Pharma Outsourcing: Regulatory Scenario

The authors craft a background of the current scenario in pharma outsourcing in India and discuss how these outsourcing operations are bound by mandatory agreement with the many regulatory norms in place.

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India, due to its skilled resource, is able to effectively contribute to contract research and manufacturing process, and due to its large patient population and genetic pool, has become a hub for cost-effective and speedy clinical trials for investigational new drugs. These significant advantages that India offers has compelled multi-national pharma companies to outsource operations in the fields of drug discovery, contract manufacturing and clinical research to organisations in India. In 2012, the Indian pharma outsourcing industry was valued at USD 1.2 billion and is growing annually at a rate 15-20 per cent.

Nature of Work

Outsourcing in pharmaceutical industry takes place on two levels: Research and Manufacturing. Research outsourcing covers a wide range of services, including the drug development process, medical writing, pre-clinical and clinical trials, clinical trial monitoring, and clinical data management. The organisations to which research is outsourced carry out research under a contract, and hence, these organisations are popularly referred to as Contract Research Organisations (CROs). Manufacturing outsourcing includes bio manufacturing and the custom manufacture of pharmaceutical ingredients as well as formulations.

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Legal and Regulatory Compliance

The important legislations and regulatory instruments covering various regulatory aspects related to clinical research and manufacture are:

1. Drugs & Cosmetics Act of 1940 and Rules of 1945.
2. Guidelines on Similar Biologics, 2012 prepared by Central Drug Standard Control Organisation (CDSCO) and the Department of Biotechnology.
3. Mashelkar Committee Recommendations, 2006 adopted by Ministry of Environment and Forest (for regulation of organisms modified by r-DNA techniques to be used as pharmaceutical products).
4. Director General of Foreign Trade's (DGFT) Notification regarding bar- coding of exported pharmaceutical products.
5. Information Technology (Reasonable security practices and procedures and sensitive personal data or information) Rules, 2011 issued under Information Technology Act, 2000.
6. Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002 issued under the Medical Council Act, 1956.
7. Good Clinical Practice Guidelines issued by CDSCO.
8. Ethical Guidelines for Biomedical Research on Human Participants, 2006 issued by Indian Council for Medical Research (ICMR).

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Drugs Controller General of India (DCGI), is the apex authority under the Ministry of Health and Family Welfare which regulates pharmaceutical and healthcare industry in India. Each State regulates manufacture of drug within its territory through the State Food and Drug Administration (FDA). The Genetic Engineering Approval Committee (GEAC) functions under the Ministry of Environment and Forest as a statutory body for review and approval of activities involving large scale use of genetically engineered organisms (also referred as living modified organisms) and products thereof in research and development, industrial production, environmental release and field applications. All clinical trials involving the use of biotech products would be referred by DCGI to GEAC for recommendations regarding environmental safety.

Some of the key regulatory requirements which must be borne in mind by CROs are:

1. All clinical trials must be registered with the Clinical Trial Registry of India.
2. Disclosure or transfer of identifiable medical or health related data of trial subjects without their written permission is prohibited.
3. All clinical trial of new drugs requires strict compliance with Good Clinical Practice Guidelines.
4. CROs may become liable for medical management of trial subjects and may have to pay compensation for clinical trial related death or injury to the subject if it has obtained to permission to conduct clinical trial in India on behalf of the sponsor.

Some of the key regulatory requirements which must be borne in mind by CMOs are:

1. Manufacturing of different categories of drug may require separate license from State FDA.
2. All manufacturing records pertaining to each batch of drugs must be maintained for a period of five years.
3. Export of drugs requires primary, secondary and tertiary level bar-coding as prescribed by DGFT.
4. The manufacturing activity must be in compliance with Good Manufacturing Practices prescribed under Schedule M of the Drugs and Cosmetics Rules, 1945.

Issues and Concerns

The CRAMS industry faces numerous regulatory challenges today. The regulations governing this sector are evolving rapidly resulting in significant transition cost. Delay in obtaining approvals and permissions is a major cause of concern for the CRO industry. While 262 clinical trials were approved in 2012, only six clinical trials were approved between January and June this year. More so, there is a cloud of mystery surrounding definition of sponsor of a clinical trial, and CROs constantly run the risk of being categorised as Sponsors unless appropriate documentation exists to indicate otherwise. Furthermore, though regulatory framework prescribed under the Drugs and Cosmetics Rules, 1945 is applicable only to clinical trial of new drugs; it is possible that the authorities may demand compliance of the Rules to even those clinical studies which do involve a new drug.

The CMOs also face unique regulatory challenges. A simple change in name, or even change in share- holding, is required to be reported immediately to the authorities and must be followed by an application for issuance of fresh license for manufacture. Many a times, the standards imposed through regulations are India specific and not in tune with the global standards. This poses a concern since a large number of CMOs focus on exports.

Consequently, CMOs are forced to match Indian as well as global standards. There are other concerns which require attention too, like taxation issues connected to transfer pricing, taxation as an association of persons, creation of Indian private establishment of foreign enterprise, service tax liability etc.; IP issues connected to technology transfer, joint ownership, licensing, assignment, royalty payment, honoring of intellectual property etc. and contractual issues connected to sub- contracting, confidentiality, audit rights, indemnity, governing law etc.

Conclusion

Non-compliance with the regulatory requirement may have severe consequences ranging from suspension of license to imprisonment and prohibition from conduct of business in India. Therefore, regulatory compliance must be taken seriously. Non-compliance with regulatory requirements is not option for the CRAMS Industry! ■

[1] *As per Times of India news report available on http://articles.timesofindia.indiatimes.com/2013-02-22/india-business/37241193_1_contract-research-pe-funds-domestic-market (last accessed August 19, 2013).*

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