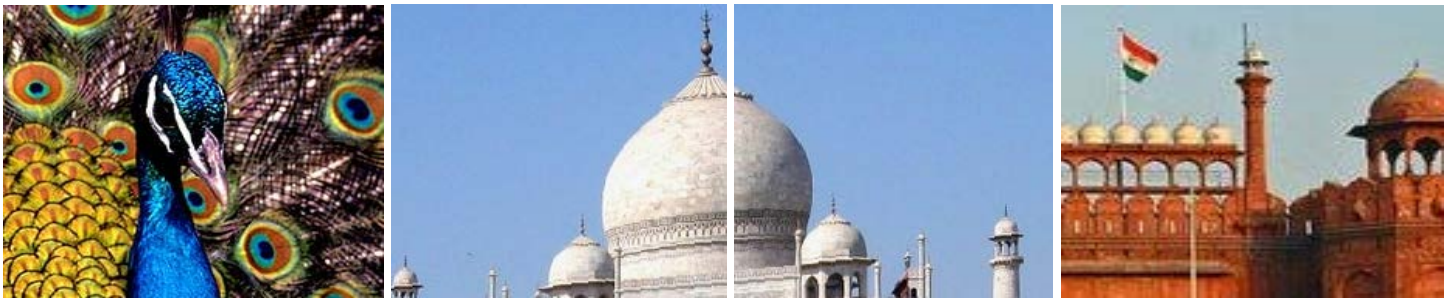

CONUNDRUM OF MEDICAL DEVICES APPROVAL PROCESS IN INDIA

By Neeraj Dubey

The development of medical devices has extended the ability of physicians to diagnose and treat diseases, and has made great contributions to health by improving the quality of life of patients. Generally, medical devices would include any instrument, apparatus, machine, appliance, implant, *in vitro* reagent or calibrator, software, material or other similar or related article. However, in India, the medical devices employed in internal or external use in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals are considered to be "drugs" as notified by the central government in its official gazette after consultation with the Drugs Technical Advisory Board. Those medical devices not notified as drugs only require an import or manufacturing license and no quality check system exist for them.

REGULATORY FRAMEWORK

At the moment, in India there is no single comprehensive specific law regulating medical devices. The import, manufacturing, sale and distribution of medical devices are regulated under the Drugs and Cosmetics Act, 1940 ("India Act"), the Drugs and Cosmetics Rules, 1945 ("Rules"); and the Central Drugs Standard Control Organization ("CDSCO"), under the Ministry of Health and Family Welfare ("Ministry") is the principal regulator. A draft Bill on "Regulation of Medical Devices" ("the Bill") has been pending since 2006. Once implemented, it will, perhaps, streamline the medical devices sector. Until such time, one has to refer to multifarious regulations.

With effect from March 1, 2006, the Ministry approved a set of procedures for the import as well as manufacture of medical devices in India. The Drugs Technical Advisory Board, which provides technical guidance to CDSCO, proposed certain changes in the Rules, which among others provides a categorization of medical devices into four classes. This classification is based on the risk level, intended use and on adverse effect of the devices on the human body based on the potential risks associated with the technical design and manufacture of these devices. The classes of devices are: (i) Class A: Low risk devices and equipment such as thermometers and tongue depressors; (ii) Class B: Low to moderate risk devices including hypodermic needles and suction equipment; (iii) Class C: Moderate to high risk equipment like lung ventilators and bone fixation plates; and (iv) Class D: High risk devices such as heart valves and implantable defibrillators. The regulatory control becomes stringent with each progressive class and the conformity assessments are proportionate to device classification.

IMPORT OF MEDICAL DEVICES

Presently, the import of medical devices is largely unregulated and medical devices can be freely imported into India. The purchaser (whether it is a government hospital, a private hospital or a doctor) evaluates the quality of the product being purchased. Normally, the U.S. Food and Drug Authority ("FDA") and the European Conformite Europeenne ("CE") approved products are preferred because of their better quality and performance. It is necessary to follow the procedures for registering and obtaining a license as laid down under the Rules. Import licenses are conditional and granted for a period of three years. Breach of any of the stipulated conditions may lead to the cancellation of the license.

To be registered in India, the imported device must be approved for sale in the manufacturer's country of origin. If the device has already received approval from an agency abroad, such as, the U.S. FDA, evidence of

such approval must be provided along with a copy of quality standard ISO/EN certification which assesses the quality and risk of the devices manufacturing facility. Medical devices with prior approval from any of the recognized regulatory authorities, like FDA and CE are subjected to an abridged evaluation in India.

If a device is not approved for marketing in the country of origin, the importer has to submit additional evidence such as reports of clinical trials, details of sales, certificates of satisfactory use from medical specialists about the use of the device and details of product complaints, if any. If a device incorporates a medicinal product, which is likely to act upon the body in conjunction with the device, it is pertinent to provide relevant data on the safety, quality, and usefulness of the medicinal substance used along with data on compatibility with medicinal products, clinical data and published articles, if any.

The manufacturer must also have complied with product standards and home country quality control requirements. The manufacturer of the devices, the importer or his agent must file an application to obtain a registration certificate with respect to the premises where the devices are manufactured and with regard to the devices. The product information and the undertakings with respect to product standards, safety and effectiveness requirements and quality systems in the country of origin are necessary to be furnished. Crucially, a brief description of the device, its intended use and method of use, medical specialty in which the device is used, the qualitative and quantitative particulars of the constituents, device master file with details of the manufacturing process/flow chart and the component/material used and risk assessment as per ISO 14971 are necessary to be provided. Once a medical device reaches the market in India, the manufacturer has to adhere to requirements of post-marketing surveillance ("PMS") norms to systematically monitor the performance of the device. PMS involves procedures for maintenance of records, complaint handling, adverse incident reporting and procedures for product recall.

MANUFACTURE OF MEDICAL DEVICES

The manufacture of medical devices in India requires a license from the government. An application for the license is made with a brief description of the manufacturing process, details of the manufacturing standards and "best practices" that will be followed by the company, as well as product evaluation, standards, and procedures for testing the device. The Rules prescribed in Schedule M-III list mandatory "good manufacturing practices" that manufacturing companies must follow. The law provides that any manufacturing can be done under the direction and supervision of only a whole-time employee of the manufacturer and who is qualified to do so. India has several stringent industrial and labor laws that make the occupier of the manufacturing plant responsible for any breach in compliance. The occupier is generally the managing director of the company that runs the manufacturing unit or a director on the board of directors and can be fined up to INR 0.2 million or imprisoned up to two years for any non compliance.

As proposed under the Bill, the regulatory authority sets up an expert committee to consider proposals and evaluate medical devices that do not have any benchmark certification. The committee after completing its assessment forwards its opinion regarding suitability of the device to the competent licensing authority which can grant permission for the device to be launched in the market. The licensing authority after joint inspection and verification forwards the license to Central License Approving Authority ("CLAA ") for approval. The license is finally issued in form 28 of the Rules after due approval of CLAA. The stockist and retail sellers of medical devices are also required to obtain sales licenses from the respective state licensing authorities for medical devices.

CLINICAL INVESTIGATIONS

At present, clinical trial studies are not regulated in India. However, a set of good clinical practices guidelines laid down by the CDSCO govern clinical trials and specify the responsibilities, inter alia, of sponsors, investigators, and ethics committees. In 2010, CDSCO released a guidance document on the requirements for conducting clinical trials of medical devices in India ("Guidance"). It is necessary to file an application with the CDSCO before conducting the study and the application should indicate the precise intent of the application (e.g. whether the application is

for a feasibility study or a safety and efficacy study, or a post market study). The entity sponsoring the study must also submit a declaration on its letterhead prescribing the extent of delegation of responsibilities to an individual who is appointed as the Principle Investigator. It is also necessary to provide the global regulatory status of the device (particularly when 5 Global Harmonization Task Force ("GHTF ") countries i.e. U.S.A., Australia, Japan, Canada and European Union are involved) along with detailed technical data.

Though the document is still non-binding, it provides sufficient procedural information regarding the method to all stakeholders.

MEDICAL DEVICES: QUALITY STANDARDS

According to the Guidance, all medical devices sold in this country should carry the ICAC mark (Indian Conformity Assessment Certificate) to indicate their conformity with the provisions of the schedule of the Guidance to enable them to move freely within the country. CLAA adopts and recognizes quality standard BIS 15575 or its revisions and quality standard ISO 13485 in respect of the specifications to be followed for quality for the manufacturer to demonstrate conformity with the relevant regulatory requirements. Any reference to the harmonized standards includes the monographs of the Indian pharmacopoeia and U.S., EU pharmacopoeia wherever applicable, notably on surgical sutures and on combination of pharmaceutical and devices.

It is necessary that the labels on the packaging material for medical devices comply with the relevant ISO standards. It is also necessary to denote internationally accepted symbols regarding sterilization, single use etc, as per ISO 15223-1:2007. When medical devices are sold in bulk the packaging material of individual devices do not have to bear the date of manufacture, which must appear on the bulk packaging material.

In light of the growing usage of medical devices, stringent regulatory standards are essential to ensure that the devices are tested, safe and with minimum adverse reactions. Standards regarding safety, risk elements, effectiveness, efficiency and performance of the medical devices need to be well established. It will be interesting to see how the regulatory scenario changes if and when the Bill is enacted into law. Apart from the Bill, there are different proposals for regulating India's medical devices sector by different regulatory bodies, like amending the India Act and Rules proposed by the Ministry. The inter-governmental dispute is a cause for concern and confusion for India's medical devices industry.

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