Online Real Time Metal Analysis during Pharmaceutical Manufacturing

M. Garcia and N. Kumar

nanoRANCH-UHV Technologies, Inc., 1708 Jaggie Fox Way, Lexington, KY, USA 40511

The ability to rapidly measure metals at the low ppm levels is becoming increasingly important in pharmaceutical manufacturing and there is a need to develop low cost instruments that can be used for real time online detection and analysis during manufacturing of pharmaceutical drugs and compounds. In general, there are three methods of incorporation of metallic impurities in the product during manufacturing.

Metallic catalysts are extensively used during manufacturing of pharmaceutical drug compounds. These include metals such as Palladium, Rhodium and Iridium, which must be removed after the steps involving catalysis to avoid incorporation of these metals in to the final products. Another source of impurities is the metal particles and broken pieces (e.g. broken sieves etc.) from the production equipment such as reactors, tanks, filters and pipes. These metals can include Iron (Fe), Copper (Cu) and Zinc (Zn) in addition to stainless steel (made of Fe, Cr and Ni) and platinum. Lastly, the metal impurities can come from the raw materials (plants, animal proteins, rDNA, etc.) and excipients (stabilizers, fillers, binders, release agents, flavors, colors, coatings, etc.)

Ensuring the removal of these metal impurities is required to avoid toxicity associated with heavy metals. The best method for this will be an online instrument that can be used at point of use in the manufacturing line to continuously detect, measure and analyze metallic impurities. An improved approach would allow low ppm metals analysis to be performed at point of use, employing affordable, robust equipment that would be easy to operate by any lab technician.

UHV has developed an XRF instrument to detect low ppm levels of the entire suite of metals commonly used in modern synthetic organic chemistry (Pd, Rh, Cu, Zn, Fe, Ir, etc.) within active pharmaceutical ingredients (APIs), powders, syrups and liquids. This instrument has been shown to measure palladium and rhodium with a sensitivity of 2-3 ppm in pharmaceutical samples. The design of the instrument and latest results from the work to date on this XRF technology will be presented in this paper.

* This project is funded in part by the US National Institutes of Health