Experience with CEPs from the perspective of Indian manufacturers

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We Trust

- The EDQM is a highly respected and much appreciated member of Council of Europe family wherein protecting public health is a key priority.
- The standards and texts elaborated by the experts of European pharmacopeia commission are instrumental in guaranteeing and protecting human life.
- The certificate of suitability confirms that active pharmaceutical ingredients or medicine substance are developed according to European Pharmacopoeia monographs.
- The advantages are : Confidentiality, centralized evaluation , recognition by all European member states as well as other countries, reduced complexity as compared to ASMF.

Today the EDQM and Health care is a world leader in its field of expertise thus plays a major role in developing, manufacturing and trading medicines and also with major responsibility to ensure highest possible quality standards.

India – Business hub

- India is one of the strong leader in the number of CEPs granted by EDQM due to its strong presence in generics and API approvals.
- By 2020 the pharmaceutical market is anticipated to more than double to US $1.3 trillion (1/5th of global sales) with the E7 countries — Brazil, China, India, Indonesia, Mexico, Russia and Turkey
- India rates higher than other countries on cost efficiency which is visibly reflected in the manufacturing costs of US FDA-approved plants in India .
- India with its apt chemistry skills and low cost advantages, both in research and manufacturing coupled with skilled manpower will attract a lot of business in the days to come.

Indian Government's Initiatives

- The Department of Pharmaceuticals has prepared a "Pharma Vision 2020" document for making India one of the leading destinations for end-to-end drug discovery and innovation.
- The vision is to project India into one of the top five pharmaceutical innovation hubs by 2020 &
- The Government has also been taking various policy initiatives for the pharmaceutical sector.
  - These include tax-breaks to the pharmaceutical sector and weighted tax deduction at 150% for the R&D expenditure incurred.
  - US$ 149.11 million to support start-ups in the research and development in the pharmaceutical and biotech industry.
  - Indian Government has launched two schemes
    - New Millennium Indian Technology Leadership Initiative
    - Drugs and Pharmaceuticals Research Program—specially targeted at drugs and pharmaceutical research.
- Indian government has promoted development of special economic zone (19 SEZ) for pharma sector, which are under various stages of development .
- Eight mini drug-testing laboratories across major ports and airports in the country.

Industrial Expectations from EDQM
(Speedy introduction of generic drugs into the market)

- CEP is the tool through which MAA provide data on active ingredients, prepared by synthesis, fermentation or semi-synthesis
  - All the requirements including CMC
  - All the potential impurities
  - Control over contaminations related to manufacturing process
  - Stability requirements

Average time taken to obtain a CEP is about 15 -18 months.

- ✓ Target time for initial assessment is 5 M.
- ✓ Additional information request & Response is 6 M.
- ✓ Target time for response assessment is 4 M

This can be reduce to 12 months as USFDA provide a Goal Date of about 10 month.

Industrial Expectations from EDQM
(Speedy introduction of generic drugs into the market)

- Inclusion of new and Non-Pharmacopoeial molecules into the European pharmacopeia so as to facilitate CEP filings.
- Availability of EPCRS (Solvents & impurities) and if possible in bulk quantities upon request.
- To quantify impurities in sample, EP specify to use diluted test solution, however as per USP, reference standard shall be used.
  - We expect a harmonized system to avoid multiple time preparation of diluted test solution.(e.g. If number of samples are more for testing)
  - Harmonization of monographs across Pharmacopoeia (EP/BP/USP) .

Industrial Expectations from EDQM
(Speedy introduction of generic drugs into the market)

- Inclusion of drug product into EP, specifying the impurities to be tested and assure the availability of reference standards
- Currently BP and USP is referring to drug product and many a times related impurities test is not part of monographs specifically topical.
- Formulator find it difficult to obtain the impurities reference standard for method development. Sometimes API manufacturers does not support for supply of impurities.
- Formulator find it difficult to identify excipient (IR test) due to non-availability of reference standard.
  - ✓ It will be of great help if Reference IR spectrum library is published for listed monograph.
- Inclusion and acceptance of alternate technique like NIR, Raman spectroscopy for quick identification of bulk material.

Challenges faced by Formulation manufacturers

- High fragmented Industry
  - Market is over loaded with generic manufacturers
- Drug Price control
- Stronger IP regulation
- Low input for R&D due to pricing norms
- Compliance issues and GMP

- Pharmaceutical manufacturers have become eager to learn where and how the API is manufactured and no longer accepts just documentation part and also growing control measures by the relevant health API authorities to enforce safety cGMP compliance.

- Formation of links between suppliers and customers providing full transparency in pricing, origin, and quality has become essential to provide efficacious and safe products to public

Challenges faced by Formulation manufacturers

Expectation from API manufacturer:

- API development starts with intense evaluation on
  - Synthetic route, structural elucidation
  - Impurity profile
  - Degradation products
  - Potential Mutagenic & other related impurity
  - Carryover of impurities from KSMs to intermediates to API
- Risk Management Summary on elemental impurity
- GMP assurance at KSM and intermediates manufacturing sites
  - Inadequate and missing information
  - Poorly justified specification
  - Reluctance for Quality audit by API manufacturer or formulator
  - Reluctance to improve infrastructure – cost viability

Challenges faced by Formulation manufacturers

Some deficiencies in API (existing/new)

- Identification, isolation or synthesis are not addressed including theoretical impurities.
- No proper degradation pathway communication so as to assess its impact on formulation.
- Particle size distribution with trend data to design bioavailability of drug product.
- Changes in CEP and timely submission to Agency and Formulator
- Frequent changes (addition/deletion in process , batch sizes, equipment, site changes etc)
- Timely response to critical deficiency letters

Challenges faced by Formulation manufacturers

Way-forward:

- Effective partnership between the Formulator / API manufacturer / Agency
- Timely communications on all changes having direct or indirect impact on the Formulation.
- Joint audit of intermediate and KSM supplier by API and Formulator
- Effective coordination in identifying new suppliers.
- Transparency in providing details of KSM, intermediate supplier to Formulator to facilitate QP assessment for GMP compliance and risk management.

To Create the future we desire ,we need a language,
we must speak from the heart and in the language of Soul

A language of trust, faith and higher values of
inner growth, love and listening

Make a Great Day !!

Thank You !