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Pharmaceutical Industry and the Role of an Analyst

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Editorial

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Editorial

Analytical chemistry prospers because it is continuously evolving and hence changing. The users of analytical instruments increasingly are exploiting their inventiveness as chemical measures to learn, to measure and investigate diverse phenomenon that collectively regarded as "Measurement of Chemical System". Pharmaceutical industries are working diligently for the betterment of humans in the society. These industries produce and monitors the drug in various dosage form, average duration of drug manufacture, keep a close check on stability in different formulations and perform impurity determination. Emergence of pharmaceutical industries has led to the demand for the development of analytical methods. Being decisive element for the quality of active pharmaceutical ingredients and formulations it is very important to develop efficient and accurately validated methods for pharmaceutical analysis as per guidelines [1]. Analytical method development should aim at delivering reliable measurements within a given application. For a successful method development, it is important to understand method fundamentals and how they may influence the analysis. It takes approximately 15 rigorous years for a medicinal product to come to the market and these years are associated with distinct phases of drug development. The requirement of quality, quantity, purity and safety of pharmaceutical products warrants a careful thought by everyone associated with this area. The pharmaceutical industry is required by the Food, Drug, and Cosmetic Act to establish the identity and purity of all marketed drug products. The United States Food and Drug Administration (FDA) and other regulatory bodies around the world require that impurities in drug substance (active pharmaceutical ingredient) and drug product (formulation) when present at threshold levels recommended by the International Conference on Harmonization (ICH) be isolated and characterized. Analytical method development for the quantification of low level impurities present in pharmaceuticals can be considered a three step process.

a) Selection of the sample for analytical method development.
b) Screening of chromatographic conditions and phases, typically using the linear-solvent-strength model of gradient elution.
c) Optimization of the method to fine tune parameter related to ruggedness and robustness.

Assuring the safety of a new pharmaceutical compound or drug substance demands that new drug substance must meet the established purity standards as a chemical entity or when mixed with animal feeds for toxicity studies or when formulated with or without pharmaceutical excipients for human use. Due to easy availability of sub-standard drugs and medicines in the market it is crucial to assay the drugs in bulk and dosage forms. Hence development of rapid, simple and cost-effective analytical methods for the analysis of drugs is the need of the day in public defense /interest.

The role of laboratory analyst in the in the development process is to provide data to establish the identity, potency purity and overall quality of the active pharmaceutical ingredients and the finished product. Figure 1 depicts a versatile role of an analyst during the drug development process. Analytical methods are required to establish equivalency of different formulations and batch sizes during the development process. An analyst supports process development, characterization, scale up and process validation activities. The developed method by the analyst should have sufficient controls and proper documentation to ensure the accuracy and reliability of the data.

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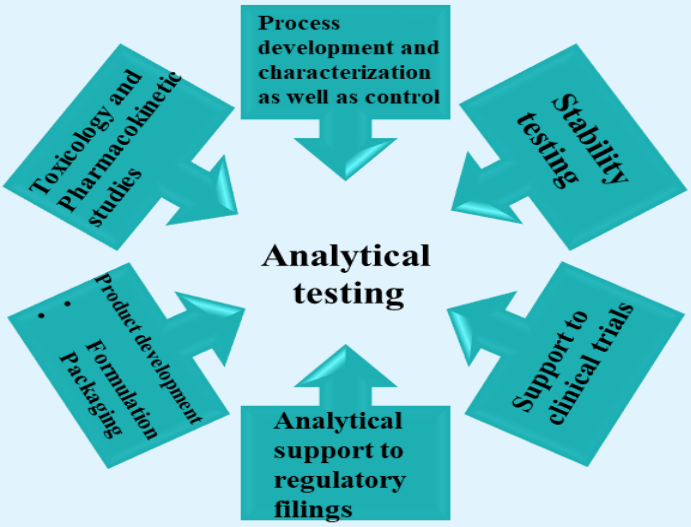

Figure 1: Role of the laboratory analyst in the development of a drug molecule.

The discovery of drug (pharmaceutical concern) lies on separate phases of drug development. At the end of each phase suitable registration documents are submitted to the regulatory authorities for getting allowed to move on to further and up-to clinical trial phases. Figure 2 showing the flow block diagram of a drug development process.

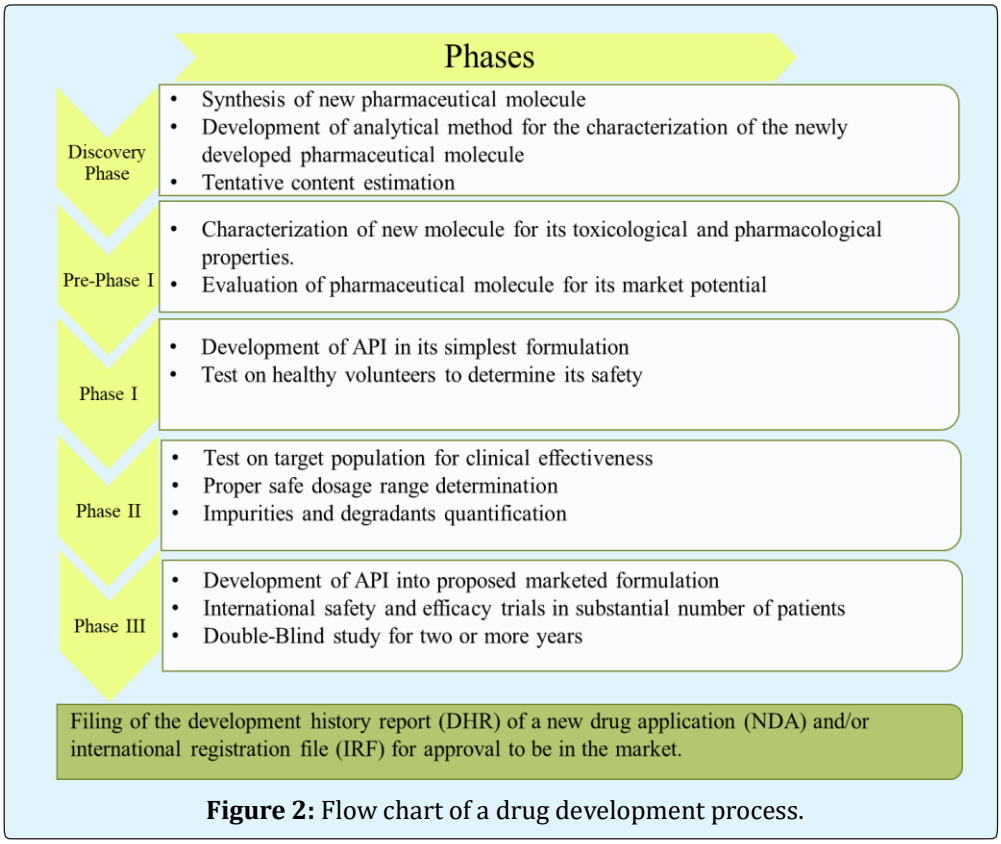

Figure 2: Flow chart of a drug development process.

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New drug development requires that meaningful and reliable analytical data be produced at various stages of the development. From the analytical chemistry and process laboratory prospective, Figure 3 is showing the step wise requirements and their inter-connections for the generation of the development history report (DHR) for filing purpose to regulatory authorities. During drug development key decisions are based on the data obtained from the analytical test methods. Therefore, results from these processes must be both accurate and precise. The developed test methods by the laboratory analyst are used in the evaluation of product safety, dosage form's bioavailability, establishment of specifications for drug substance, intermediates and drug product, stability of the API / formulation, identification, quantification and qualification of impurities, and support to preclinical and clinical studies for product safety and efficacy.

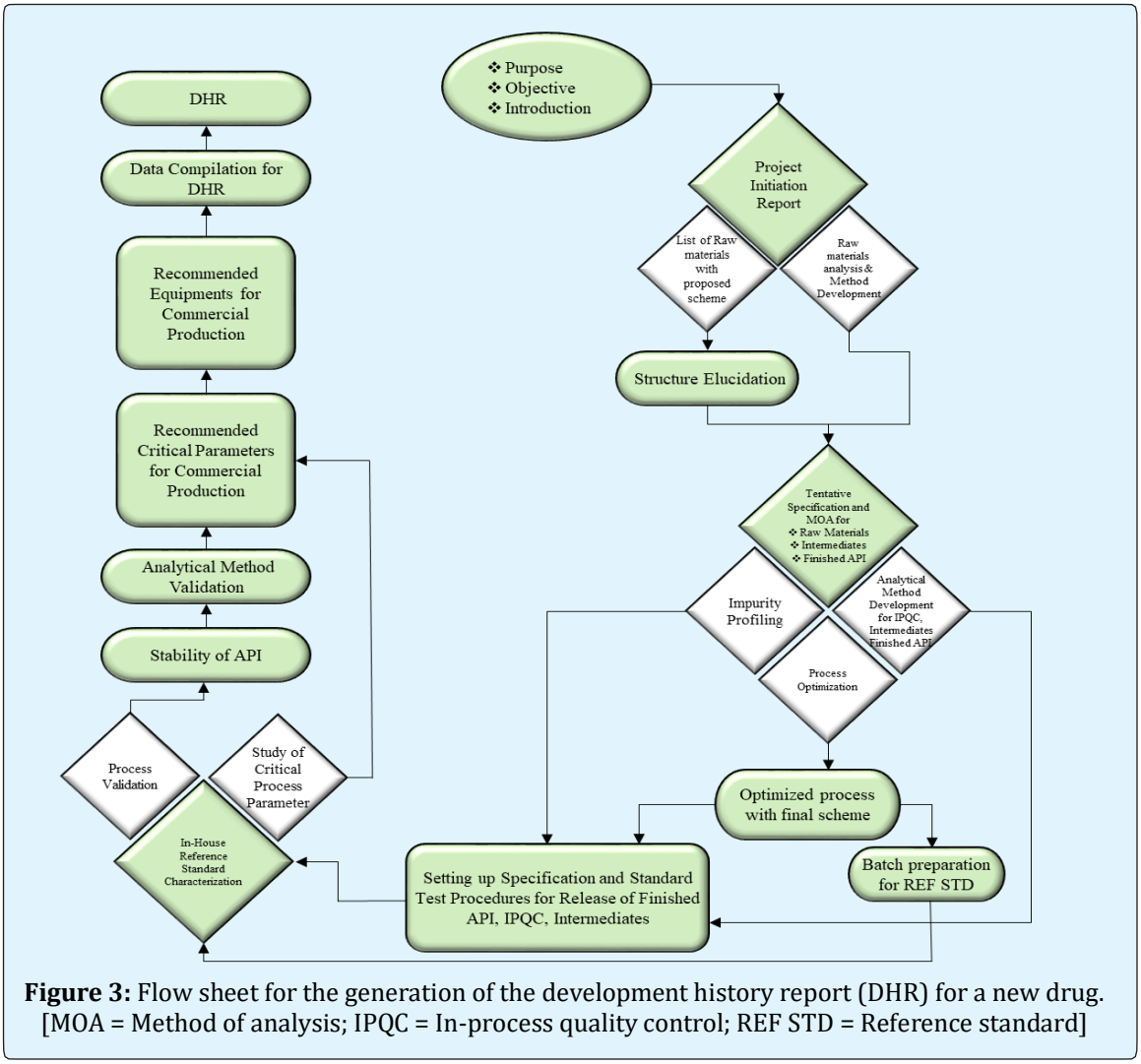

Figure 3: Flow sheet for the generation of the development history report (DHR) for a new drug. [MOA = Method of analysis; IPQC = In-process quality control; REF STD = Reference standard]

Analytical method validation has evolved successfully over a number of years into the formalized, well founded process and now it's recognized [2,3]. The key elements of method performance (accuracy, precision, sensitivity etc.) are well established for laboratory based pharmaceutical analysis [4-6]. While advances continued to be made in measurement technology within existing, well established pharmaceutical techniques, the basic requirement of method validation for such techniques remains largely unchanged. Special attention must be given to the robustness of the analytical methods, especially for those methods that will ultimately has to be transferred from

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R&D laboratory to quality control laboratories or stability testing laboratories. Therefore, robustness is a part of the initial new drug application (NDA) / international registration filing (IRF) method development. Robustness should not be compromised as the method will be carried out by several groups during its progress from development to validation. A key analytical contribution to a NDA filing is the method validation package. During the development of an analytical method the major required factors are the involvement of the skilled analysts, availability of qualified analytical instruments which requires periodic calibration and preventive maintenance and the method development section must be cGMP compliant. Figure 4 shows the inter-related elements that are required for the generation of reliable data. The mentioned factors for the development process ensure successful application of an analytical method worldwide as required.

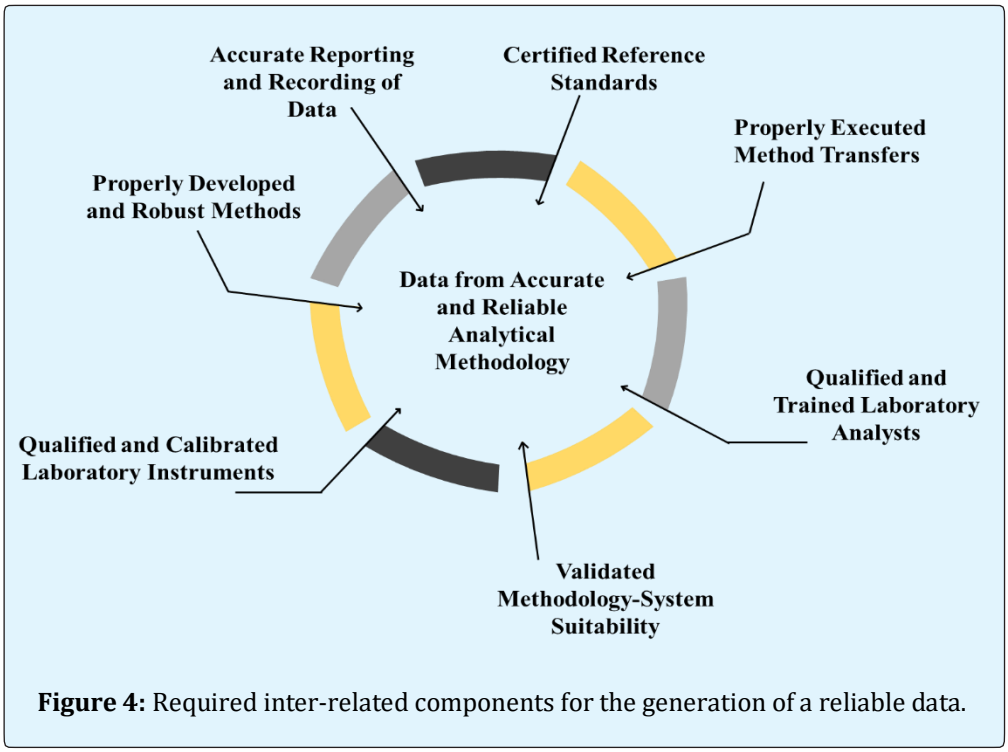

Figure 4: Required inter-related components for the generation of a reliable data.

It is observed that same formulations are being produced by various companies according to their set standards. Therefore, validation of each of the method is necessary to stand international competition and maintaining the standard of product in commercial and dosage form. Name of the international regulatory agencies that have fixed the standard and protocol to agree with the reference for approval, authentication and registration are mentioned below

a) United States Food and Drug Administration (US FDA)
b) Current Good Manufacturing Practice regulations
c) Good Laboratory Practice regulations.
d) The Pharmaceutical Inspection Cooperation Scheme's (PIC/S)
e) The International Conference for Harmonization (ICH)
f) Quality Manual ISO/IEC 17025 issued by International Organization for Standardization.
g) World Health Organization (WHO)

Pharmaceutical manufacturers ensure the safety and efficacy of drug products by coupling the tight control of raw materials and manufacturing process with well executed toxicological and clinical trials for new drug applications (NDAs). The testing and quantification of drug substance should continue in such a way that the necessary documentation (internal and external reports, certificate of analyses, stability reports supporting raw data) is complete from both a regulatory and scientific standpoint at the time of the NDA filing.

Regulatory dossiers compiled by the laboratory analyst, particularly for new active substances, tend to

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reflect state-of-the-art analytical techniques from a few years prior to the application because the drug development takes place over a relatively long time scale. The chosen method should be reproducible, simple and convenient. It meets the demands required at each stage of drug development, so they can be applied in quality control laboratories for analysis of studied drug.

The laboratory analyst needs to be aware of the basis of drug development efforts and the effect that drug / formulation may have on testing of the final product. Consequently, the quality and composition of inactive materials begin to have more importance to analytical testing. Often, complicated formulations (extended release, polymer extrude or coated microspheres, complexes) that presents further analytical challenges during drug /formulation development and its characterization.

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