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Overview of Regulatory Guidelines for Medical Devices

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Abstract: Medical devices are becoming more important in the health care unit. Diversity and intricacy of medical devices in last two decades. Regulation of these devices has also advanced due to the requirement for a steady regulatory perspective. One of the major issues for companies developing and producing medical devices is to be updated on the regulatory requirements and implement them in the process. This thesis examines the regulatory requirements for medical devices in Australia, Brazil, India, Japan, Russia, MENA countries and compares them with the requirements in the European Union. The conclusion of this thesis is that most countries have similar requirements for registration of medical devices and are striving to harmonize with the GHTF guidelines. Now with the availability of different regulations of the countries or region on medical devices, there is a need to harmonize regulations in order to curtail regulatory hurdles and expedite access to high quality, safe and efficacious medical devices. Most countries are trying to harmonize the regulatory guidelines for medical devices through their participation in Global Harmonization Task Force (GHTF). Harmonized regulation of medical device will lead to the availability of the quality product.

Keywords: Medical Device, GHTF, Regulatory Requirements, Harmonization.

INTRODUCTION

Medical Device

A medical device is according to the European definition “any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of: - Diagnosis, prevention, monitoring, treatment or alleviation of disease, - Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap, - Investigation, replacement or modification of the anatomy or of a physiological process, - Control of conception, and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means”⁽³⁾.

Classification System for Medical Devices ⁽⁴⁾

The control of medical devices will be based on a risk assessment and risk management. The level of regulatory control applied to the medical device is proportional to the degree of perceived risk associated with the device. The requirements of the review process differ for each class, type, and technology of medical device.

Medical devices may be classified into 4 classes: Class I (low risk), II and III (medium risk) or IV (high risk).

- **Class I Devices** – those needing the lowest level of regulation because of low risk to the patient except sterile products. They are subject to the General Controls requirements. Declaration of conformity is accepted from the legal manufacturer.
- **Class II Devices** are a medium risk. These devices are invasive in their interaction with the human body, but the methods of invasion are limited to natural body orifices. The category may also include therapeutic devices used in diagnosis or in wound management
- **Class III Devices** are a medium risk. They are either partially or totally implantable within the human body and may modify the biological or chemical composition of body fluids.
- **Class IV devices** are high risk and require design/clinical trial reviews, product Certification and an assessed quality system involving clinical trials. These devices affect the functioning of vital organs and/or life-support systems. Devices are

usually invasive, life-sustaining, life-supporting, or is used "in preventing impairment of human health or if the device presents a potential unreasonable risk of illness or injury".

In-Vitro Diagnostic medical devices are based on the potential risk involved in their use and interpretation clinically, classification rules.

In-Vitro Diagnostic medical devices may be classified into 4 classes:

- Class A (Low Individual Risk and Low Public Health Risk).
- Class B (Moderate Individual Risk and/or Low Public Health Risk).
- Class C (High Individual Risk and/or Moderate Public Health Risk).
- Class D (High Individual Risk and High Public Health Risk).

The Company Registration Requirements

1. The company applying for registration shall make application in writing by completing an official form Annex 4, which is to be signed by duly authorized representative of the company and by the local authorized representative.
2. Company Business License includes their manufacturing site issued by the competent authority in the country of origin.
3. If the company has multiple manufacturing sites, each manufacturing location Should be identified indicating the manufacturing step carried out in as follows (see application for company registration):
 - A. Design
 - B. Production
 - C. Sterilization (if applicable)
 - D. Packaging
 - E. Labeling
 - F. Final Release.
4. Site Master File for each manufacturing site (if applicable- mainly required for pharmaceutical product manufacturers).
5. Warehousing & dispatch General Information on Manufacturing Site and quality Management system follows.
6. Organization of Quality Assurance system.
7. Notarized copies of certificates pertaining for Quality Accreditations from recognized notified bodies (section above) for each manufacturing facility that involved in the manufacturing of the medical device intended for registration in UAE.
8. For pharmaceutical products/class I (non-sterile) / IVD A manufacturer GMP certificate (or equivalent) and manufacturing License (or equivalent after endorsing that equivalent document by DR&CD) for each of the manufacturing sites is required.
9. For classes III & IV / IVD C & D manufacturer: Copies of the Design Examination, Type Examination certificates or equivalent health authority approvals issued for these devices should be provided as a proof of compliance with the company with best practices.
10. Report of a Recent audit by other auditing organization includes the nonconformities points and evidence of corrective action program and supporting documentation (if applicable).
11. For Sterilization process: Full verification that processes are appropriate to produce sterile products should be submitted; including the controlled condition; evidence that process records for each sterilization batch are maintained and traceable to each batch; validation studies including qualification of the sterilizer. Proofs that the process is operating within specific limits; if the sterilization process is software controlled, the validation of the software should be submitted; proves and SOPs that shows that the equipment used has been adjusted, calibrated and maintained.
12. Post marketing surveillance general plan.
13. General profile including the following Information:
 - Company name, address, including the corporate structure as well as all company names of the company and its manufacturing site used.
 - Contact name, telephone, fax numbers and e-mail addresses.
 - A total number of employees (all shifts) covered by the scope of the audit.
 - Product range and class of medical devices being manufactured (The class of a medical device may differ from one regulatory authority to another).

Current trends in the use of standards in medical device regulations:

International standards are a building block for harmonizing regulatory processes to assure the safety, quality, and performance of medical devices. To achieve this purpose, the following principles are recommended:

- Regulatory Authorities and industry should encourage and support the development of international standards for medical devices to demonstrate compliance with "the Essential Principles of Safety and Performance of Medical Devices" (GHTF document SG1 NO20R5 referred to hereafter as the Essential Principles).
- Regulatory Authorities developing new medical device regulations should encourage the use of international standards.
- Regulatory Authorities should provide a mechanism for recognizing international standards to provide manufacturers with a method of demonstrating compliance with the Essential Principles.
- When an international standard is not applied or not applied in full, this is acceptable if an appropriate level of compliance with the Essential Principles can be demonstrated.
- While it may be preferable for harmonization purposes to use international standards, it may be appropriate for Regulatory Authorities to accept the use of national/regional standards or industry standards as a means of demonstrating compliance.

- Standards Bodies developing or revising standards for use with medical devices should consider the suitability of such standards for demonstrating compliance with the Essential Principles and to identify which of the Essential Principles they satisfy.
- The use of standards should preferably reflect current, broadly applicable technology while not discouraging the use of new technologies.
- Standards may represent the current state of the art in a technological field. However, not all devices, or elements of device safety and/or performance may be addressed by recognized standards, especially for new types of devices and emerging technologies.

AIM

The aim is to find out the regulatory requirements for medical devices in Australia, Brazil, India, Japan, Russia, MENA countries and to compare them with the requirements in the USA and the European Union.

OBJECTIVE

- The regulatory requirements for medical devices shall concern laws and regulations, standards and the product registration process including classification of medical devices and the implementation of quality systems.
- The information in this work primarily concerns general medical devices but information concerning active implantable medical devices and in vitro diagnostic devices might in some cases also be mentioned when it has been easily found.

METHODOLOGY

Literature search

- Understanding the different regulatory aspects in various countries.
- Searching regulatory websites of such countries with special emphasis on the regulatory requirements, review process, documents, time lines, fee requirements that are required throughout the lifecycle of the medical devices.
- Various published articles related to regulatory strategies, the most critical regulatory concerns that drive the regulatory submission in those countries.

Regulatory submissions

- Types of Registration and application forms required for the countries.
- Time lines involved in the approval
- The various documents need to be submitted along with the application forms for the specific countries manufacturing, export, and import.

Drawing the conclusion

Information collected from different regulatory websites and articles was reviewed and based on the different concerns, the conclusion was made separately for each country and recommendations are made for each country.

DISCUSSION

Most countries have similar requirements for registration of medical devices and are striving to harmonize their requirements with the GHTF guidelines. A company can go far by following the requirements of the European Union, USA or GHTF. The main requirements are usually a local representative, a Certificate of Free Sale from the country of origin, import license from the competent authority in the import country and registration of the company and the product. Technical documentation is also necessary and shall in most cases be submitted with the registration application. This is where the requirements differ. The classification systems for general medical devices are mainly the same, usually divided into three groups as in the USA or four groups as in the EU or according to the GHTF guidelines.

Brazil who is members of Mercosur (South America's variant of the European Union) follow the European classification rules but use the product classes I to IV instead. The class I to IV generally corresponds to the Australia use the same classification terms as in the EU but with the difference that AIMDs are treated as class III devices and not as a separate group. India, Japan, Russia have their own classification systems although medical devices in Japan are divided into class I to IV medical devices. Good manufacturing practice is required by all countries. An ISO 13485 certificate is in most countries the way to demonstrate compliance with the quality system requirements. Some countries, like Brazil, Russia, and Japan require a manufacturer of a medical device to be GMP certified according to their specific system. In these cases, an ISO 13485 certificate might be enough to demonstrate compliance with the quality requirements but it must be approved by the local certification body.

The regulatory environment in these countries is very different. Publicly accessible written legislations are limited, sometimes only available in the local language (most Arabic) and leave room for interpretation. In order to support the information, the author of this master thesis sent a questionnaire to the corresponding local Regulatory Affairs Managers (nine countries) of a globally operating Medical Devices company.

MENA region specification Document legalization

The health ministries of foreign countries, where a company wishes to market its products, requires assurances that the products are safe, effective and in conformance with current Good Manufacturing Practices (GMP). The ministries often require copies of the company's US FDA approval certificates or ISO certification or FSC to document that the products in question are free from defects. To prove these documents are authentic, they must be certified, authenticated, legalized or apostilled depending on the national health ministry's requirements. The countries of the MENA region are divided into Apostiile and none apostiile countries:

1. Document legalization in Apostile countries:

The only Apostile countries in MENA region are Oman and Israel. The mentioned certificates only need an Apostile to legalization for both countries.^(13,14)

2. Document legalization in non - Apostile countries:

The remaining 17 MENA countries are not- Apostile countries. For any on- Apostile country, the document must be sent to the chamber of commerce and the respective embassy for consular legalization.

In Germany the legalization process for these countries is different for the two following groups:

1. Iran and Palestine

The documents for these countries must first be sent to the district court (Landgericht), then to the chamber of commerce (IHK) and finally to the Embassy of the foreign countries.

- 2. Algeria, Egypt, Bahrain, Iraq, Jordanian, Kuwait, Lebanon, Libya, Morocco, Qatar, Saudi Arabia, Syria, Tunisia, UAE and Yemen.**

1. MEDICAL DEVICES IN RUSSIA

General Information

Russia is an unstable market both politically and economically. The economy is slowly getting better and the medical device market is growing⁽¹⁵⁾. In 2003 the medical device market was estimated at 1.4 billion dollars. However, in 2002 only about one fifth of the population had access to quality healthcare. The public healthcare stood for 3.7% of GNP in 2002⁽¹⁶⁾.

Today it is relatively easy to import and market a medical device in Russia⁽¹⁷⁾. The domestic production of medical devices is concentrated to cheap low-tech products which make the demand for imported high tech devices large. In 2003 imported products stood for about 75% of the medical device market. Most of the medical devices are imported from Germany, with the USA on the second place.

Regulation

The Federal Service for Control over Healthcare and Social Development (Roszdravnadzor) is the competent authority in Russia for registration of medical devices. Foreign manufacturers work through the Department of Registration of Foreign Medical Equipment and Devices⁽¹⁸⁾. In June 2000 a new instruction No. 237 on registration procedures for foreign-made medical equipment and devices was introduced.

Foreign manufacturers of medical devices must register their product with the competent authority, obtain a GOST-R quality and safety certification and obtain a sanitary and epidemiological conclusion.

Classification

Medical devices are divided into medical equipment and supplies. The definitions of the product types are unclear and medical equipment can, therefore, be registered as a supply or medical equipment. Medical equipment is classified and given nomenclature according to the General Classification Codes (OKP system). Russia does not use any of the international classification systems. All import and export of medical devices are however subject to Foreign Trade Classification (TNVED) codes.

Product Registration

Medical devices need to be registered with the Federal Service for Control over Healthcare and Social Development before entering the Russian market. A manufacturer needs to have a local office, distributor or consultant that handles the communication with the authority. The business language at these meetings is Russian. The product must be defined as a medical device and classified according to the OKP system for registration and TNVED for importation. Manufacturers of medical devices must meet the Russian quality and safety standards set by Gosstandart. Foreign manufacturers shall submit a certificate of applied international standards with the registration application and send samples of the device for testing to special accredited laboratories. To get a permit to import a product the manufacturer of a medical device must have a GOST-R quality and safety certificate and sanitary and epidemiological assessments. A product will not be approved by the Department of Registration of Medical Equipment and Devices has reviewed and approved the test results. Risk management is a part of the GOST-R certificate⁽¹⁹⁾.

The first step in the registering procedure is for the authorized local representative to have a meeting with an expert from the Department of Registration of Foreign Medical Equipment and Devices. Necessary documents for the registration shall be submitted to the meeting. The department examines the documents and decides what kind of tests is necessary. The next step is to send samples of the product to an accredited test laboratory in Russia. The testing period often lasts more than three months⁽²⁰⁾. The results of the tests are sent to the Department of Registration of Medical Equipment and Devices for a final review. The authority approves the product and issues a certificate or denies the registration.

The required documentation submitted with the application for registration is:

1. A letter from the manufacturer describing the manufacturer's intention to apply for registration of the product (the official language of the manufacturer and a Russian translation).
2. A Power of Attorney to the authorized representative (a legal entity) to conduct registration. The document shall be legalized in the manufacturer's country of origin and if the country is part of the Hauge Convention of 1961 the application shall have a stamp called Apostille.
3. Reference material on the medical product. The reference material shall contain information on the medical device such as the purpose and area of application of the product, a brief description of its usage and information on when the product was developed and launched into production and which world markets it is sold in. The document must be in Russian or have a Russian translation.

4. An exact and complete description of the product and its components (if necessary).
5. A picture of the medical device
6. Advertising illustrative materials. This material can be provided in another language than Russian.
7. Documents on registration of the manufacturing company in the country of origin and/or third countries. Examples of required documents are Certificate of Company Registration or patent for the right to conduct the certain business activity. The documents mentioned here are not manufacturing licenses.
8. Documents on the registration of a product in the country of origin as a measurement device. These documents are required if they are available.
9. National or international documents confirming the conformity of the medical device to the requirements of national and international normative documents and describing the manufacturing process. Some examples are a Declaration of Conformity, Certificate of Free Sale and standards certificates.
10. Manufacturer's operational manual in Russian and manufacturer's price list on its letterhead

The documents described in the last four points shall be originals or notarized copies which have undergone legalization or have an Apostil from the Russian Consulate office in the country of origin. Most of the documents must be in Russian. The registration certificate for medical equipment is valid for ten years while the registration certificate for a supply is valid for five years.

2. MEDICAL DEVICES IN INDIA

General Information

The Indian medical device market ranks top 20 in the world and top four among the Asian countries⁽²¹⁾. The economy in India is growing rapidly. GDP is now growing at a rate of 10% per year and the medical device market is following the trend⁽²²⁾. In 2005 the medical device market in India was estimated to 1318 million US dollars⁽²³⁾. In 2007 Pacific Bridge Medical expected the medical device market in India to grow by 12-16% for the next five years. The expanding middle-class population and the rich population demand high tech products for reasonable prices. Low tech products are produced domestically to very low cost and are therefore not of interest for foreign companies. The purchase of medical devices is done through global tenders issued by government owned and private hospitals⁽²⁴⁾.

Regulation

The Department of Health under India's Ministry of Health and Family Welfare is responsible for the jurisdiction over the regulation of medical devices. The Central Drug Standard Control Organization (CDSCO) in the Ministry of Health is primarily responsible for regulation of drugs but also medical devices, diagnostic devices, and cosmetics. India has no specific regulation for medical devices.

Medical devices are freely imported into India, except for implantable devices, diagnostic kits and sterile devices which are required to be registered⁽²⁵⁾. Products that do not require registration are evaluated by the purchaser in term of quality. Pharmaceuticals and medical devices defined as drugs are regulated under the Drug and Cosmetics Act 1940 and the Drugs and Cosmetic Rules 1945 and must be registered before they can be sold in India. Medical devices defined as drugs require a registration certificate and an import license before being sold on the market⁽²⁶⁾. In 2006 a proposal for a new legislation was published for review. The proposed act is called The Medical Devices Regulation Bill 2006. The new act will come into force 31st of December 2009⁽²⁷⁾.

Classification

The Ministry of Health classifies the medical devices. There are two types of classes; life-saving medical equipment and not life saving medical equipment. If a medical device is classified as a life saving medical equipment it will have reduced duty. Sterile devices are defined as drugs.

In the Medical Devices Regulation Bill 2006 medical devices are proposed to be classified as class A, B, C and D according to the GHTF guidelines. India has as a member of the Asian Harmonization Working Party adopted the Global Medical Device Nomenclature (GMDN) system

Product Registration

Medical devices defined as drugs must be registered with the Ministry of Health and have an import license to be sold in India. Other devices are not subject to this yet but will be under the new legislation. Medical devices not defined as drugs only require an import license. Medical devices defined as drugs are subject to the current legislation the Drug and Cosmetics Act and the Guidelines for Import and Manufacture of Medical Devices.

Quality systems for medical devices do not exist, although CE-marked or FDA approved products are preferred because of their quality and performance. Manufacturers of medical devices defined as drugs must apply Good Manufacturing Practices (GMP) and conduct suitable tests to prove the product quality. The quality systems shall concern design, development, and manufacture. This kind of devices also requires risk management in form of ISO 14971. The registration shall be done according to Rule 24A of the Drugs and Cosmetic Act and Form 40 shall be filed. The applicant can be the manufacturer, the importer or the responsible agent in India.

The Drugs Controller General India (DCG (I)) wants applicant details such as name, address and contact number of the applicant. The department also wants name and addresses of the manufacturer and the manufacturing premises, the importer, the local authorized representative and the local manufacturer if there is one. A copy of the Plant Master File shall be submitted with the application. The information required in the Plant Master File is described in the Clarifications on Guidelines for Import and Manufacture of Medical Devices. Information on approval in other countries such as US clearance, CE certificate or approval in

Australia, Canada or Japan shall be documented and copies of ISO or EN certificates submitted. A list of countries where the product is sold and a list of countries where the product has been withdrawn from the market and the reasons for the withdrawal are required.

Product information, a GMP certificate and a master file are necessary. The master file shall have a description of components and materials used and information on the manufacturing process including flow charts, quality assurance procedures and process controls, risk management according to ISO 14971 and test protocols and reports for stability, biocompatibility, toxicology and validation/verification of sterilization where these tests are applicable.

Labeling of devices according to GHTF guidelines or ISO specifications is accepted⁽²⁹⁾. Manufacturers of medical devices shall have documented procedures for distribution records; complaint handling, adverse incident reporting and product recall. A registration of a medical device defined as a drug is valid for five years⁽³⁰⁾.

3. MEDICAL DEVICES IN BRAZIL

General Information

The medical device market in Brazil ranks among the top ten in the world. The year 2006 the Brazilian medical device market was valued at US\$ 2,585 million and the Brazilian economy was ranked as the 12th largest in the world year 2007, according to Epsicom. The medical device market is estimated to exceed US\$ 3 billion in the year 2011. The import is low but the demand of more high tech medical devices increases the market⁽³¹⁾. Medical devices are sold through public bids⁽³²⁾. Brazil has a well-established medical device industry with local and multinational companies, supplying about 70% of the market. Most of the companies are situated in southeastern or southeast Brazil in São Paulo or Paraná⁽³³⁾. Brazil is a member of the Southern Common Market (Mercosur) together with Argentina, Paraguay and Uruguay.

Regulation

The National Health Surveillance Agency (ANVISA) or in Portuguese Agencia Nacional de Vigilancia Sanitaria (ANVISA) is the competent authority for medical devices in Brazil. All medical devices, diagnostic kits, immune-biological products and sanitation products must be registered with ANVISA before getting out on the Brazilian market⁽³⁴⁾. Medical devices are regulated by Law No. 6360 of 1976, Decree 74.094/97⁽³⁵⁾. Resolution RDC-185 of October 22, 2001, is the main resolution for medical devices. This resolution describes the required documents for registering a product and it contains a registration protocol. Resolution RDC No. 206 of November 2006 describes the requirements for registering in vitro diagnostic devices⁽³⁶⁾. Classification Medical devices are divided into Class I, Class II, Class III and Class IV. Class I devices represents the lowest risk and Class IV devices the highest risk. This is according to the GHTF proposals and the Brazilian Class I represents the European Class I, Brazilian Class II represents the European Class IIa, Brazilian Class III represents the European Class IIb and the Brazilian Class IV represents the European Class III. The classification rules are found in Annex II of Resolution RDC 185, October 22, 2001. The Brazilian rules are identical to the European rules except for Rule 8 and 13⁽³⁷⁾. Brazil has adopted the Universal Medical Device Nomenclature System (UMDNS). In vitro diagnostic devices are divided into six different groups together describing a total of 87 families of devices according to the document "Families de Products Diagnostics de use In Vitro" at the ANVISA homepage.

Product Registration

To register a medical device with the Brazilian Ministry of Health the manufacturer must have an office in Brazil or have a local distributor in Brazil authorized by the Brazilian authorities to import and distribute medical devices. The distributor is responsible for registering medical devices. The Brazilian importer of medical devices must have an import license, a so called Automatic License, or if requested a Non-Automatic License (LI). Manufacturers and importers of medical devices must have an "Autorização de Funcionamento" or in English called Company Working Allowance before registering their product. The product must be classified as a class I, II, III or IV device and the essential principles must be met. The essential principles are found in resolution RDC/ANVISA No. 56 of the 6 of April 2001.

A certificate of Brazilian good manufacturing practice (in Portuguese Boas Práticas) is required and a copy of the certificate shall be submitted with the registration application. Information on requirements for Brazilian GMP is found at Boas Práticas de Fabricação at ANVISA's homepage. Usually, Brazil accepts U.S. product standards and certifications by U.S. testing laboratories such as Underwriters Laboratory. Active medical devices under IEC 60601-1 must be certified by an INMETRO accredited test agency (Notified Body) and display the INMETRO marking⁽³⁸⁾.

Risk management is mandatory for all implantable devices, intrauterine devices and plastic bags for blood. Brazil has adopted the risk management standard ISO 14971 as a national standard. Requirements for risk factors are found in the essential principles.^{(39), (40)}. New products and products with innovative technology require clinical trials⁽⁴¹⁾. A post marketing surveillance system is required and adverse events shall be reported with special electronic forms found at NOTIVISA at the ANVISA homepage.

The required documentation for registration of a medical device is:

- A copy of payment bank receipt provided by ANVISA. A "Declaração do Porte da Empresa" or in English a "Declaration of company fee" shall also be submitted with the application.
- Identification of the manufacturer or importer and its medical device according to Annex III A, III B and III C in RDC 185/01 declaring the technical and legally responsible.
- A copy of authorization of the manufacturer to import and commercialize its medical device in the country. When authorized to export or import the commercial relationship between the exporter/importer and the manufacturer must be described.

- A copy of registration or certificate of free trade or equivalent document issued by the competent authority where the product is manufactured and/or commercialized. In Portuguese it is called “Registo ou certificate de livre comércio do product no exterior”.
- A declaration of conformity.

Medical devices class I only require the documentation in the first two points and the last point. Two label samples shall be submitted with the application and two copies of instructions for use shall be submitted with the application. Medical devices of class I and II do not need this information if they can be used safely without it. The information shall be in Portuguese.

4. MEDICAL DEVICE IN AUSTRALIA

General Information

Australia represents a large and highly advanced medical device market. Australia ranks as the 11th largest healthcare market in the world and counts as one of the richest in the Asia-Pacific region. The medical device industry has a growth rate of 15% per year and has a market capitalization of about 4 billion Australian dollars. Public hospital purchasing is varying from state to state. Generally, purchases are conducted centrally but there are exceptions. In some states, hospitals are allowed to purchase medical equipment within their own budget. A small company is recommended to have a local distributor ⁽⁴²⁾⁽⁴³⁾.

Regulation

The Therapeutic Goods Administration (TGA) is the competent authority for medical devices in Australia. TGA is a unit of the Australian Government Department of Health and Ageing and is responsible for administering the provisions of the legislation under the Therapeutic Goods Act 1989 (the Act). This act covers both medical devices and AIMD's. The organization is divided into several parts where the Office of Devices, Blood, and Tissues is responsible for medical devices.

On 4 October 2002 a new GHTF harmonized regulatory system was introduced by the Therapeutic Goods Regulations 2002, here called the Regulations ⁽⁴⁴⁾⁽⁴⁵⁾. The transition period for the new system ended on 4 October 2007 ⁽⁴⁶⁾. Medical devices must be registered in the database Australian Register of therapeutic Goods (ARTG) before entering the Australian market. Sponsors are recommended to use the Devices Electronic Application Lodgment system (DEAL) for the applications. Sponsors have the responsibility for all activities concerning medical devices while manufacturers have obligations to fulfill the requirements ⁽⁴⁷⁾.

Classification

Medical devices are divided into five classes; class I, class IIa, class IIb, class III and Active Implantable Medical devices (AIMD). Class I represents the lowest risk and class III and Active Implantable Medical devices the highest risk. Class I devices include low-risk devices that are sterile and/or have a measuring function. AIMDs are treated as class III devices.

In vitro-diagnostic devices (IVDs) are divided into four different classes; class I, II, III and IV. Class, I devices present no public health or a low personal risk. Class II devices present a low public health risk and moderate personal risk. Class III devices present a moderate public health risk or high individual risk. Class IV devices present a high public health risk ⁽⁴⁸⁾. Medical devices are given Global Medical Device Nomenclature (GMDN) codes ⁽⁴⁹⁾.

Product Registration

The sponsor is responsible for registering the medical device in the ARTG ⁽⁵⁰⁾. Before doing this the medical device must be classified according to the Australian system and suitable quality management systems must be applied and risk analysis been done to comply with the Essential principles described in Schedule 1 of the Therapeutic Goods (Medical Devices) Regulations 2002 ⁽⁵¹⁾. A post marketing surveillance system is an obligation on the manufacturer but the sponsor is the responsible legal entity and shall, therefore, participate in the system ⁽⁵²⁾.

A quality management system is required for medical devices class IIa, IIb, III and AIMDs to get a conformity assessment certificate approved. Standards are recommended to use but are not mandatory. Australia has its own standing orders but the international ISO standards can be used. Standards for quality management systems (ISO 13485), risk management (ISO 14971), clinical trials (ISO 14155) and biocompatibility (ISO 10993) are recommended depending on the type of medical device ⁽⁵³⁾. The manufacturer is required to have made a documented risk analysis of the product. This is according to the Australian Essential principles 1 and 2, ensuring the safety of the medical devices.

There are three documents that are necessary to register a medical device in Australia; a conformity assessment certificate which can be issued by TGA or an overseas notified body, a Declaration of Conformity and an application to include the medical device in the ARTG ⁽⁵⁴⁾. The conformity assessment certificate is not required for medical devices class I that does not have a measuring function or are intended to be supplied in a sterile state ⁽⁵⁵⁾. Manufacturers with a CE certificate must give TGA following information:

- Copies of the current CE certificates hold by the manufacturer
- Copies of the Initial Certification audit report
- Copies of the current CE design Examination Or Type Examination Certificate, if applicable
- Copies of the Design Examination or Type Examination reports issued by the Notified Body in support of the certificate, if applicable
- Evidence of close out of nonconformities

The manufacturer is also required to submit the information required under Quality System Documentation (Section 5.0 of the attached form), a completed essential principles checklist, risk management report, clinical evidence, and labeling, instructions

for use and advertising material. For class III devices and AIMDs, the manufacturer shall also submit a Design Dossier which is a compilation of quality management system design and development records showing conformity to essential principles.

TGA may on a review of this information conduct a reduced assessment of the quality system or may in some cases do an on-site audit⁽⁵⁶⁾. Information provided with the medical device shall at least be in English. If a device belongs to class I or II and the device can be used safely for its intended use without instructions a document of instructions for use need not be provided with the device. The registration is valid for five years⁽⁵⁷⁾.

4. MEDICAL DEVICES IN GCC COUNTRIES

5.1 Kingdom of Saudi Arabia (KSA)

a) Medical Devices Regulation:

As KSA is an active member of AHWP, the most Medical Devices regulations are based on IMDRF and consequently GHTF requirements. These regulations ensure that only Medical Devices that have been authorized by one of the founding IMDRF members have access to the Saudi Arabian market. The Saudi Arabian Food and Drug authority (SFDA) was established in 2003 and is still constructing the regulatory infrastructure for Medical Devices registration. The SFDA is operating through a Medical Devices Interim Regulations (MDIR) system. The SFDA is an independent authority that reports to the council of ministers and is responsible for the regulation of Medical Devices in Saudi Arabia⁽⁶⁵⁾.

The MDIR is facilitated through a set of Electronic systems⁽⁵¹⁾ [Country Questionnaire, 2014] and solutions to enable manufacturers, Authorized Representatives, Importers, Distributors, and other parties to communicate efficiently with the SFDA. The electronic application forms (Annex V) are found on the Medical Devices Marketing Authorization (MDMA) portion of the SFDA's website⁽⁶⁶⁾ [Country Questionnaire, 2014].

The Medical Devices interim regulation applies to the following parties and products:

1. Manufacturers, authorized representatives, importers, and distributors.
2. All Medical Devices and their accessories that will be supplied to the KSA market.
3. Contact lenses and laser surgical equipment for cosmetic rather than medical purposes, and their accessories.

Medical Devices may be placed on the market only if they comply with the applicable provisions of this MDIR^(68, 69). A local representative is required to handle the registration application on behalf of the foreign manufacturer.

b) Required documentation:

According to article 18 of MDIR, in order to register a Medical Devices, the applicant is asked to submit the following documentation to SFDA

1. Application form (Annex V);
2. Letter of Authorization (LOA);
3. Manufacturer and Saudi Authorization representative details;
4. GMP certificate or QM- system certificate (ISO 13485, ISO 9001);
5. Recent Audit Report;
6. Other Certificates as required by the Devices class;
7. Documents supporting the market authorization in reference IMDRF market;
8. Declaration of Conformity, written in English;
9. The declaration of conformity clearly identifies to which Medical Devices it applies and attests that the Medical Devices complies with the regulatory requirements of the relevant IMDRF Founding Member and also complies with the national provisions of MDIR.

Moreover, the following Technical documents are requested for submission:

- ❖ A copy of the Medical Devices information including labeling, Intended use, instruction for use (IFU) and marketing materials, in English and/ or Arabic language;
- ❖ Specifications or similar documents that ensure, that the Medical Devices are correctly stored, transported, installed and maintained in the KSA, and users can be trained in their proper use;

c) Pre-Owned Medical Devices:

Used or refurbished medical equipment is allowed entry into Saudi Arabia. However, the Ministry of Health and other Saudi government hospitals keep away from purchasing such equipment.

d) Post Marketing Surveillance:

The NCMDR receives reports of suspected Medical Devices adverse events and confirmed product recalls from healthcare practitioners and Devices suppliers within the Kingdom of Saudi Arabia⁽⁷⁵⁾.

MEDICAL DEVICES IN WESTERN ASIA COUNTRIES

6.1 Israel

Medical Devices definition

Medical Devices defined as Instrument, Devices, software, chemical, biological or biotechnological

- ❖ Used in treatment; or
- ❖ Needed for the activation of a Devices or apparatus that is used for treatment and not mainly intended to work on the body as a drug.

a). Medical Devices Regulation:

Although Israel is geographically part of the Middle East, because of political issues there is no regulatory relationship with any of the countries around it. In Israel, medical Devices are regulated by the Division of Medical Devices and Accessories

under the Israel's Ministry of Health (IMOH) by the "AMAR" unit. AMAR is responsible for certification of all activities concerning medical Devices import, sale and export. In order to import or sell a Medical Device in Israel, the manufacturer shall hold an AMAR registration for the Devices concerned.

The MOH recognizes the Food and Drug Administration (FDA) certification and the European Union CE Mark and approves products carrying such certifications without further requirements. Furthermore, MOH implements FDA's recommended indications for the Devices ⁽⁸⁵⁾

b). Required documentation:

Companies wishing to export medical equipment or Devices to Israel must have a local Israel agent or distributor who should request a Pre-Marketing Approval (PMA) from the IMOH.

The PMA request should be accompanied by one of the following documents:

- The U.S. Food and Drug Administration (FDA) 510(k) marketing authorization or PMA.
- Biological Devices fall under Medical Devices classification required FDA's Centre of Biologics Certificate.
- In most cases, the CE Mark (European Union) and Canadian documentation are also accepted by IMOH.

For any imported medical Devices, the Israeli importer must submit a registration application to the MOH Department of Medical Devices. Registration of Medical Devices in Israel is based on having prior approval in one of the five founding IMDRF countries: Australia, Canada, EU, Iceland, Norway, New Zealand, Switzerland, Japan or USA. If such a certificate is not available, the registration can be processed but will take a longer period of time, and the MOH will determine what type of testing is needed.

The application should be submitted on the special form designated for this purpose and shall include the following data and documents ^(87, 88) Name and address of the manufacturer and of the importer as applicable, intended use of the medical Devices and of its medical indications.

- A certificate attesting the safety of the Devices, issued by a competent authority of one of the following countries: Australia, Canada, European Community (EC), Israel, Japan, and USA.
- FSC.
- CE Certificates.
- ISO 9001 and ISO13485 certificates.
- Description of the technical and maintenance services, including periodic checks and inspections.
- Declaration of the local manufacturer/importer, and of the foreign manufacturer.
- Details of the standards to which the Devices complies and
- The latest audit report.

Moreover, the following technical documentation is required for submission:

- ❖ Technical details of the medical Devices and of its components,
- ❖ Information on any risk which may be associated with the use of the Devices,
- ❖ IFU of the Devices,
- ❖ Catalogues of and brochures for the Devices,
- ❖ Labels and accompanying material.

Furthermore, the Israeli MOH – AMAR requires a checklist of information from a foreign medical Devices manufacturer for the registration or the renewal of the registration, according to the information from a local representative in 2014.

c). Pre-Owned Medical Devices:

The Israeli market for used medical equipment is very small and considered insignificant for US exports. There is no special tariff that applies, and the official import requirements are the same as for new equipment. However, in practice, the Ministry of Health (MOH) permits the import of used/refurbished equipment only by specified end-users and does not issue registration certificates for imported used equipment.

CONCLUSION

The regulation of medical devices around the world is very diverse. There has been an upsurge in the number, diversity, and intricacy of medical devices in last two decades. Regulation of these devices has also advanced due to the requirement for a steady regulatory perspective. Medical Devices and are striving to harmonize with the IMDRF guidelines, in others the MD regulation is still in its infancy. Although the US is still the dominating regulator, the EU regulation becomes continually more impact on harmonization. This corresponds to the growing exports of EU countries in the MENA region. Most countries are trying to harmonize the regulatory guidelines for medical devices through their participation in GHTF. The endowments of GHTF, Latin American Harmonization Working Party LAHWP and Asian Harmonization Working Party (AHWP), will play an important role in the harmonization of regulatory guidelines of medical devices. Harmonized regulation of medical device will lead to the availability of the quality product. Non-harmonization of medical device regulation might lead to serious concerns. Some studies in public domain illustrate that regulatory reforms are required to promote high-quality evidence in approval of higher risk devices.

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