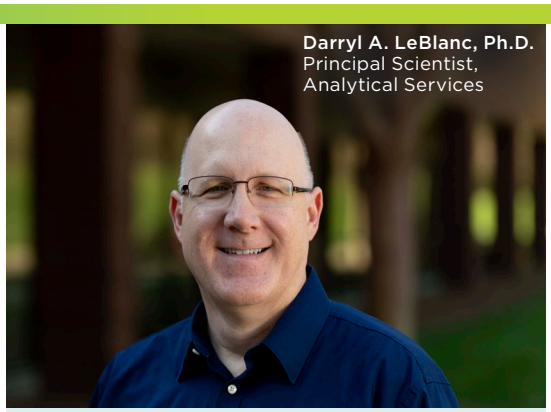
Cambrex

Case Study
Analytical Services

Rapid characterization of impurities



Managing impurities in drug development with swift isolation, synthesis, and analysis.

Eliminating potential risks: Identification is the first step

Impurities in drug products can arise at various time points during the manufacturing process or during storage. Without swift identification to assess potential risk, they can stall critical clinical timelines or cause a product recall. Understanding the nature of an impurity is a critical first step in determining whether the substance is recognized as a high-risk genotoxic impurity, a low-risk trace elemental impurity, or an unknown contaminant. However, identifying impurities can be complex, because they often surface as unknown peaks in a routine chromatogram. Their chemical nature can include both organic and inorganic molecules, and they can originate from multiple sources including starting materials, reaction intermediates and side products, or degradants.

To address the presence of an impurity, drug makers must first understand its chemical structure and the point in the process where it originated. Naturally, most drug manufacturers are focused on production efforts and do not also house the analytical resources to perform comprehensive characterization and synthesis of impurities. Cambrex fills this gap by fully supporting clients in rapid identification of impurities in their drug substances or drug products and prompt synthesis of standards for those impurities.

ICH guidelines established a scale of detection thresholds to ensure that impurities which pose a potential risk to patients are addressed prior to product release. There are distinct thresholds for reporting, identifying and qualifying impurities in drug substances and drug products. For impurities that need to be routinely controlled for safety purposes, detection above the threshold requires further toxicology studies. In this case, a client discovered an impurity during ongoing stability studies that exceeded a qualification limit set forth by ICH guidelines.

Strength in numbers: Dual teams and multiple synthetic routes

Impurities related to the drug substance are typically addressed by the time a drug product undergoes stability studies. Drug product impurities can surface during accelerated stability tests, and in this case, the client required rapid identification of the impurity to determine

Peak performance.

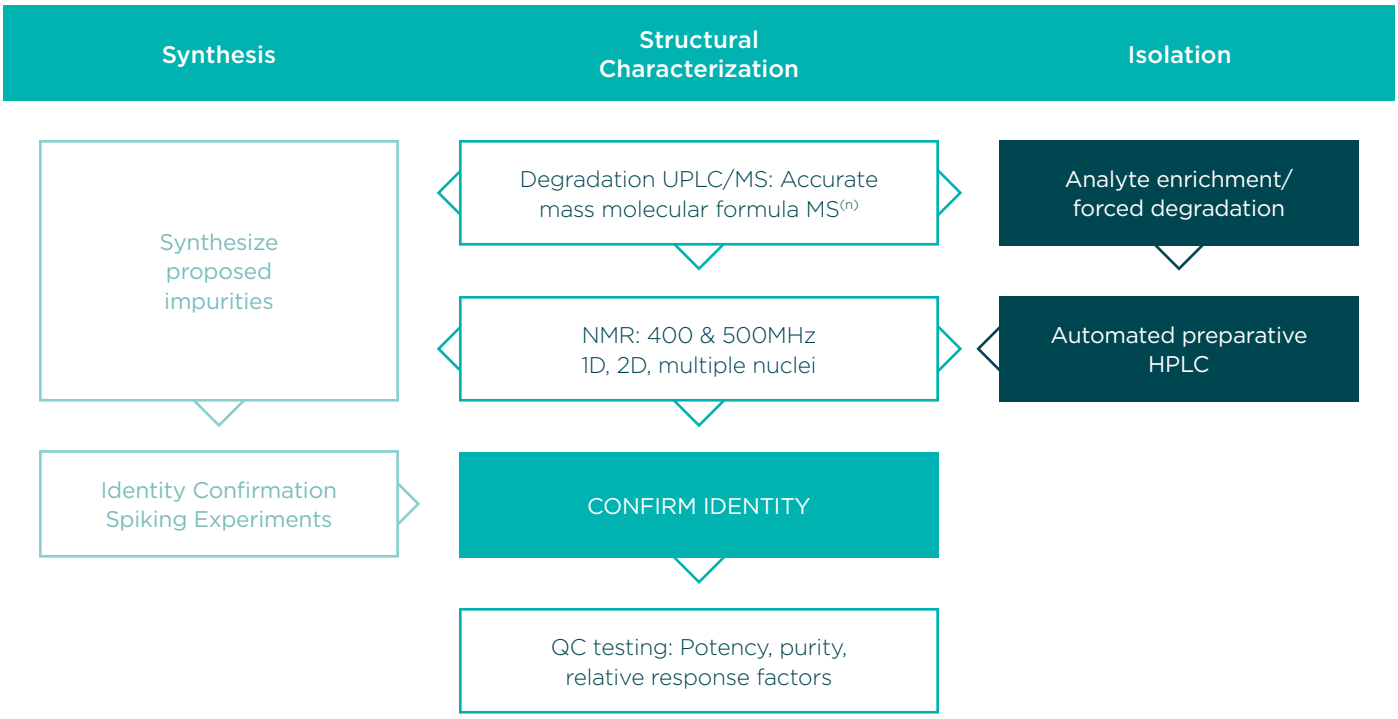
Cambrex provides the fastest route to qualified reference standards of impurities.

About Cambrex

Cambrex is a leading global contract development and manufacturing organization (CDMO) that provides drug substance, drug product, and analytical services across the entire drug lifecycle.

With over 40 years of experience and a growing team of over 2,200 experts servicing global clients from North America and Europe, Cambrex is a trusted partner in branded and generic markets for API and finished dosage form development and manufacturing.

Characterization of impurities



Dual in-house teams tackle impurities in parallel

Cambrex's analytical chemists and synthetic chemists work alongside each other to provide the fastest and most thorough characterization of impurities. We perform all steps of the isolation and identification of the impurity along with the synthesis and analysis in our state-of-the-art facility.

whether further toxicology studies were needed. Cambrex's expert chemists took immediate action to enrich the analyte through forced degradation and isolate the peak of interest. Our facilities are equipped to use a combination of the most advanced instrumentation, including UPLC, HRMS and NMR, to confirm the identities of materials. Moreover, Cambrex wields a competitive advantage by teaming our analytical chemists and synthetic chemists under the same roof for close collaboration.

With a proposed structure in hand, chemists initiated synthesis of the impurity. For this client, the short timeline triggered evaluation of four possible routes of synthesis in parallel, and the team was able to quickly deliver the structural identity within 10 days of beginning work. This allowed the client to provide evidence to regulatory authorities that the impurity did not compromise the toxicology profile of the product.

Once the impurity's identity was confirmed, the newly synthesized material was qualified as a reference standard and its Relative Response Factor (RRF) determined to allow accurate quantification. The quantitative results revealed a level of 0.1%, which is below the ICH Qualification threshold for impurities. Cambrex exceeds standard industry expectations in impurity characterization and synthesis. In addition to providing confirmed structural identity in under two weeks, the successful synthesis allowed our experts to support rapid analysis in future stability studies. The client minimized interruption to ongoing studies by providing evidence of the impurity identification to the FDA, and they are now equipped with a qualified reference standard to evaluate the presence of this impurity in their drug product in the future.

Authors

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