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Analytical development-role of innovative and differentiating technologies

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Perspective

Analytical development-role of innovative and differentiating technologies

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Abstract

India is today, one of the top emerging markets in the global pharmaceutical landscape. The sector is highly knowledge-based and its steady growth is positively affecting the Indian economy. The targets of the global pharmaceutical companies are always "First to File" with "Right time-first time" approach. A successful organization always differentiates itself for their process. It works with a vision, leveraging on new technologies and ideas. In order to have more confidence in data and to understand the analytical development process better, we need to introduce some orthogonality in our analytical development process like the *mass detectors*. In order to automate and fasten the process of method development and transfers, Pharmaceutical scientists uses UPLC's. It is an LC system with inbuilt features to support faster method developments like automated solvent/pH/salt blending and has softwares assisting in method transfers across LC platforms. The adoption of UPLC methods for various tests by different regulators like US-FDA, EMEA as release methods or alternative methods and adoption of UPLC by EP and USP in their monographs (NF and MC) clearly reflects the reason for the increase in trend with respect to its implementation. Hence, Pharmaceutical companies can leverage upon the new technologies to increase the throughput efficiency and differentiate oneself in this competitive world.

Keywords: HPLC, Pharmacopoeia, Characterization

India is today, one of the top emerging markets in the global pharmaceutical landscape. The sector is highly knowledge-based and its steady growth is positively affecting the Indian economy. The organized nature of Indian pharmaceutical industry is attracting several companies that are finding it viable to increase their operations in the country. India is expected to be the third-largest global generic active pharmaceutical ingredient (API) merchant market in coming years, with 7 per cent market share approximately.[1]

The Indian pharmaceutical sector accounts for about 1.4 per cent of the global pharmaceutical industry in value terms and 10 per cent in volume terms. The country's pharmaceutical industry is expected to expand at a Compounded Annual Growth Rate (CAGR) of 14.5 % over 2009-2020 to reach US$ 55 billion. The generics market in India is expected to grow up to US$ 26.1 billion by 2016 from US$ 11.3 billion in 2011.[1]

The targets of the global pharmaceutical companies are always "First to File" with "Right time-first time" approach. A successful organization always differentiates itself for their process. It works with a vision, leveraging on new technologies and ideas. Apart from the analytical instruments like High Performance Liquid Chromatography (HPLC), for an analytical lab to be successful, it requires analytical aptitude and expertise amongst its scientists. The technologies like HPLC, Gas Chromatography (GC), Ultraviolet (UV) and Infrared Radiation (IR) are conventional and mandatory technologies today and their usage in analytical laboratories may not be a differentiating feature anymore.

In order to differentiate from competition and meeting the targets like "First to file" and "Right

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time-First time", an organization needs to believe and invest in new technologies and ideas. Analytical scientists need to intensify their awareness for new technologies and solutions that are in the market, so that they are appropriately utilized. This article discusses new technologies that can differentiate your lab from the rest, speed up the development process and also ensure success.

In a typical analytical development process, we have three major requirements - confidence in data, robustness of the method and speed of development process.

So, how does one verify that the analytical development process is on right track? Is implementation of Quality by Design (Quds) approach in analytical lab feasible without compromising on time? For example, in a related substance method development, we need to address some of the following aspects such as characterisation of peak, identification of non chromophoric impurities, tracking/identifying of peaks during forced degradation studies, screening and scouting of different chromatographic conditions as per QbD principles and ensuring that analytical method indicates stability. Does our current analytical method development process cover all these aspects and face no compromise? So, how does one verify that the analytical development process is on right track? Is implementation of Quality by Design (Quds) approach in analytical lab feasible without compromising on time? For example, in a related substance method development, we need to address some of the following aspects such as characterisation of peak, identification of non chromophoric impurities, tracking/identifying of peaks during forced degradation studies, screening and scouting of different chromatographic conditions as per QbD principles and ensuring that analytical method indicates stability. Does our current analytical method development process cover all these aspects and face no compromise?

In an analytical development process, we typically rely on UV-PDA detector as detector of choice and live with the limitations of the same. In order to have more confidence in data and to understand the analytical development process better, we need to introduce some orthogonality in our analytical development process like the mass detectors. The new generation of such orthogonal universal mass detector are designed so that any scientist/analyst who operates HPLC can use *mass detection* irrespective of his prior knowledge about mass spectroscopy. The usage of such mass detectors during the analytical development ensures confidence in the data.

The challenges in UV/PDA based developments can be resolved using such orthogonal universal Mass detectors. The term orthogonal refers to not only alternative but also techniques which can verify the correctness of primary technologies. The new generation Mass detectors are not spectrophotometers and has been purposefully designed to enable chromatographers/analysts to readily incorporate mass detection within a UV-PDA chromatographic workflow. The simplicity of such new generation Mass detectors is such that it can be handled easily by the chromatographers who have no Mass Spectrometry (MS) experience.

Once switched on, the new generation mass detectors are ready to be used in less than 25 minutes. They can be controlled through chromatography software, and hence enabling scientists to do various tasks like peak tracking and identification, analyzing non-chromophoric impurities, understanding mass-balance related issues, performing MS finger printing and confirming peak purity data

Figure 1: Acquity® QDa Mass detector

One of the major limitations of Mass Detector is its incompatibility with phosphate buffers. Most of existing pharmacopoeial or non pharmacopoeial methods have non-MS friendly mobile phase. In order to analyse such samples with Mass detectors,

we can utilize the 2D technology to clean-up the samples. In addition, 2D chromatography can help to streamline the sample preparation process by processing smaller sample volumes. Hence, 2D chromatography also helps to improve the sensitivity, accuracy and precision of the analysis.

Figure 2: 2-D UPLC

The above descriptions show how orthogonal detectors and technologies like 2D LC can help to address the aspect of "confidence in data" in analytical development process. Now, let us discuss the role of another innovative technology which has changed the outlook of industry with respect to throughput in LC analysis and brought the concept of "speed" in analysis with "no compromise", in its Ultra Performance Liquid Chromatography (UPLC).

In order to automate and fasten the process of method development and transfers, Pharmaceutical scientists uses UPLC's. It is an LC system with inbuilt features to support faster method developments like automated solvent/pH/salt blending and has softwares assisting in method transfers across LC platforms. UPLC has capabilities of performing both UPLC and HPLC applications. This flexibility has translated UPLC H-Class technology into one of the best example for "Future-proof" investment in Pharmaceutical industry.

Following QbD approach during analytical method development process was emphasized by US-FDA in their latest guidance on "Analytical Procedures" (effective July 2015). QbD recommends us to perform multivariate experiments by screening and scouting of different variables using Design of Experiments (DOE) approach. Screening and scouting can be done on UPLC by using multiple buffers, solvents and column chemistries.

The adoption of UPLC methods for various tests by different regulators like US-FDA, EMEA as release methods or alternative methods and adoption of UPLC by EP and USP in their monographs (NF and MC) clearly reflects the reason for the increase in trend with respect to its implementation. Here are some of the products having official UPLC methods in *USP- Glycopyrrolate, Tramadol HCl extended release tablets, Ganoderma Lucidum, Sulindac, Aminolevulinic acid, Schisandra Fruit, Almotriptan tablets. Reference UPLC methods official in EP are Quetiapine fumarate and Nevirapine.* The recent revision of USP Chapter <621> allows the conversion of HPLC methods to UPLC without the need of complete validation.

Hence, Pharmaceutical companies can leverage upon the new technologies to increase the throughput efficiency and differentiate oneself in this competitive world. To summarize, in order to have a bigger and stronger impact in pharmaceutical market, organizations need to adopt and implement usage of innovative and differentiating technologies like UPLC's and new generation compact mass detectors, which not only increases the productivity but also reduces the risk of products failure.

Reference

1. Pharmaceuticals. Indian Brand Equity Foundation (IBEF). March 2015.