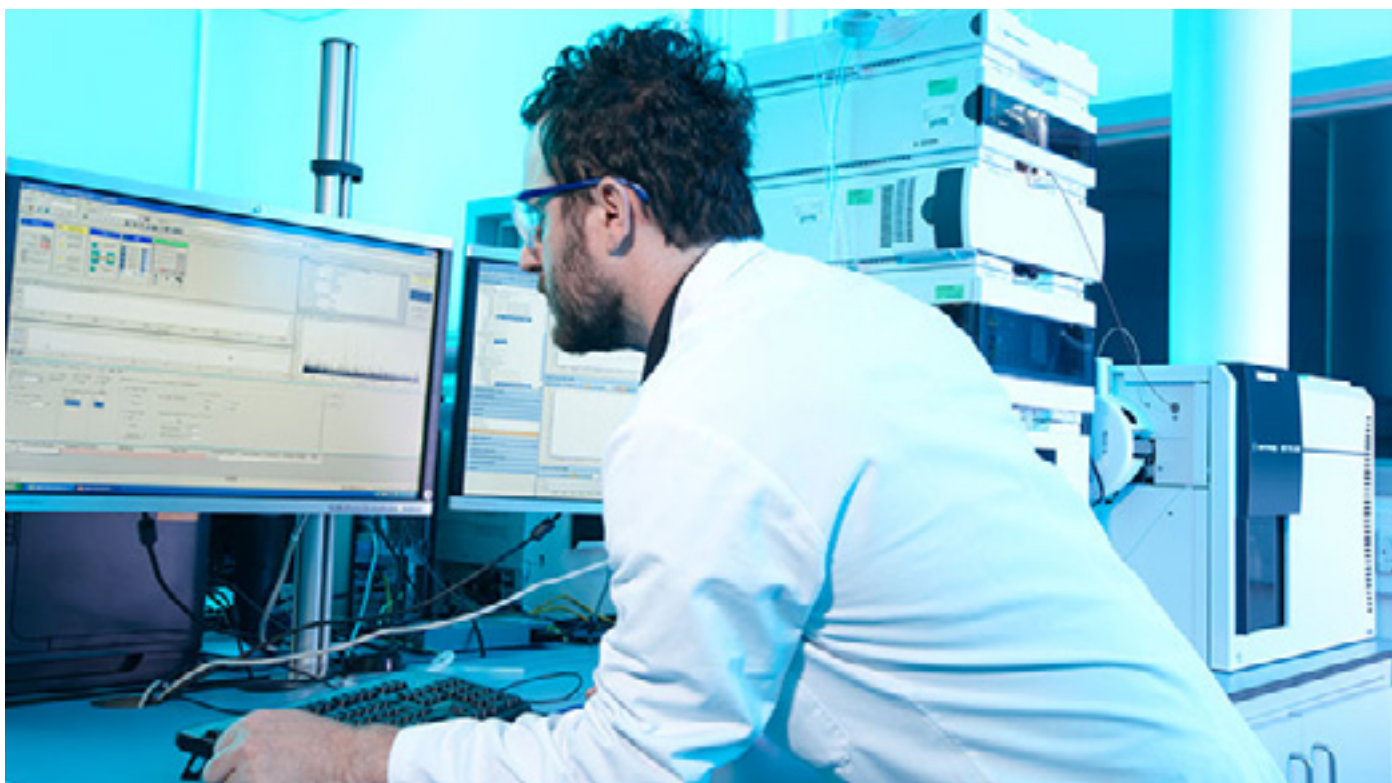


Exploring ICP-MS expertise at Almac

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A discussion about Inductively Coupled Plasma Mass Spectrometry (ICP-MS) and its importance within drug development.



Almac Sciences, a member of the contract development and manufacturing organisation Almac Group, provides integrated services from development to commercial scale of advanced intermediates and Active Pharmaceutical Ingredients (API). One of our key offerings is our analytical services, a group that employs over 170 highly skilled analysts working in GMP / GLP environments globally with significant experience in the analysis of both small and large molecules.

This article will discuss [Inductively Coupled Plasma Mass Spectrometry \(ICP-MS\)](#) and its importance within drug development. The author, Anna Cousens, joined Almac Sciences in 2012. She is part of the Global Analytical BD team that engages with clients worldwide on behalf of Almac's three analytical facilities based in the UK, Europe (Ireland) and USA (PA).

What is ICP-MS and why is it important?

ICP-MS is a spectroscopic analytical technique with applications in the detection of metals within drugs. It is one of the many different analytical techniques used by the industry to ensure that all drugs on the market are safe to use and manufactured to a high standard free from impurities. These impurities can come from different chemical bonds forming in the manufacture, degradation of raw materials or finished products, or from the presence of residual catalysts or foreign objects from any apparatus used. Different types of impurities require different testing methods, and Almac performs a wide range of these testing methods for clients. For impurities relating to the API or drug product, HPLC testing is frequently used. HPLC release methods for these compounds often capture common impurities and detect their presence right

down to low levels, however when potential impurities are of a different nature, spectroscopic tools are often required. Almac uses a variety of these tools to interrogate unknown impurities, often using many orthogonal tests to narrow down the options, in order to achieve successful elucidation of the full structure of the impurity.

When conducting tests for metal impurities in drugs there are two methods that can be deployed, the traditional wet chemistry assay, or a new highly specific ICP-MS.

ICP-MS is a relatively new technology which came into mainstream use three years ago when new United States Pharmacopeia regulations were implemented regarding limits on heavy metals in pharmaceutical products.

What were the new regulations?

All drugs are subject to tight controls on their quality and purity, and the standards followed depend on which country a product is being manufactured or sold in. There are three key bodies involved which set the criteria with which to comply: the EP (European Pharmacopeia); JP (Japanese Pharmacopeia) and the US (United States Pharmacopeia, or USP). More recently, the International Council for Harmonisation (ICH) has brought consensus between these three pharmacopeias in order to simplify the requirements.

Regarding Elemental impurities, the USP developed the “gold standard” of testing in this area. This standard covers a wide range of analysis, but it is chapters <232> Elemental Impurities-Limits and <233> Elemental Impurities-Procedures which specify limits and procedures for elemental impurities in drug products. In chapter USP <233> method implementation, validation and quality control during the analytical process are described. In 2018, these much-needed new chapters were implemented to address a myriad of issues with the traditional wet chemistry methods of quantification of elemental impurities. Although, from a technical perspective it was a welcome change, companies needed to adapt quickly to a new technology that wasn’t in routine use and was expensive to buy.

So these regulations drove changes in the market?

Yes, these regulations impacted CDMOs and Pharma companies

in how these analyses were performed. In the last three years, there has been significant activity in this space as manufacturers sought to comply with the new regulations. Any pharmaceutical product sold in the US needed to comply with these regulations hence its effects were felt industry wide across all drug delivery platforms: from tablets and capsules, to vials, injectables and even devices. In addition, the impact had repercussions for all suppliers into this market as the final product manufacturers performed risk assessments of where these elemental impurities could originate. This led to a significant increase in the number of enquires to API, raw material and excipient suppliers and manufacturers requesting information about their procedures. The entire industry had to update their testing regimes to include the new ICP-MS standards. Some companies with very low risk of elemental impurities performed a risk assessment which limited the amount of testing required, whilst others had to completely rethink their approach and develop and validate new ICP-MS methods for their complete product portfolio. With an increased demand in testing, sales of equipment exponentially grew driven by demand from finished product manufactures, big pharma and CDMOs.

How did Almac respond?

Almac was proactive to ensure the increasing client demand would be met. Significant investment was made in purchasing state of the art equipment, expanding and improving facilities and training our already skilled employees in order to conduct the required development and validation of methods. In addition, the Aglient 7900 was installed, validated and qualified for GMP use which is used to support in-house API and drug product manufacture, as well as supporting clients as a contract service.

The increased volume of samples tested at Almac has led to further investment and the purchase of a second ICP-MS instrument, a Thermo iCAP RQ which has also been qualified for GMP use and has allowed Almac to increase the volume of analyses it can support.

What is Almac’s experience in this area?

Almac has developed a wealth of experience in this area:

- Performed **57 validations**: from Phase I to commercial release and stability support.

- QC support for **>30 APIs**.
- Customer analysis: approx. **60 different test articles** including drug substance/API, Excipient/ drug product and raw materials for various projects at different stages of development.

Almac has a comprehensive and practical understanding of the new regulations providing robust methods to support our growing client base.

What is next in this space?

In the coming months, new guidance will be issued on Nitrosamines and will present a new set of challenges to analytical professionals globally.

Almac is already working to adapt to these changes and has methods in place to support clients in this area, having over 20 years’ experience using LCMS equipment. This equipment is managed by Almac’s spectroscopy team – a 30 strong group of employees that manages an extensive range of equipment (including 2D LCMSMS equipment, GCMS and NMR) that is fully GMP compliant. The team has extensive knowledge, not only of the equipment and our library methods, but also structural interpretation and data processing to ensure the correct experiments are run for each project. The Pharma industry, as a whole, is no stranger to change. Almac, with its wealth of knowledge, expertise, and ability to adopt and adapt as required, offers a straightforward solution to any challenge.

[Learn more about Mass Spectrometry expertise at Almac](#)