Residual Solvents Analysis in 5 - Batch (Case Study)

The term "Residual Solvents" in pharmaceuticals/ pesticides are defined as organic volatile chemicals which are present in minute quantities, during the production of drug/ pesticide substances/ excipients. Most of the times, traces of these solvents are difficult to remove and are carried forward till the end-product. The residual solvents' analyses are an essential part of 5-batch study for determining and quantifying the compositional % of active ingredient and its impurities. It is the first step and key towards determining the composition of a technical grade product and defining its specification.

As defined in the ICH Q3C, the Permissible Limits (PL) or Permitted Daily Exposure (PDE) of residual solvents, belongs to one of the three classes, based on its toxicity:

- Class 1 solvents: Need to be avoided - known human carcinogens, strongly suspected human carcinogens and environmental hazards, e.g. benzene…..
- Class 2 solvents: Need to be limited - on-genotoxic animal carcinogens or possible causative agents of other irreversible toxicity such as neurotoxicity or teratogenicity. Solvents suspected of other significant but reversible toxicities, e.g……
- Class 3 solvents: Need no health- based exposure limit due to its low or negligible toxic potential to human life; Class 3 solvents have PDEs of 50 mg or more per day.

Most of the generic drug/ pesticide substances have similar residual solvents' impurities. However, to discriminate them in a given product calls for development and validation of specific analytical methods, based on the individual drug /pesticide substances and the physicochemical properties of the impurities. JRF has invested time and resources to develop a single gas chromatographic GC method is validated for the determination of common residual solvents' impurities (viz., methanol, dichloromethane, n-hexane, trifluoroacetic acid, isopropyl alcohol, acetonitrile, acetone, acrylonitrile, acrylamide, acrylic acid, toluene, ethyl acetate, tetrahydrofuran, dimethylformamide, chloroform, cyclohexane, benzene, diisopropylamine, heptane, p-xylene, n-octanol, etc.) This method can quantify up to 0.1 mg/L of residual solvents using single analytical method for different drug/ pesticide products.

About The Author

Mr . Ashok S. Amruskar, with specialization in Chemistry is a senior research officer, in the Department of Chemistry. He has contributed commendably as a Senior Scientist in the developing and validating analytical methods, and conducting 5-Batch and Physico-Chemical studies for agro-chemical compounds. He is having an experience of over 18 years in CRO industry.

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The key services of JRF are dedicated to the establishment of the discovery and development of a drug, as well as the efficacy and safety of products, in our well established and highly credible state of the art research facilities, pertaining to the Analytical, Bio-analytical chemistry, and Organic synthesis, IND enabling Mammalian Toxicology and Mutagenicity under endorsement of the OECD GLP."

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