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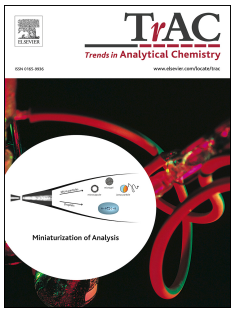

Analytical Control Strategies for Mutagenic Impurities: Current Challenges and Future Opportunities?

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Analytical Control Strategies for Mutagenic Impurities: Current Challenges and Future Opportunities?

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1. Abstract

The last decade has seen continued development and refinement of guidance related to mutagenic impurities (MIs); culminating in June 2014 with the publication of ICH M7. This has seen an introduction of factors such as durationally adjusted limits and emergence of alternative approaches to demonstrate control, such as purge factor calculations, Teasdale et al.

This review examines the impact of these changes on the approaches taken to the analysis of MIs. Observed is the emergence of platform approaches; methods that can be applied to a class of MIs rather than simply to individual analytes. Another observation and concern is the continued development of highly specific sensitive methods for analytes, where appropriate knowledge of the status of the analyte (i.e. it is actually non-mutagenic), would have precluded the necessity to do so. This illustrates the need to conduct a thorough review of the available literature before analytical method development is commenced.

2. Introduction

Regulatory guidance relating to mutagenic (genotoxic) impurities (MIs) has evolved significantly over the last decade. Ten years ago the EMEA's (now EMA) control strategy could be simplistically summarized as: avoidance > reduction > control, in terms of a hierarchal strategy [1]. In retrospect, avoidance of MIs was never really tenable as a strategy; as complex, multi-functional active