



The pharmaceutical industry has registered tremendous growth & progress in the past few years. However, despite its success, the industry faces several unique challenges involving expanding costs, increasing competition, drying product pipelines & inability to replenish these pipelines, regulatory failures, etc. Amid these challenges, the industry is also required to comply with the ever-evolving stringent quality & safety norms. It is gradually getting more apparent that the compliance to the world-class quality norms is the key to success in this business, finds out **Saloni Vora**.

Today, the pharmaceutical industry is one of the fastest-growing knowledge-driven industries in the world and is continuously in a state of dynamic transition. In today's competitive scenario, company executives and decision makers attribute high importance to designing innovative marketing strategies and implementing strategic R&D plans, considering these to being the prime drivers of the industry's profitability & growth. On the other hand, the quality of operations sometimes takes a backseat, thereby affecting the bottomline of the company.

An article recently published in McKinsey Quarterly, highlights the fact that poor quality and compliance-related issues have cost the industry more than \$ 700 million in fines since 2001. Also, many a times, there are instances where the entire manufactured batch of products has been recalled due to inadequacies in expected product quality. These situations not only result in revenue losses but also loss of valuable time & effort. Thus, the implementation of stringent quality norms in various pharmaceutical operations is important, as these products are used for the treatment of ailing patients. On the same lines, Milind Pitale, vice president – Quality Systems, Inventia Healthcare, avers, "Human life is very precious and hence, pharmaceutical products should be of a high quality. Stringent quality norms should be imbibed throughout the process of product development right from conception to delivery."

For this, various pharmacopoeia guidelines act as a rich source of reference, and guide personnel on the required quality standards for a particular product with respect to its manufacturing, quality control & assurance and packaging. Says Dr Krishna Solanki, senior vice president – Quality, Unimark Remedies Ltd, "The pharmacopoeia specifications & guidelines are used to check &

Milind Pitale

vice president – Quality Systems, Inventia Healthcare



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control the quality of the products. In addition to these specifications, USDMF and EDQM CEP holders also require to control the toxic & non-toxic impurities and carcinogenic solvents. All such controls go a long way in providing quality medicines to a global population."

Over the years, there has been an evolution and revision in various quality norms followed in the pharma industry.

Evolution of GMP

The concept of GMP introduction can be traced back to 1960-1961 when the thalidomide disaster occurred, which resulted in the death of over 10,000 babies whose mothers had consumed the tranquiliser thalidomide. This disaster occurred due to negligence in studying the effects of the drug thalidomide and ambiguous rules & regulations to monitor the manufacturing aspects of drugs and their quality during the process and upon completion.

In India, The Drugs and Cosmetics Act was brought into effect in 1945 for monitoring the safety, quality and efficacy of drugs. Since then, many amendments have been made in this Act, to avoid the various incidences and mishaps that have taken place with respect to the manufacturing of pharmaceutical products. For example, the revised Schedule M gives a detailed and exhaustive list of GMP requirements that need to be followed by companies with respect to premises, equipment use, air quality and surroundings while manufacturing pharmaceutical products.

However, there is still a perception that quality of Indian products is not superlative and the country supplies cheap products by cutting corners. To convince people otherwise, a recent amendment was made in 2009 in the Drugs and Cosmetic Act (D&C Act) in relation to the manufacture & sale of spurious drugs, wherein the penalties for indulging in these activities has been increased to a minimum imprisonment of 10 years, which may extend to a life term. Moreover, a minimum fine of Rs 10 lakh or three times the value of the drugs confiscated, whichever is higher, has also been enforced. This would help in strengthening awareness across the world that Indian rules & regulations for supplying quality & genuine products are at par with international standards. Feels Dr Solanki, "The changes made in the Act are in line with international



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Dr Krishna Solanki

senior vice president – Quality, Unimark Remedies Ltd



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awareness. Further, these changes and awareness created globally will have a strong impact on the international trade of spurious drugs."

Earlier, in some critical cases, some offences were non-cognisable and bailable in nature, but this has now been amended. Such cases have been made cognisable and non-bailable in nature. Hence, this recent revision is an illustration of updating the outdated regulations and thereby plugging the loopholes in the law to ensure that quality of pharmaceutical products being manufactured is of high standards. Opines Pitale, "The recent amendments in the D&C Act with respect to spurious drugs will definitely reduce the instances. However, stringent punishment implementation, special courts for taking faster decisions, publishing the awareness of this regulation for the common man

through different media shall help to bring down the number of these cases even more. In addition, the intervention of the branch cell will be helpful for the FDA in the implementation of this regulation and will go a long way in restricting the circulation of spurious drugs in and outside the country."

Rising to the challenge

According to a recent pharma industry report by the global consulting firm KPMG, India, with its intrinsic advantages, is one of the preferred destinations for carrying out an array of pharmaceutical activities like drug development and manufacturing operations for many pharmaceutical companies across the globe. Avers Sujay Shetty, associate director, Pricewaterhouse Coopers, "Today, Indian pharmaceutical companies are well received by MNCs for their CRAMS business. Moreover, India has the largest number of USFDA approved plants in the world, after the US."

However, despite this global success, Indian companies providing these services face a multitude of challenges, the most important of them being obtaining approval from international regulatory bodies like the USFDA, UKMHRA, etc, to manufacture and market their drugs in the international community.

Avers Pitale, "Issues like ineffective implementation of quality systems, inadequate laboratory controls, testing non-compliance, stability problems, cleaning, hygiene & safety issues, inconsistent quality of starting

materials, unawareness of the updates on cGMP norms and non-adherence to the maintenance of the equipment, instrument and facility, are the main areas of challenges encountered by the companies while getting regulatory approvals from international bodies."

The only way to combat these challenges is to bridge the gap during the effective implementation at the research & manufacturing sites with respect to premises, production systems, material systems, quality systems, laboratory control systems, packaging & labelling systems, etc. According to Pitale, continuous updation of the above six systems with continuous training of the personnel and implementation of good documentation practices, scheduled self-audits, agency audits, risk analysis and placing more emphasis on the preventive measures rather than corrective action, will result in a quality products in the international market."

In addition, pharma companies also have to comply with different requirements that vary from country to country for a particular drug. Dr Solanki opines, "Although the ICH is working towards the harmonisation of requirements, the speed at which it is done needs further acceleration. Moreover, facing audit programmes from regulatory bodies is also a challenging job because the requirement of regulatory bodies varies from agency to agency. Keeping the facility and systems as per cGMP, regular monitoring of systems & records and updating the same as per current guideline remain a challenge."

Good clinical practices

Clinical research, which involves testing of drugs that are yet to be established as safe or efficacious, also has to be conducted in accordance to specific quality norms. Feels Shashikant Bhat, head – Clinical Quality Assurance, SIRO Clinpharm, "Since clinical research operations involve testing of drugs



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on human volunteers or patients, it is important to protect the rights, safety and well-being of these participants. Hence, quality norms in clinical research provide the necessary requirements to protect these research subjects and also scientifically assess the new drug for its safety & efficacy. The latter is important as ultimately, these drugs will be given to a large population after its approval for use and hence would impact their health & well-being."

Over the past few years, a few revisions have been made in the laws regulating clinical trials in India. "In India, the last key changes in regulations were implemented in 2005 to the Schedule Y of the Drugs & Cosmetics Rules. These changes provided new norms to evaluate proposals to conduct clinical trials as well as specified broad requirements for maintaining quality & compliance. Moreover, it included allowance for simultaneous trials with other countries for new drugs discovered outside India except phase I. These changes also introduced specific requirements in certain areas like functioning of ethic committees, requirements to provide safety reports and commitments to be provided by investigators," avers Bhat. Since the last year, inspections at clinical investigator sites have been initiated to assess compliance. He adds, "This practice will contribute to preventing complacency. Further, a registry of trials has also been set up, which is publicly available and provides vital information regarding trials."

As India is looked upon as an upcoming destination for clinical research, education & training of the personnel engaged in conducting clinical trial functions is one of the steps that need to be taken to ensure that the manner in which clinical data is obtained is credible. For this, it is essential that proper training programmes are organised for the employees, where they are equipped with the skills and knowledge for carrying out these functions in an appropriate manner.

Sujay Shetty

associate director, Pricewaterhouse Coopers



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Quality-driven culture

In an organisation, it is important to create a culture among the employees where the importance of quality & quality practices is emphasised and promoted at all times. Bhat says, "The commitment to quality is a basic necessity. Hence, it is important that this is demonstrated to the staff clearly, right from the time they resume services." Moreover, to drive such initiatives in an appropriate manner, the top management of a company plays a crucial role. Dr Solanki states, "ICH Q 7 demands that cGMP should start from the top management, which is the source to implement quality practices in a company. Moreover, they should monitor that these practices are being implemented by the quality departments and appreciate the same. Further, the management should not view cGMP practices as a hindrance to productivity, but consider them as indispensable tools for achieving & maintaining quality."

The top management also has the responsibility to ensure that effective pharmaceutical quality systems

are in place to achieve the quality objectives. Pitale opines, "For this, the roles, responsibilities and authorities should be well-defined, communicated and implemented throughout the company. Further, the senior management should participate in the design, implementation, monitoring & maintenance of an effective system and advocate continual improvement to all employees." Such support & encouragement of top management can go a long way in promoting quality practices in a company.

Importance of training

In the midst of a challenging regulatory environment, today, many pharmaceutical companies and clinical research organisations need to review their quality policies. Avers K R N Moorthy, joint managing director and head – API, Wanbury Ltd, "Pharma companies should stress more on the identification of the training needs of employees involved in manufacturing activity and train them as per the need."

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employees, as such programmes would help the company evaluate the type & number of training programmes that are required to update the employees regarding quality issues. Accordingly, the same can be devised and conducted for the employees, where they are informed about the quality regulations and advised about the ways of implementing them. Pitale says, "GMP training is considered an essential tool for human resources management for ensuring the work force is appropriately qualified to perform its duties. Further, during training, the awareness of the workforce contribution towards the quality goal of the organisation needs to be ensured. In addition, effective training will help in reducing the quality complaints, recalls, rework, reprocess and also help in optimal utilisation of resources, ultimately contributing to the business and reputation of organisation."

Training programmes for GCP are imperative, as it would make the employees familiar with the application

of the theoretical knowledge imbibed on a practical basis. Opines Bhat, "Sound GCP training is crucial, as it would equip the personnel not just with the plain theory of information but also provide the ability to understand conceptual aspects. This also helps them give the right advice to others, thereby propelling the importance of quality throughout the company."

In addition, companies should also design initiatives where the staff can discuss the quality-related issues & problems with their peers & seniors, and thereby indulge in the learning process. Moreover, according to Bhat, the importance of the right training cannot be emphasised enough, as it is an ongoing process and hence, organisations must have sound processes to institutionalise ongoing learning."

Future trends

Even in the future, pharmaceutical companies are likely to witness an evolution in quality norms on a regular basis. Shetty explains, "Quality being the most important aspect in the pharmaceutical industry, cannot and must not be compromised at any time. For this, pharmaceutical companies should take all the necessary steps & precautionary measures to ensure that products manufactured are as per the required quality standards.

At the same time, they should keep updating and complying with the evolving quality norms."

In addition, the regulatory requirements for export of pharma products have continuously increased since the last 15 years. Says Dr Solanki, "Initially, the industry was managing with the available facilities and acceptable GMP systems. Gradually, the facilities, systems & procedures were updated and they have reached world-class standards. The future trend would focus on automation, CFR-part 11 compliance, online documentation and implementation of process analytical techniques. Also, today, there is a lot of draft guidance available on the harmonisation of different country regulations that would help in bridging the gap between understanding & implementation of quality norms by manufacturers." According to Pitale, this will enhance the number of international certifications resulting in uniform quality of the drug or drug product across the globe and ultimately improve the economy & the reputation of the country.

On the clinical research front, a harmonisation process exists in the ICH framework in three developed regions. However, ICH guidelines are used in other regions of the world. Bhat avows, "These organisations might eventually participate in the process, contributing their own unique experience. Also, a number of guidelines exist today that cover a variety of topics affecting the clinical research industry and the several processes it employs. Yet, there are differing requirements across regions too. While multinational pharmaceutical companies or CROs have been largely successful in implementing global standards, there might be greater cooperation between regulatory agencies to share information from inspections. This will impact how quality is regulated in the future." 



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