SUCCESS STORIES

EXSYN
ESSENTIAL CHEMISTRY

ICH Q3D(R) elemental analysis: Successfully developing a customized and cost-effective ICH Q3D analytical method along with risk assessment for an inhalation grade drug undergoing clinical trials in the EU.

OVERVIEW

ICH Q3D is key to the patient's safety: 24 elemental or metal impurities need to be controlled in pharmaceutical products depending on their permitted daily exposure (PDE). Q3D elemental analysis and methodology is the backbone to determine a PDE by incorporating scientific mechanisms to control elemental impurities which may be either introduced through the raw materials or the drug processing equipment and cannot be controlled by routine heavy metals tests carried out by manufacturers. Depending on the route of administration of the drug and its daily dose, the maximum permissible exposure of the various element's changes, hence the reviewing authorities requested our customer to implement USP <232> and <233> along with ICH Q3D for the determination of metal elements in their inhalation grade API.

KEY TAKEAWAYS

Y ExSyn conducted a scrutiny and proposed a suitable option of Indian CRO having expertise in performing analytical method development activities for elemental analysis (ICHQ3D)

Y By integrating and prioritizing key objectives of customer's specific requirements, the laboratory developed a scientific roadmap that required analytical method by ICP-MS and subsequently validated methods based on the risk-based approach, providing a rational assessment mechanism to the customer.

Y Studies were performed under a GMP-qualified laboratory.

THE CHALLENGE

In order to develop controls for elemental impurities for inhalation grade, the main challenge for the CRO was to design a protocol based on principles of quality risk management and the classification scheme as per ICHQ3D guidelines. The classification of elements is as follows:

Class 1: As, Cd, Hg and Pb

Class 2: Elements in this class are generally considered as route-dependent human toxicants. Class 2 elements are further divided in subclasses 2A and 2B based on their relative likelihood of occurrence in the drug product.
→ **Class 2A:** Co, Ni and V
→ **ClasS 2B:** Ag, Au, Ir, Os, Pd, Pt, Rh, Ru, Se and Tl

Class 3: Ba, Cr, Cu, Li, Mo, Sb and Sn

Other Elements: Al, B, Ca, Fe, K, Mg, Mn, Na, W and Zn

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THE SOLUTION

Y ExSyn's effective management of this standalone project was based on customer-centric approach, wherein a team of scientists from the CRO used their wide industrial experience and know-how to develop a feasible ICHQ3D method by ICP-MS for an inhalation grade API.

Y The CRO was able to run qualitative experiments based on ICHQ3D guidelines and develop a protocol which not only focused on the risk assessment of those elements that are the most toxic ones but also had a reasonable probability of inclusion in the final drug product.

Y Subsequently, the conclusive outcome of the methodology was verified on three different lots through validation and batch analysis. The obtained linearity, method precisions, accuracy at different levels, intermediate precision, LOQ precision and LOD confirmed that resulting parameters were well within the acceptable limits. A complete system suitability using target elements helped establish a suitable specification of ICHQ3D limits for the inhalation grade API.

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> "After implementing ICHQ3D elemental impurities based on a scientific approach, we were able to achieve a fully developed ICH Q3D analytical method along with the risk assessment for our drug application for inhalation grade undergoing clinical trials in Europe."
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> European Finished Dosage Formulator
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> "With ExSyn's precise targeting capabilities to effectively handle standalone and FTE analytical projects, coupled with time bound solutions for your analytical needs, we make sure that you get the most representative and customized ICHQ3D cost-effective solutions."
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> ExSyn Corp
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