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An Elemental Impurities Excipient Database: A Viable Tool for ICH Q3D Drug Product Risk Assessment

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ABSTRACT

To support the practical implementation of the ICH Q3D guideline, which describes a risk-based approach to the control of elemental impurities in drug products, a consortium of pharmaceutical companies has established a database to collate the results of analytical studies of the levels of elemental impurities within pharmaceutical excipients. This database currently includes the results of 26723 elemental determinations for 201 excipients and represents the largest known, and still rapidly expanding, collection of data of this type. Analysis of the database indicates good coverage of excipients relevant to real-world drug product formulations and tested element profiles consistent with ICH Q3D recommendations. The database includes the results from multiple analytical studies for an excipient and thus incorporates within it an indication of both excipient supplier and batch-to-batch variability as well as any variability associated with the different testing organisations and methods employed. The data confirm the findings of earlier smaller studies that elemental impurity concentrations in excipients are generally low and when used in typical proportions in formulated drug products are unlikely to pose a significant patient safety risk. The database is now in active use as one line of evidence in ICH Q3D risk assessments.

Keywords: Analytical chemistry, Excipients, Formulation, Mass spectrometry, Regulatory science

INTRODUCTION

The International Council for Harmonisation (ICH) Q3D guideline describes a risk-based approach to the control of elemental impurities in drug products.[1,2] The first step of the risk assessment requires the identification of known and potential sources of these impurities. The focus within this work is on the consideration of excipients used in drug product formulation. According to ICH Q3D, evidence collected in the risk assessment can be derived from numerous sources which, other than the results of testing, may include data and information provided by a supplier and the use of published literature. However, currently, in the case of excipients, supplier information relating to elemental impurity determinations is often limited[2] and published literature is also sparse. Barin and co-workers, for example, undertook a literature review of published studies