NDSRIs). Nitrosamines are small nitrogen-based compounds that may form through unintended nitrosation pathways during synthesis, storage or degradation, and are closely monitored because many nitrosamines are potent mutagens and probable human carcinogens. Their control is therefore essential for patient safety, regulatory compliance and the integrity of the pharmaceutical supply chain.

The publication is freely accessible to scientists and industry stakeholders worldwide at: https://pubs.acs.org/doi/10.1021/acs.oprd.5c00223
It appears in *Organic Process Research & Development* (OPR&D), a leading peer-reviewed journal focused on chemical process development and scale-up for industrial applications, issued by the American Chemical Society (ACS).

In the article, authored by **Anna Simonetto**, *R&D Researcher*, **Gabriele Razzetti**, *Global Director of R&D*, and **Simone Mantegazza**, *Research Laboratory Manager*, **at Dipharma Francis**, together with **Prof. Enrico Monzani at the University of Pavia** (Italy), the research team presents an innovative method that overcomes the limitations of traditional mass-based techniques. By integrating the nitrosation assay procedure (NAP) with ^{15}N-enriched nitrosating reagents and ^{15}N-NMR spectroscopy, the authors provide a selective and sensitive technique to detect and characterize nitrosamines, including challenging NDSRIs, even in complex matrices or when dealing with isomeric or degradation-derived species.

This strategy offers a robust and early-stage tool for assessing nitrosamine formation during API development and manufacturing, supporting impurity profiling, process understanding, and alignment with evolving regulatory expectations.
For both innovator and generic pharmaceutical companies, this research represents a significant step forward in proactively identifying and addressing nitrosamine-related challenges and ensuring long-term product reliability.
Dipharma congratulates the authors for this achievement, which reinforces the Company's commitment to science-driven solutions and to enabling customers to make informed, sustainable decisions throughout the API development lifecycle.

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"*This publication strengthens Dipharma's long-term strategy for nitrosamine control, which is grounded in multidisciplinary scientific investigation and combines advanced analytical solutions, a robust Risk Assessment Protocol, and proactive measures designed to safeguard compliance and product safety," said* **Gabriele Razzetti**, Global Director of R&D at Dipharma Francis S.r.l. *"Thanks to our innovative approach, we can confirm or exclude nitrosamine formation with exceptional clarity, even in the most complex scenarios. For our partners, this means having a reliable foundation for risk assessment, regulatory justification, and mitigation planning. It also gives them the confidence that Dipharma is fully aligned with their objectives for safe, robust and future-proof API manufacturing, supported by continuous collaboration and a strong commitment to supply continuity. This study further demonstrates the excellence of our R&D team, whose scientific rigor and problem-solving capabilities continue to drive our success."*

About the Dipharma Francis group

The Dipharma Group is a global CDMO and a leading manufacturer of APIs and Intermediates, with about 600 skilled and highly committed employees, 4 cGMP plants, located in the U.S.A. and Italy, plus sales offices in Italy, the U.S.A. and China. The fully equipped R&D Centers develop innovative chemical processes and crystalline forms for the most prominent pharmaceutical companies worldwide. As a third-generation family-owned company, Dipharma has a long history of stability, commitment, and financial solidity. Dipharma has the right size and variety of scale-up capabilities to act as a global player and manage processes efficiently, while offering flexibility and agility to promptly solve any challenge. **Experience you can trust.**

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