**Mass Spectrometry in the pharmaceutical industry – the amazing impact on the delivery of medicines to patients**

Tony Bristow

Chemical Development, Pharmaceutical Technology and Development, Operations, AstraZeneca, Macclesfield, UK

Mass spectrometry (MS) is applied across AstraZeneca and the broader pharmaceutical industry. It is a business critical analytical science technology with impact from discovery, through early and late stage development and out to quality control in the operations and manufacturing.

During the discovery phase MS is essential in terms understanding a biological target, the structural design of a molecule and evaluation of drug metabolism and pharmacokinetics (DMPK). As a potential new medicine moves into the early and later stage development, specialist qualitative and quantitative MS application turns to the understanding of the impurity profile of the active pharmaceutical ingredient (API - the drug substance) and the formulated drug product. This knowledge is foundational for the development of the drug substance and drug product manufacturing processes. The resulting control strategy for the new medicine, demonstrates its quality and safety and is informed by MS data. The MS data is also applied in the authoring of a regulatory submission. More broadly MS plays a key role in method development for multiple chromatographic approaches and is democratised broadly though open access MS technologies.

Though strongly established in many areas of AstraZeneca (examples include DMPK, extractables and leachables), the application of trace analysis has expanded since 2018, driven by the risk of the presence of trace nitrosamine impurities in drug substance and drug product. High resolution LC-MS/MS and GC-MS methods have been developed to meet strict regulatory safety criteria, with requirements for both LOQs and LODs as low as single digit parts per billion (ppb). A number of methods have required analytical technology transfer to internal operations quality control (QC) laboratories. This has delivered on-going testing of drug products to demonstrate safety and to maintain the release of the medicines to patients.

Though these examples demonstrate the current impact of MS, it is clear that the role and impact will continue to grow in AstraZeneca and across the pharmaceutical industry. This is driven by the increasing diversity of both biological and synthetically generated molecules, that are the medicines of the future. The next generation of molecules are larger, increasingly complex and include small molecules, oligonucleotides, peptides, proteins, antibody-drug conjugates, other conjugates and mRNA. Therefore, innovation in MS for the pharmaceutical industry remains essential and will arise from in-house developments and those delivered through collaboration with academia and many instrument/technology manufacturers.

This presentation will illustrate the impact of MS across AstraZeneca, with multiple examples of innovation and application from all phases in drug discovery, development and medicine supply