

DETERMINATION OF ELEMENTAL IMPURITIES IN ACTIVE PHARMACEUTICAL INGREDIENTS ACCORDING TO CURRENT LEGISLATION BY USING X-RAY FLUORESCENCE SPECTROMETRY

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The determination of potential impurities in different stages of the pharmaceutical manufacturing processes, and especially in the final product, is necessary to prevent potential risk to human health. Metals can be introduced in the active pharmaceutical ingredients (API) through different sources (e.g., naturally derived plant or mineral raw materials, catalysts or other equipment used in manufacturing). Consequently, they are potential impurities in the drug substances and are routinely monitored.

All pharmacopoeias include a test for heavy metals, which is commonly carried out by sulfide precipitation in a weakly acidic medium and visual comparison of the color of a simultaneously and similarly treated standard solution of lead. The compendial method is nonspecific, insensitive, time-consuming, labour intensive and mostly yield low recoveries. Further serious limitations of the visual heavy metals test are the lack of selectivity and the inability to detect some metals as platinum, palladium, iron or nickel (frequently used as catalysts) which have to be determined. Therefore, great effort is currently being devoted to the development of new procedures to control metals in pharmaceuticals that rely on modern analytical methodologies. For instance, the United States Pharmacopoeia (USP) describes a new testing approach in a recent Pharmacopoeial Forum article [1] and suggests spectroscopic techniques based on plasma (optical or coupled to mass spectrometry) as reference technique. However, when using these techniques, a prior digestion of the solid drug sample is required, leading to a time consuming and elaborated sample treatment. A promising alternative could be the use of solid state techniques such as X-ray fluorescence spectrometry (XRF).

This work gives an overview of the state-of-the-art of X-ray fluorescence spectrometry for the determination of some metal impurities in APIs according to current legislation [3]. Special attention is paid to current instrumentation, and the advantages and limitations of each configuration mode are highlighted. Typical validation characteristics that should be considered for the approval of alternative procedures according to the USP are also evaluated.

References:

[1] <232> Elemental impurities-Limits, <233> Elemental impurities-Procedures. Pharmacopoeial Forum Vol.36(1) [Jan-Feb.2010]

[2] E.Marguí, K.Van Meel, R.Van Grieken, A.Buendía, C.Fontàs, M.Hidalgo, I.Queralt. Anal.Chem.81(2009)1404-1410.