INTRODUCTION

The quality of product may deviate from the standard required but in carrying out an analysis one also has to certain that the quality of the analysis itself is of the standard required. Quality is integral to all modern industrial processes and the pharmaceutical industry is no exception. Testing a pharmaceutical product involves chemical, physical and sometimes microbiological analysis. Pharmaceutical analysis procedures may be used to answer any of the questions outlined.

ICH GUIDELINES

The requirements for control of the quality of methods of analysis (validation) have been addressed by the International Conference on Harmonization of Technical Requirements for registration of Pharmaceuticals for Human Use or more briefly, the ICH (www.ich.org). The ICH was initiated in Brussels in 1990 and brought together representatives of regulatory agencies and industry association of Europe, Japan and the USA. The purpose of the organization was to standardize the requirements for medicines regulation throughout the world. The standardization of the validation of analytical procedures is one area that the ICH has addressed. The ICH indicated that the most important analytical procedure that require validation are

IMPURITY PROFILE

Impurity:

Any component of the new drug substance that is not the chemical entity defined as the new drug substance.

Impurity profile:

Impurity profile is a description of the identified and unidentified impurities present in a typical batch of API (Active Pharmaceutical Ingredient) produced by a specific controlled production process. It includes the identity or some qualitative analytical designation (e.g. retention time), the range of each impurity observed, and type of each identified impurity.

Sources of impurities in pharmaceutical manufacture.
During the course of the manufacture of a pure drug substance, impurities may arise as follows:

i. Present in the synthetic starting materials

ii. Result from residual amounts of chemical intermediates used in the synthetic process and form unintended side reaction.

iii. Result from reagents, solvents and catalysts used in manufacture.

The process used to produce the formulated drug substance may introduce impurities as follows:

i. Particulate matter from the atmosphere, machines and devices used in the manufacturing process from containers.

ii. Impurities that are present in the excipients used in the formulation

iii. Cross contamination may occur from other processes carried out using the same equipment, e.g.: from mixers

iv. Microbial contamination may occur

v. The drug may react with the excipients used in the formulation

vi. Impurities may be introduced from packaging, e.g.: polymeric monomers.

According to ICH guidelines, impurities associated with API’s are classified in to the following categories:

. Organic impurities (process and Drug-related)

. Inorganic impurities

. Residual solvents

Organic impurities may arise during the manufacturing process and/or storage of the drug substance. They may be identified or un-identified, volatile or non-volatile, and include the following.

1) Starting materials or intermediates
2) By-products

3) Degradation products

The importance of impurity analysis in pharmaceutical products:

To purity a material and remove the excess impurities one should first recognize that whether they are actually present and what their nature is. In the fast this was not always done. But presently drug analysis and pharmaceutical impurities are the subjects of constant review in the public interest. The international conference on harmonization (ICH) guidelines achieved a great deal in harmonizing the definitions of the impurities in new drug substances. It is necessary to perform all the investigations on appropriate reference standards of drug and impurities to get meaningful specification. In order to meet the challenges to ensure high degree of purity of drug substance and drug products, a scheme is proposed for profiling drug impurity. Finally, analytical methods based on analytical instrumentation must be employed to quantitate drug substance and its impurities.

HIGH-PRESSURE LIQUID CHROMATOGRAPHY

For most pharmaceutical analysis, separations are achieved by partition of compounds in the test solution between the mobile and stationary phases. Systems consisting of polar stationary phases and non-polar mobiles phases are described as normal phase, while the opposite arrangements, polar mobile phase and non-polar stationary phase is called reverse-phase chromatography. Partition chromatography is almost always used for hydrocarbon-soluble compound of molecular weight less than 1000. The affinity of compound for the stationary phase, and thus its retention time on the column, is controlled by making the mobile phase more or less polar. Mobile phase polarity can be varied by the addition of a second, and sometimes a third or even a fourth, component.

Columns used for analytical separations usually have internal diameters of 2 to 5 mm; larger diameter columns are used for preparative chromatography.

Detectors:
Many compendial HPLC methods require the use of spectrophotometric detectors. Fixed, variable, and multi-wavelengths detectors are widely available. Fixed wavelengths detectors operate at a single wavelength, typically 254 nm, emitted by a low-pressure mercury lamp. Variable wavelength detectors contain a continuous source, such as a deuterium or high-pressure xenon lamp, and a monochrometer or an interference filter to generate monochromatic radiation at a wavelength selected by the operator.