A Report on Meeting with US FDA Team on 18th March, 2015

Hyatt Regency, New Delhi

1. Background:

A meeting of the CEOs /Quality Heads of the pharmaceutical industry, the leaders of industry assocaitions such as IDMA, BDMA, FOPE, Indian Pharmaceutical Association, ABLE and of professional bodies such as ISPE, AIDCOC, PDA, and key members of Pharmexcil was organised in coordination with the officials of US FDA India office by the Secretariat of Pharmexcil.

In order to ensure that the current issues of concern are represented in an objective manner, it was decided to hold a discussion with the key professionals of the industry. Accordingly under the guidance of Dr Appaji, DG, Pharmexcil a telecon was organised by Pharemxcil. This telecon was planned and lead by Mr S.M.Mudda, COA Member of Pharmexcil and Head of Regulatory issues on 11th March, 2015.

Based on the inputs of the participants, a draft representation was prepared by Mr Mudda that was circulated to all concerned. The night before the FDA meet, a meeting of a few members of Pharmexcil and other Associations was held at New Delhi, to prepare a final representation. After a through deliberation and several corrections the note that emerged came out with a positive tone stating that the Industry understands the importance of Drug safety for the patient and has pledged itself to follow an action plan aimed at creating a Culture of Quality across the industry.

2. Agenda received from US FDA for the meeting held on 18th March, 2015

Prior to the visit of the US FDA team Dr. Appaji, DG, Pharmexcil and Delhi team coordinated the details of the visit and the agenda of the visit was received. The focus of the meeting as stated by FDA was for conveying to the Indian Regulators and the industry FDA's vision of strengthening safety of the medicinal products and to enhance engagement with the Indian Regulators.

AGENDA

U.S. FDA's vision to strengthen the safety of medical products and cosmetics exported from India to the United States by reinforcing FDA's mission, which has global impact, to ensure that U.S. consumers have access to safe, high quality and effective products. Also share your vision of building enhanced relationships.

- *The Pharmaceutical Quality System including: Sound Lifecycle, scientific and Risk-based Approaches, maintains a state of control, monitors performance and product quality and creates real "fixes" (long-term, systemic).*
- *The importance of US FDA's collaboration with the DCGI.*
- *U.S. FDA's Inspection/Compliance Program.*
- *The challenges Indian pharmaceutical manufacturers are facing in India and globally.*

3. A Brief Report of the meeting:

In the Interactive Meeting that began at 10.30am, the following participants were present

3.1 List of participants from U.S. FDA

1. Mr. Howard R. Sklamberg, Deputy Commissioner for Global Regulatory Operations and Policy
2. Ms.Cynthia Schnedar, J.D., Director, Office of Compliance, CDER
3. Ms.Dara Corrigan, J.D., Assistant Commissioner for Global Regulatory Policy
4. Mr. Carl Sciacchitano, Senior Advisor for Scientific International Affairs
5. Mr. Mathew T. Thomas, M.B., B.S.,, Acting Director, India Office
6. Mr. Solomon Yimam, Intl. Program & Policy Analyst
7. Mr. Thomas Arista, Sr. Investigator
8. Dr. Shiva Naga Vara Prasad Bathula, Food and Medical Product Safety Coordinator

3.2 List of participants from Government of India.

1. Mr. Sudhanshu Pandey, Joint Secretary, Ministry of Commerce
2. Dr. G. N. Singh, Drugs Controller general (India)
3. Mr. R. Chandrasekhar, Deputy Drugs Controller
4. Dr. V.G. Somani, Joint Drugs Controller
5. Mr. Ashutosh Gupta, Chairman - Pharmexcil
6. Dr. P.V. Appaji, Director General - Pharmexcil

In addition to the above, Shri Veerramani, President-IDMA, key representatives of various industry associations and officers from Pharmexcil participated in the meeting.

Welcome and Introductions : The meeting began with the welcome address by Shri. Sudanshu Pandey (Jt.Secretary, Ministry of Commerce, Government of India). Shri. Pandey appreciated the initiative of the visiting US FDA team for identifying opportunities for collaboration with the regulators and the industry for the common objective of manufacturing high standard medicines in India and for export to various countries including USA. He also appreciated the active participation of US FDA in training sessions conducted in various parts of the country for providing education related to US FDA's Inspection & Compliance Programme and challenges associated with quality of the generic drugs. He expected to see an increase in this pro-active engagement with the industry in the coming years.

In the speech that followed Dr. G N Singh, Drug Controller General of India (DCGI) welcomed the Regulators from US FDA and expressed satisfaction on the discussions held with US FDA officials in the meeting held on the previous day.

Thereafter, Dr Appaji, offered flowers to all the dignitaries

Mr. Sudhanshu Pandey called upon Mr. S M Mudda to present the industry issues and view points to the visiting US FDA team. Mr. Mudda handed over a written representation note to all the dignitaries and presented/ read it out in the meeting. Please refer to **Annexure 1** for "**PHARMEXCIL REPRESENTATION TO US FDA"**

Mr. Howard Sklamberg, Deputy Commissioner for Global Regulatory Operations and Policy, in his talk reiterated the need to ensure the highest quality of generic medicines by the manufacturers and stated that when necessary enforcement would be used as an appropriate tool for dealing with faulty information.

He also shared the FDA's proposed plan to create a new approach to facility inspections that will not only identify the deficiencies in GMP compliance but also will note a firm's Quality Management System that exceeds the minimum regulatory expectations.

This approach will possibly incentivize the companies having a long term focus on enhancing their own quality culture by way of the frequency of inspection, regulatory flexibility around post- approval manufacturing changes etc. He also appreciated the initiative by Government of India in introducing Track & Trace Systems for authentication of medicinal products ahead of many other countries of the world.

This was followed by Question & Answer sessions that brought out the need for ensuring on-going GMP compliance for maintaining the highest quality of generic drugs supplied to USA and also brought to the fore the welcome initiatives of the Indian Pharma Industry that would ultimately lead to creating a sustainable quality culture.

Mr. Ashutosh Gupta, Chairman – Pharmexcil thanked the visiting team of US FDA personnel and for active engagement with the industry.

The meeting was followed by lunch that provided further opportunity for the participants for informal discussions with the FDA Personnel. The industry was happy with the interactive meeting with the US FDA officials and thanked the US FDA team and US FDA India office for encouraging an open and transparent dialogue during the meeting.

The outcome of the meeting was reported in FDA's official blog "FDA Voice" under the title **"From New Jersey to New Delhi, a global focus on quality".** It is stated based on the discussions held with the regulators and industry leaders that India intends to be part of the global community that is committed to produce the highest quality of drugs possible. Please refer to **Annexure 2** for the blog.

Panel Discussion with Industry Representatives

Mr. Mudda presenting industry views

Annexure 1

PHARMEXCIL REPRESENTATION TO US FDA

India Pharma CEOs Meeting with Dy.Commissioner & Senior Officials of US FDA

Mansion Oval Room, Hyatt Regency, New Delhi,
18th March 2015

1. INTRODUCTION

Pharmaceutical Export Promotion Council of India (PHARMEXCIL) welcomes US FDA delegates and thanks for providing an opportunity for making a representation that provides an overview of the current challenges of the industry, the actions taken and the expectations from the agency for encouraging the industry in meeting with the evolving Agency policies and regulatory requirements.

Pharmaceutical Export Promotion Council of India (PHARMEXCIL) is the authorized agency of the government of India for promotion of pharmaceutical exports from India. It was set up under the provisions of Foreign Trade Policy by the Ministry of Commerce and Industry in May 2004. Various pharmaceutical products, namely, bulk drugs, formulations, biotech products, herbal products, diagnostics etc. are covered under its purview. PHARMEXCIL takes up several external trade promotion activities by organizing trade delegations outside India, arranging buyer-seller meetings and conducts international workshops and seminars on the issues confronting the industry.

2. OVERVIEW OF INDIAN PHARMACEUTICAL INDUSTRY AND ITS MARKET SHARE IN USA

India is one of the major suppliers of medicines to USA today. The pharmaceutical industry has acquired a commendable position in the global pharma market as a supplier of high-quality, low-cost generic drugs. Since the year 2000-01, USA has been the largest exporting partner of India's pharmaceuticals year after year. India holds approximately 5% market share of USA's generic market by value and can be estimated 15% share by volume. India's exports to USA have increased from USD 105 million in 2001-02 to USD 3,963 million in 2013-14 with a compound annual growth rate of 35%.

3. CURRENT CHALLENGES

Despite the sustained growth of the industry, we are aware of the challenges before the industry for demonstrating improved compliance with Good Manufacturing Practices (GMPs).

We are also aware of the regulatory requirements that in addition to ensuring compliance with the quality and safety attributes of the product, it is equally important to ensure compliance with the quality attributes of data generated over the entire product life-cycle. We are aware of the importance of maintaining and assuring the accuracy and consistency of data supporting product quality.

4. INITIATIVES TAKEN BY INDUSTRY FOR IMPROVED GMP COMPLIANCE

- Majority of the leading manufacturers of the industry have taken a serious note of the regulatory requirements and have initiated measures for adopting a quality systems and risk-based approach for addressing the underlying systemic causes of the deficiencies observed in quality compliance. Equal focus is being placed on the behavioral and technical aspects to identify the underlying contributing factors and initiate long term preventive actions rather than initiating remedial actions aimed at providing symptomatic relief for the deficiencies observed.
- Going by these initiatives it is understood that the industry has acknowledged the importance of adopting a proactive approach for implementing Quality Systems with a visible and demonstrable senior management involvement that will help in creating a sustainable quality culture and ensure ongoing compliance with the GMPs.

- The remedial measures taken towards achievement of these objectives by some of the leading Indian companies for assuring the accuracy and consistency of data are:

    - ✓ Implementation of Global Remediation Action plans involving senior management
    - ✓ Utilizing the electronic platforms (LIMS, Electronic Batch Records and QMS Software's etc) to reduce errors due to human intervention.
    - ✓ Focus on development of managerial and supervisory level leadership that represents the quality intent of top management in letter and spirit
    - ✓ Educating the operational staff at all levels in making them realize the importance of the data

- Further, to build awareness of the current challenges and changing expectation of creating a culture of quality, the industry and professional associations like IDMA, ISPE, PDA, PHARMEXCIL etc have been conducting several workshops, conferences and seminars to propagate the proactive approach to quality, responsibility of senior management, sustainable quality culture and the need to adopt science and risk-based approach throughout the product quality life cycle.
- The initiatives taken by the leading companies will be followed by many others in the times to come and a focus will continue to be placed on ensuring a sustainable GMP compliance by creating a culture of quality.

5. OFFICE OF THE PHARACEUTICAL QUALITY and QUALITY METRICS

The industry appreciates the new initiatives by USFDA in establishing a separate Office of Pharmaceutical Quality and new initiatives arising out of FDASIA. We are committed to educate and develop personnel for adopting the requirements of quality metrics.

6. COLLABORATION BETWEEN US FDA and THE INDUSTRY

- We believe that an active engagement of the senior leadership of the industry with USFDA will provide a much-needed opportunity in presenting the progress done by the industry towards ensuring on-going compliance with the GMPs. This will also help the industry to seek Agency's guidance in implementing the evolving regulatory requirements and to create new initiatives for improved compliance.
- Pharmexcil will be happy to coordinate this collaboration and requests for at least two interactive discussions between the industry and US FDA annually. More frequent interactions on periodic basis may be held with US FDA India office.
- Additionally, Pharmexcil is committed to create a long term education programme aimed at providing an on-going education to the industry professionals in technical, regulatory and behavioral aspects. An active participation of US FDA in such education programmes will provide an opportunity for the professionals to understand the changing regulatory expectations and increase their capabilities.
- We are aware that an ongoing education of the industry professionals for ensuring GMP compliance and that of the senior Management for creating and supporting a Pharmaceutical Quality System alone will help create a Sustainable Culture of Quality, where every individual in the organization involved in activities having direct or indirect impact on the quality understands his responsibility for protecting the quality and safety of the products manufactured by the company.
- Finally, we sincerely believe that US FDA through their engagement with the industry will find the evidences of the progress made in these areas and will acknowledge the efforts and guide the industry form time to time for improved compliance with GMPs.

Annexure - 2

From New Jersey to New Delhi, a global focus on quality

Posted on March 24, 2015 by FDA Voice

By: Howard Sklamberg and Cynthia Schnedar

As we walked through the bustling, ancient city streets of Old Delhi last week, teeming with tourists and shop keepers selling spices and saris, we were struck by how resplendent this country is, and just how much it offers the world.

Howard Sklamberg, J.D., FDA's Deputy Commissioner for Global Regulatory Operations and Policy

This is certainly true about prescription drugs. India is a significant exporter of generic drugs to the United States. The American people benefit tremendously from generic drugs, as more and more generic medications reduce costs for patients, and the American healthcare system. The rise of India's pharmaceutical star is one of the reasons why our trip to India is so important.

While here, we have had a chance to meet with our regulatory counterparts in the Indian government, as well as the drug manufacturers that are either based here, or who have facilities in the country. Needless to say, we are learning a great deal.

It's no secret there have been challenges associated with the quality of generic drugs coming out of some facilities in India. Some people have asked us here if the FDA is "singling out" India for increased inspections. We simply reply that increased exports to the U.S. result in increased inspection, no matter where you are in the world. FDA inspections ensure that when a firm wants to export drugs to the United States, the drugs meet FDA standards and will be of the quality patients and consumers want and deserve.

Cynthia Schnedar, J.D., Director of the Office of Compliance at FDA's Center for Drug Evaluation and Research

And we've been happy to hear that this focus on quality is, in fact, a shared goal, held by both the Indian — and India-based — regulators and pharmaceutical manufacturers with whom we've met. They understand what we mean when we tell them the FDA is interested in helping to build a global network of quality; that it doesn't matter whether a drug is made in Hoboken or Hyderabad, if it is intended for use in the United States, the drug, and the way and under what conditions it's produced, will be reviewed using the same standards and levels of scrutiny.

That scrutiny, by the way, doesn't always have to have negative results. The inspections associated with drug production have been a central discussion point on this trip, and we've brought news that has been well-received, especially by the drug industry. We shared our proposed plan to create a new approach to facility inspections, one that will not only note problems, but will also allow our inspectors to document where a firm's quality management system exceeds what would be required to meet

regulatory compliance. To put it simply: the inspections can yield also carrots, and not just sticks.

Last week, FDA's Howard Sklamberg and Cynthia Schnedar participated in a panel discussion on drug quality with drug associations in India

So what are the carrots? These findings could be used to influence the frequency of our inspection of a particular facility, and possibly even support regulatory flexibility around post-approval manufacturing changes. These kinds of decisions would be anchored by data that proves that the risks of manufacturing problems in a certain facility are minimal.

We have often said we cannot inspect our way to absolute drug quality. Many of our discussions on this trip have focused on the importance of firms enhancing their own "quality cultures." And, to that end, we know there are initiatives we can take to help them succeed. For example, we will be piloting a new questionnaire that could be used to further standardize inspections, with the goal of uniformly harvesting the kind of data that supports accurate measures of quality. We believe that by improving the inspection process in this way, future "metrics" that define quality will be understood and aspired to by manufacturers — no matter where they are in the world.

Last week, FDA's Howard Sklamberg and Cynthia Schnedar met with pharmaceutical CEOs in India to discuss drug quality

Of course, enforcement has been, and will continue to be, an important part of our program to ensure drug quality. Enforcement is a particularly appropriate tool when a firm does not submit accurate data to us. FDA relies on information to do its job, and faulty information means that we cannot ensure the quality of the drugs that the firm produces.

It is already clear to us, after speaking with regulators and industry leaders here, that India intends to be part of that global community that is committed to producing the highest quality of drugs possible. Through workshops and joint inspections, we continue to work with the Indian government to raise awareness and understanding of our inspections processes. And to the industry leaders we have met with here, we have pledged to continue to collect their feedback on how we might be able to help them improve regarding quality issues, and to incentivize them to do so.

India has a significant spot in the constellation of drug-producing nations. As one Indian official so eloquently said to us, we have "a galaxy" in common. And, we are happy to add, that the brightest star in that galaxy may just be our shared commitment to a global system of drug quality.

Howard Sklamberg is FDA's Deputy Commissioner for Global Regulatory Operations and Policy

Cynthia Schnedar, J.D., is Director of the Office of Compliance at FDA's Center for Drug Evaluation and Research