PREAMBLE:

Impurities in pharmaceuticals are the unwanted chemicals that remain with the active pharmaceutical ingredients (APIs), or develop during formulation, or upon aging of both API and formulated APIs to medicines. The presence of these unwanted chemicals even in small amounts may influence the efficacy and safety of the pharmaceutical products. Impurity profiling (i.e. the identity as well as the quantity of impurity in the pharmaceuticals), is now getting receiving important critical attention from regulatory authorities.

In general, according to ICH guidelines on impurities in new drug products, identification of impurities below the 0.1% level is not considered to be necessary unless the potential impurities are expected to be unusually potent or toxic.

Definition “Impurity”

“(1) Any component of the new drug substance which is not the chemical entity defined as the new drug substance. (2) Any component of the drug product which is not the chemical entity defined as the drug substance or an excipient in the drug product.”

(ICH Q6A: Specifications)

IMPURITIES ARE CLASSIFIED AS BELOW IN ACTIVE PHARMACEUTICAL INGREDIENTS (API)

Impurities can be classified into the following categories:

- Organic impurities (process- and drug-related)
- Inorganic impurities
- Residual solvents

Organic impurities can arise during the manufacturing process and/or storage of the new drug substance. They can be identified or unidentified, volatile or nonvolatile, and include:
Starting materials

By-products

Intermediates

Degradation products

Reagents, ligands, and catalysts

Inorganic impurities can result from the manufacturing process. They are normally known and identified and include:

Reagents, ligands and catalysts

Heavy metals or other residual metals

Inorganic salts

Other materials (e.g., filter aids, charcoal)

Solvents are inorganic or organic liquids used as vehicles for the preparation of solutions or suspensions in the synthesis of a new drug substance. Since these are generally of known toxicity, the selection of appropriate controls is easily accomplished.