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COMPREHENSIVE ADMINISTRATIO FOR THE COMPLIANCE MANUFACTURING AND MARKETING OF MEDICAL DEVICES IN MENA COUNTRIES

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ABSTRACT

During the development and registration process, several parties need to interact with each other. Local authorized representatives or agents play a key role in medical Devices registration in all MENA countries. They are required as per the regulations and they help to overcome barriers for foreign companies, like language issues and the know-how of local requirements and processes as well. Often websites and local regulations are only available in local language (mostly Arabic) and local agents can benefit from participation in local regulatory or industry networks. As the requirements for Medical Devices are not homogeneous throughout the MENA countries, different types of dossiers will have to be prepared. The technical documentation will cover the requirements of the majority of countries, however not internationally named as ‘design dossier’ or STED. Beside the technical documentation, the main requirements are usually GMP or QM-System certificates, a FSC from the Country of Origin, a Letter of Authorization, EC certificates, and Declaration of Conformity, a Certificate of Analysis the finished product, a statement about the status of Devices distribution, a local application form and country specific declarations. The FSC is a key document in the registration process of Medical Devices in most MENA countries, which must be legalized by the chamber of commerce and the embassy of the foreign importing country in C.O.O. (see Annexes II, III and IV)). Annex II-IV illustrate which countries need a FSC for submission and which countries do not required a FSC. The Devices needs to be classified very early in the development process in order to determine the path forward. Medical Devices in general usually are divided into three groups as in the USA (class I, II and III) or four groups as in the EU (class I, IIa, IIb and III) or according to the GHTF guidelines (class A, B, C and D). The main MENA countries accept both EU and FDA definitions. In vitro diagnostic Devices are seen as a separate group and the classification of these products vary a lot.

KEYWORDS: Medical Devices, MENA countries, GMP or QM-System.

1.0. INTRODUCTION

Define the regulatory environment for Medical Devices in the Middle East and the North African countries (MENA), to show their limits and their prospects. The Medical Devices market in this area presents unique challenges and opportunities to international manufacturers in the health care sector. Although the Medical Devices market in the MENA region is very diverse most of the individual economies have shown sustainable growth. This growth is driven by several factors including a growing population of 400 million people, the price of oil and energy, an increase of the Gross Domestic Product (GDP) and the income per capita, an improved literacy rate, a larger middle class and also a higher disease rate. In this market Medical Devices are one of the most important health intervention tools available for the prevention, diagnosis and treatment of diseases and for patient rehabilitation. The growth of demand for sophisticated pharmaceutical and medical products in the MENA region seen in recent years is only likely to continue. Despite of the overall positive economic development in most of the MENA countries the regulatory environment can be challenging. Publicly accessible written legislations are limited in these countries, sometimes are only available in the local language (mostly Arabic) and leave room for interpretation. Also important to mention in this context are the barriers for the continuing evolution of the regulatory environment in some of these emerging countries due to their political instability, non-transparency and corruption. Against this background the efforts of the Global Harmonization Task Force (GHTF) to harmonize the Medical Devices regulation, offer a valuable contribution to ease the regulatory interconnection and intercommunication between the individual countries and the international economic operators of the Medical Devices industry. The follower of GHTF - the International Medical Devices Regulators Forum (IMDRF) - builds on the strong foundational work of the GHTF and accelerates the international Medical Devices regulatory harmonization and convergence. The impact of the EU on the harmonization in these countries is rising.

1.1 Definition of MENA countries

The Middle East & North Africa (MENA) region is bordered by Morocco in the south (respectively west) to Iran in the north. There is no standard definition of the Middle East. The Word Bank defines the MENA region as Algeria, Bahrain Djibouti, Egypt, Iran, Iraq, Israel, Jordan, Kuwait Libya, Morocco, Oman, Qatar, Saudi Arabia, Syria, Tunisia, United Arab Emirates (UAE), West bank and Gaza and Yemen.[1]

The MENA countries consist of three general sub-regions[2,4]:

Arabian Peninsula: Bahrain, Kuwait, Oman, Qatar, Saudi Arabian (SA), United Arab Emirates (UAE) and Yemen. This region is also defined as Cooperation Council for the Arab States of the Gulf (GCC).

Western Asia: Iran, Iraq, Israel, Jordan, Lebanon, Palestinian Territory and Syria;

North Africa: Algeria, Egypt, Libya, Morocco, Tunisia.

2.0. AIM AND OBJECTIVE OF WORK

The purpose of this Master Thesis is to define the regulatory environment for the MENA region. This includes regulatory provisions like registration requirements and processes, guidelines as well as predictive approval timelines.

As the Medical Devices registration in most countries of the MENA region is based on having a prior approval in one of the GHTF countries, this paper will describe briefly the regulatory environment according to the GHTF and WHO for Medical Devices regulations and its implementation in MENA countries.

METHODOLOGY

3.1. Medical Devices regulation

3.1.1. Medical Devices regulation history

The regulation of Medical Devices across the world is varies a lot, ranging from comprehensive to none. Over the past two decades, the number, range, and complexity of Medical Devices and therefore regulation of these Devices has increased. In 2001 the World Health Organization (WHO) published "A model regulatory program for Medical Devices".[21]

That was an international guide to assist member states in establishing regulatory programs for Medical Devices. The aim was to provide information to nations without Medical Devices regulatory systems that would enable the production of internationally compatible regulations. In 2003 the WHO published 'Medical Devices regulations. Global overview and guiding principles'.[22,23]

This guideline emphasized the complexity of the Medical Devices industry and identified issues related to regulation. The mentioned document provided guidance to member states wishing to create or modify their regulatory systems for Medical Devices. The WHO reported the following results from their Bangkok meeting during September 2010 about worldwide Medical Devices regulation framework.

Table 4: Worldwide Medical Devices regulation framework.[22,24]

Countries %	Medical Devices regulation
30%	These countries have a developed framework for regulation of Medical Devices.
30%	These countries partially have regulation of Medical Devices
40%	These countries are either developing a framework or do not yet have any regulation

a) International Standardization Organization (ISO)

The International Standardization Organization (ISO) was set-up in 1946 to facilitate the international coordination and unification of industrial standards. ISO is a network of national standards institutes in 163 countries, and is now the world's largest developer and publisher of voluntary international standards.

ISO standards are widely adopted on a regional and national level and support the procedures and practices of Medical Devices development, manufacture, quality control and conformity assessment requirements.

b) Global Harmonization Task Force (GHTF)

In 1992 the Global Harmonization Task Force (GHTF) was founded in response to the growing need for international harmonization of Medical Devices regulation. The GHTF was a voluntary group consisting of representatives from the Medical Devices regulatory authorities of the five members: USA, European Union (EU), Japan, Australia and Canada. In 2006, the membership was expanded to include the Asian Harmonization Working Party (AHWP), the International Organization for standardization (ISO), and the International Electrotechnical Commission (IEC).[22]

The Asian Harmonization Working Party (AHWP) was established in 1996 as a non-profit organization by a group of Medical Devices regulatory authorities and the Medical Devices industry. Its aims are to study and recommend ways to harmonize Medical Devices regulations in the Asian and other regions and to work in coordination with the GHTF and other related international organizations. The aim of this cooperation is to establish harmonized requirements, procedures and standards. Membership is open to representatives from Asia and other regions that support the above

stated goals. The following countries of the MENA region are members of AHWP: Abu Dhabi, Jordan, Kingdom of Saudi Arabia, Kuwait and Yemen.[25]

c) International Medical Devices Regulators Forum (IMDRF)

GHTF was superseded by the International Medical Devices Regulators Forum (IMDRF) that was founded in October 2011. It is a voluntary group of Medical Devices regulators from around the world. These Medical Devices regulators have come together to build up the strong foundational work of the Global Harmonization Task Force on Medical Devices (GHTF) and aim to accelerate international Medical Devices regulatory harmonization and convergence. The current IMDRF members are Australia, Brazil, Canada, Europe, Japan, and the United States of America. The membership of China and the Russian Federation is currently being confirmed. The World Health Organization (WHO) is an official observer.[26]

3.2 International Medical Devices Regulators Forum

3.2.1 Goals of the IMDRF

The goals of IMDRF are to[27]:

- Accelerate international Medical Devices regulatory convergence;
- Support innovation and timely access to safe and effective Medical Devices globally;
- Promote open discussion and the sharing of best practices among regulatory authorities responsible for Medical Devices regulation;
- Facilitate frequent exchange of policy and regulatory information of common interest to regulatory authorities;
- Provide opportunities to identify commonalities and develop approaches to overcome unnecessary regulatory barriers;
- Enhance communication, information sharing and scientific exchange among regulators and a broad range of stakeholders;
- Establish development dialogue with other relevant organizations.

3.2.2 Technical documents

The technical documents were created by the GHTF. These are final documents and are still current. As the work of the IMDRF progresses, these documents will be reviewed and published as IMDRF documents. Until then, these documents are provided for the use of interested parties.[26]

GHTF Study Group 1 - Pre-market Evaluation documents

These guidance documents describe a global regulatory model for Medical Devices. They provide principles suitable for harmonization and develop harmonized guidelines. Key terms such as “Medical Devices” and “manufacture” and the essential principles of safety and performance are defined in these documents. These documents provide guidelines concerning the principles of classification and conformity assessment such as standard format for pre-market submissions and harmonized product labelling requirements.[28]

GHTF Study Group 2 - Post-market Surveillance/Vigilance documents

This guidance is a review of adverse event reporting, post-marketing surveillance and other forms of vigilance for Medical Devices. It is an analysis of different requirements amongst countries with developed Devices regulatory

systems. The subject of these documents is to define requirements for a common Medical Devices vigilance system on a global basis.[29]

GHTF Study Group 3 - Quality Systems documents

These documents are covering the implementation and integration of a risk management system within the quality management system, process validation and the control of products and services obtained from suppliers[30] [see also 3.2.6 (1)].

GHTF Study Group 4 - Auditing documents

These documents give guidance regarding training requirements for auditors, regulatory auditing strategy and reports. Recently (September 2014), the IMDRF published a guidance intended to implement the concept of a Medical Devices Single Audit Program (MDSAP). In December 2013 the IMDRF published two documents: "Requirements for Medical Devices Auditing Organizations for Regulatory Authority Recognition" and "Competence and Training Requirements for Auditing Organizations".

These two documents are complementary documents and focused on requirements for an Auditing Organization and individuals performing regulatory audits and other related functions under the respective Medical Devices legislation, regulations, and procedures required in its regulatory jurisdiction.[31]

GHTF Study Group 5 - Clinical Safety/Performance documents

These documents focus on harmonized requirements for evidence of the clinical safety of Medical Devices and IVD Medical Devices. The subject of this guidance is a harmonized definition of clinical investigation, clinical data, clinical evaluation and clinical evidence and post-market clinical follow up study.[32]

3.2.3 Definition of 'Medical Devices' and 'In Vitro Diagnostic (IVD) Medical Devices

The GHTF proposed the following harmonized definition of a Medical Device.[33]

'Medical Devices' means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article:

Intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of: diagnosis, prevention, monitoring, treatment or alleviation of disease, diagnosis, treatment, alleviation of or compensation for an injury, investigation, replacement, modification, or support of the anatomy or of a physiological process, supporting or sustaining life, control of conception, disinfection of Medical Devices, providing information by means of in vitro examination of specimens derived from the human body; and which does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.

'In Vitro Diagnostic (IVD) Medical Devices' means a Medical Devices, whether used alone or in combination, intended by the manufacturer for the in-vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes.

3.2.4 Classification System for Medical Devices

According to GHTF/IMDRF the classification of Medical Devices is the manufacturer's responsibility. The Regulatory Authorities (RA) specifies procedures to be followed by manufacturers during the design, manufacture, and marketing of each Devices. It describes the manner in which a manufacturer should demonstrate conformity to such specified procedures. Classification of a Medical Devices has to be done carefully, because the risk class establishes the correct conformity requirements. An incorrect classification would therefore lead to a conformity assessment procedure, which is not applicable to the particular Devices.

GHTF/IMDRF established a Devices classification system consisting of four classes where Class A represents the lowest hazard and Class D the highest. The determination of class should be based on rules derived from the potential of a Medical Devices to cause harm to a patient or user and thereby on its intended use and the technology/ies it utilizes[34] (see table 5).

Table 5: Diagrammatic Representation of the Classification System.

	Class	**Medical Devices**	**IVD**	**Medical Devices**
	Level	Devices example	Level	Devices example
A	Low Hazard	Bandages / tongue depressors	Low Individual Risk and Low Public Health Risk	Clinical Chemistry Analyzer, prepared selective culture media
B	Low-moderate Hazard	Hypodermic Needles / suction equipment	Moderate Individual Risk and/or Low Public Health Risk	Vitamin B12, Pregnancy self-testing, Anti-Nuclear Antibody, Urine test strips
C	Moderate-high Hazard	Lung ventilator / bone fixation plate	High Individual Risk and/or Moderate Public Health Risk	Blood glucose self- testing, HLA typing, PSA screening, Rubella
D	High Hazard	Heart valves / implantable defibrillator	High Individual Risk and High Public Health Risk	HIV Blood donor screening, HIV Blood diagnostic

3.2.5 Essential Principles applicable to all Medical Devices including IVD Medical Devices

The worldwide adoption of fundamental design and manufacturing requirements for Medical Devices that provide assurance that the Devices is safe and performs according to its specification, offers significant benefits to the manufacturer, user, patient or consumer, and to Regulatory Authorities.

According to the GHTF Medical Devices regulatory framework, a Medical Devices has to meet certain essential principles regarding safety and performance before it can be placed on the market. The basic framework for these Essential Principles is described in one document for both Medical Devices and IVD Medical Devices.

This guidance describes fundamental design and manufacturing requirements, referred to 'Essential Principles of Safety and Performance', which apply to all Medical Devices. A manufacturer of a Medical Devices is expected to design and manufacture a product that is safe and performs as intended. There is a comprehensive list of design and manufacturing requirements separate from general requirements, which are not applicable for each Medical Devices/IVD Medical Device.

The responsibility of the manufacture is to decide which ones are relevant to his product. The following aspects are covered:

- Chemical, physical and biological properties
- Infection and microbial contamination

- Medical Devices/IVD Medical Devices incorporating a substance considered to be a medicinal product/drug
- Medical Devices incorporating materials of biological origin
- Environmental properties
- Devices with a diagnostic or measuring function
- Protection against radiation
- Medical Devices/IVD Medical Devices that incorporate software and standalone Medical
- Devices software Active Medical Devices and Devices connected to them
- Protection against mechanical risks
- Protection against the risks posed to the patient or user by supplied energy or substances
- Protection against the risks posed by Medical Devices intended by the manufacturer for use by lay persons
- Label and Instructions for Use
- Clinical evaluation

3.2.6 Conformity Assessment Procedure

The conformity assessment is a systematic examination of evidence procedures that may be used by the manufacturer to determine that a Medical Devices is safe and its compliance with the Essential Principles as intended by the manufacturer. Conformity assessment is primarily the responsibility of the Medical Devices manufacturer. However, a review of the process and the conclusions are conducted either by the relevant Regulatory Authority (RA) or a Conformity Assessment Body (CAB).

According to the documents of GHTF:

- Conformity assessment for Medical Devices
- Conformity assessment for IVD Medical Devices

The following five conformity assessment elements are applicable to all four Devices classes:

(1) Quality Management System (QMS)

The manufacturer should implement, document and maintain a QMS that ensures, that the design, manufacturing and supply to the market of the Medical Devices are safe, perform as intended and comply with the relevant requirements. Therefore, when a Medical Devices manufacturer chooses to utilize suppliers, the manufacturer should ensure control over any product or service obtained from such suppliers as defined within the QMS.[36]

The QMS can be based on international standards, such as ISO 9001 as a general management standard and ISO 13485, which include special requirements to ensure the safety and efficacy of Medical Devices. Although a full QMS is preferred, some countries or regional regulations may allow the manufacturer to choose type examination as an alternative means of demonstrating conformity with the relevant Essential Principles of safety and performance. The use of international standards is still strongly encouraged by GHTF/IMDRF, as they are generally presumed to conform to the corresponding Essential Principles and to support global convergence in regulatory system.

The requirements of a QMS have been discussed in Study Group 3 and guidance documents on the following published topics:

Quality Management System – Medical Devices – Guidance on the Control of Products and Services Obtained from Suppliers.

This guidance document is intended for Medical Devices manufacturers and it is expected that the reader is familiar with regulatory quality management system requirements within the Medical Devices sector. This guidance document may also be useful to regulatory authorities and suppliers. This guidance document is intended for educational purposes and it is not intended to be used to assess or to audit compliance with regulatory requirements.

Implementation of risk management principles and activities within Quality Management System Medical Devices manufacturers are generally required to have a QMS as well as processes for addressing Devices related risks. These processes for managing risks can evolve into a stand-alone risk management system (RMS). While manufacturers may choose to maintain these two management systems (QMS&RMS) separately, it may be advantageous to integrate them as this could reduce costs, eliminate redundancies, and lead to a more effective management system.

Manufacturers of Class A and B Devices should implement and maintain the basic elements of a QMS but have the option of eliminating the design and development controls from it. The QMS for manufacturers of Class A Devices is normally not subject to a premarket on-site audit by the RA or CAB. Manufacturers of Class C and D Devices should implement and maintain an effective QMS that includes design and development controls, and needs to be verified by the RA or CAB either by accepting existing relevant certification of the manufacturer or by carrying out an on-site audit of the facilities in question.

Process Validation Guidance

The process validation is a requirement within a QMS and has general applicability to manufacturing processes for Medical Devices. Software validation is not covered by GHTF documents. The degree of the assessment of the manufacturer's QMS by RA or CAB is influenced by the class of the Medical Devices.[37]

Detailed guidance on auditing practice is provided in the IMDRF documents. They are intended for auditing organizations[38] and an assessment method for recognition and monitoring of Medical Devices Auditing Organizations.[39]

The follow-up of corrections, corrective and improvement actions are also treated, as well as training requirements for auditors[40,41] and the competence criteria that should be met by an audit team.

(2) A system for post-market surveillance

The post-marketing surveillance system is part of the QMS and RA or CAB will confirm that such a process is in place, usually at the time of the QMS audit. Furthermore, the RA may require manufacturers to perform a specific post-marketing study of a particular type of Devices, and report the outcome to the RA. The RA will monitor any post-marketing study and consider whether any additional regulatory action is required after analyzing the outcome. The post-marketing surveillance system has to include complaint handling, vigilance reporting and corrective and preventive action according to guidance documents by Study Group 2.

4.0. RESULTS & DISCUSSIONS

4. Medical Device regulation in MENA countries

The regulatory environment in these countries is very different. Publicly accessible written legislations are limited, sometimes only available in local language (most Arabic) and leave room for interpretation. In order to support the

information, the author of this master thesis sent a questionnaire (Annex I) 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 non-Apostiile countries:

a) Document legalization in Apostiile countries

The only Apostille countries in MENA region are Oman and Israel. The mentioned certificates only need an Apostille to legalization for both countries.[46,47]

b. Document legalization in non - Apostiile countries

The remaining 17 MENA countries are non- Apostille countries. For any non- Apostille country, the document must to 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. The documents for these countries must first be sent to the district court (Landgericht), then to the chamber of commerce (IHK) and the Federal Administration Office (Bundesverwaltungsamt) depending upon the national health ministry's requirements, after that to the Arab-German Chamber of Commerce and Industry (Ghorfa) and finally to the Embassy of the foreign countries, respectively. This process is different for each country.[48]

4.1 Medical Devices in GCC Countries

4.1.1 Kingdom of Saudi Arabia (KSA)

Medical Devices Definition

The Medical Devices and In Vitro Diagnostic (IVD) definitions in Saudi Arabia are based on the IMDRF definition[49] (see section 2).

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.[50]

The MDIR is facilitated through a set of Electronic systems51 [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 [52] [Country Questionnaire, 2014].

The Medical Devices interim regulation applies to the following parties and products49: Manufacturers, authorized representatives, importers and distributors.

- All Medical Devices and their accessories that will be supplied to the KSA market.
- 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.[51,53,54] 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.[52,55-59]

- Application form (Annex V);
- Letter of Authorization (LOA);
- Manufacturer and Saudi Authorization representative details;
- GMP certificate or QM- system certificate (ISO 13485, ISO 9001);
- Recent Audit Report;
- Other Certificates as required by the Devices class;
- Documents supporting the market authorization in reference IMDRF market;
- Declaration of Conformity, written in English;

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.

Environmental statements

Statement attesting that the Medical Devices complies with the regulatory requirements of the relevant IMDRF Founding Member jurisdiction and also complies with the national provisions of this Interim Regulation (Annex VI);
The applicant shall indicate, which of the GHTF Founding Member (s) allows the Medical Devices that is the subject of the MDMA application, onto its market; and Regulatory Compliance Attestation: Statement confirming that the applicant will comply with the KSA's National Centre for Medical Devices Reporting (NCMDR) requirement and any Filed Safety Corrective Action affecting the Medical Devices is reported to KSA authorities (Annex VII).

Moreover, the following Technical documents are requested for submission

A copy of the Medical Devices information including labelling, 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; A report of any relevant adverse event, that involves the Medical Devices, be submitted to SFDA's National Centre for Medical Devices Reporting (NCMDR).[60]

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.[49,60]

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.[62]

E. Country Specifics

Enforcement of Medical Devices Marketing Authorizations

All Medical Devices & IVDs intended to be marketed in Saudi Arabia should have a valid Medical Devices Marketing Authorization (MDMA) as per the following enforcement dates.

Table 8: Enforcement date of Medical Devices Marketing Authorizations KSA.[63]

Class	Type	Enforcement Date
High Risk	In Vitro Diagnostics	1st October 2012
	Medical Devices	1st December 2012
Medium Risk	In Vitro Diagnostics	1st December 2012
	Medical Devices	31st December 2014
Low Risk	In Vitro Diagnostics	30th June 2015
	Medical Devices	31st December 2015

4.1.2 United Arab Emirates (UAE)

Medical Devices Definition

The Medical Devices and In Vitro Diagnostic (IVD) definition in the UAE are the same as in the KSA based on the GHTF definition[64] (see section 2.2.3).

A. Medical Devices Regulation

The UAE are like the KSA a member of the AHWP and the Medical Devices are regulated by the Ministry of Health (MOH) in the United Arab Emirates.[65]

UAE Medical Devices regulations are substantially orientated towards GHTF guidelines as well as towards EU requirements. Classification requirements and the evaluation of Devices follow international regulations and guidelines, mainly those of:

- The IMDRF for Medical Devices,
- The US Food and Drug Administration's Devices Regulation,
- The EU Medical Devices Directive 93/42/EEC,
- The EU in Vitro Diagnostic Devices Directive (IVDD) 98/79/EC and
- The EU Active Implantable Medical Devices Directive (AIMDD) 90/385/EEC.

The similarity between the classification of medical Devices and the registration Guideline of the MOH is shown by the fact that certain definitions are very close to those provided by the EU Medical Devices Directive.[66]

The guidelines provide for a simplified registration process for Devices that have received approval from recognized regulatory agencies, such as those in Europe, the US, Australia, Canada or Japan. The Medical Devices manufacturers must be registered with the Ministry before they can market their products in the UAE. Companies who wish to export their products into the UAE must engage a local representative or distributor with a licensed medical store for registration of their products with the MOH.

In order to register a Medical Devices in the UAE, the product as well as the company must be registered there. The appointed local representative or distributor must submit a Medical Devices as well as a manufacturer's company registration application form (Annex IIX) to the Ministry's Drug Control Department.

B. Required documentation

1. Product registration In order to register a Medical Devices, the applicant is asked to submit the following documentation in Arabic or English language to the MOH. The documentation varies depending on the Devices classification.[64]

Table 9: UAE Medical Devices regulation: the required attachments per Devices Class.[64]

Documentation	Class I/ General IVD A	Class II/ Class B IVD	ClassIII/ Cl ass C IVD	Class IV/ Class D IVD
Application Form (Annex IIX for the company and Annex IX for the product)	√	√	√	√
CE certificate and FSC (both legalized by the chamber of commerce and the UAE embassy)	√	√	√	√
Declaration of Conformity / Evidence of Conformity to the essential principles	√ Self-Declaration	√	√	√
Company registration certificate legalized by the chamber of commerce and the UAE embassy in country of origin	√	√	√	√
Status of Devices distribution	NA	√	√	√
Declaration of prices	√	√	√	√
essential principles checklist	√	√	√	√
Post-market requirements/ vigilance system and risk assessment	NA	√	√	√
Manufacturing process: • Process Validation Studies • Software validation studies (if applicable)	NA	NA	√	√
Safety and effectiveness data, risk assessment, pre-clinical and clinical studies	NA	NA	√	√
Labeling & samples • Three copies (artwork) of each product packaging, labeling and promotional material • Sample (if applicable). • Labeling and packaging must have: the product name, name and address of the company printed in English and/or Arabic, manufacturing date and/or expiration date, Medical Devices for single use must be labeled accordingly on the outer pack	√	√	√	√
Shelf life study	NA	NA	√	√

Company registration

In the UAE the company registration file should be submitted at the same time as the registration files of its product/s.[64]

Companies' registration requirements

- Application for the medical Devices company (Annex IIX),
- Company business license,
- LoA,
- Organization of the quality assurance system (flow chart),
- Notarized copies of relevant certificates for Quality Accreditations from recognized notified bodies for each manufacturing facility involved in the manufacturing of the medical Devices intended for registration in the UAE,
- 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 of the company with best practices,
- A recent audit report.

The general profile has to include the following Information:

a. Company name, address, including the corporate structure as well as all company names of the company and its manufacturing sites used,
b. Contact name, telephone, fax numbers and e-mail addresses,
c. Total number of employees (all shifts) covered by the scope of the audit,
d. Product range and class of Medical Devices being manufactured (the class of a medical Devices may differ from one the regulatory authority of one UAE country to another),
e. Types of Medical Devices sold and/or planned to be sold in the UAE and/or GCC regions for which the regulatory requirements will be assessed, including a complete list of authorizations (e.g. licenses) issued for those Medical Devices (where applicable),
f. Location and function of each site,
g. A list of activities performed at each site,
h. Special manufacturing processes, e.g., software, sterilization, etc.

Furthermore, the technical documentation is required for submission, e.g. the following documents:

- Site Master File for each manufacturing site (if applicable),
- Warehousing information and general dispatch information as well as the implemented
- Quality management system, validation and verification processes for sterilized products.
- The general post marketing surveillance plan.

If the company has multiple manufacturing sites, each manufacturing location should be identified as follows indicating the manufacturing step carried out there (see application for company registration): design, production, sterilization, packaging, labeling and final release.

C. Country Specifics

After approval of the application, a registration number is given, which is valid for five years. A registration number can be revoked,[65,67]

If the applicant requests for it or

Upon failure to meet the standards based on assessment or monitoring proving that

- The Devices are unsafe and/or harmful,
- The quality of the Devices is substandard,
- The Devices differ from the approved label.

Importation Rules

A pre-approval for importation of the consignment is issued by Drug Registration and Control Department for importation of Medical Devices. This will be only allowed for importers with a MOH medical store license.

Documents to be attached to the consignment pre-import approval application form are:

1. The legalized ISO 13485 by the UAE Embassy;
2. FSC / documentation or letters of regulatory approval / relevant CE certification/ clearance to manufacture, sale, import and export of the Medical Devices from the competent authority in the exporting country and the
3. Declaration of conformity. The control of Medical Devices will be based on an implemented risk assessment and risk management.

D. Pre-Owned Medical Devices

Used Medical Devices are not allowed for importation into and marketing in the UAE.[64]

4.1.3 Qatar

A. Medical Devices Regulation

The Ministry of Public Health (MOPH) is responsible for regulation of the Healthcare Industry within Qatar. Medical Devices registration in Qatar is conducted through the Ministry of Economy and Commerce (MEC). The registration is followed by an application request to the Ministry of Municipal Affairs and Agriculture (MMAA) for an inspection of the premises, because business activities may not be undertaken in certain prohibited areas. A local agent is required and must be registered.

Since February 28, 2011, only medical Devices that have obtained a Qatar MEC marketing authorization may be sold unless they had already obtained authorization prior to that date. Moreover, after June 30, 2011, only Qatar MEC-authorized medical Devices are allowed to be used within Qatar, while Devices in use before that date may continued to be utilized. Only Medical Devices that are authorized by one of the founding members of the Global Harmonization Task Force (GHTF) can apply for a MEC marketing authorization.[68]

4.1.4 Oman

A. Medical Devices Regulation

Medical products must be registered with the MOH. Oman accepts all medical Devices classification systems. The registration procedure is conducted by submitting an application form (Annex X) and other relevant documentation through a local representative. According to Ministerial Decision No. 109/2008, a pre-qualification of companies and

factories of medical supplies is required to register medical Devices in Oman. The medical Devices market in Oman is organized in a form of tender system.

B. Required documentation

Regarding to Article (2) of Ministerial Decision No. 109/2008 for pre-qualification of companies and factories to participate in the Ministry's tenders, the following requirements should be fulfilled.[69,70,71]:

1. The company shall be either a manufacturer or assembler and licensed to manufacture medical devices in the country of origin (C.O.O);
2. The company shall follow the principles of GMP in the manufacturing of its products.
3. The company's products shall be in circulation in the C.O.O or marketed in one of the developed countries.
4. The company is subject to a periodical technical inspection by the concerned authorities in the C.O.O.
5. There shall not be a history of judicial verdict against the company in the C.O.O or in any other country with regard to crimes of fraudulence or forgery.
6. Payment of pre-qualification fees has to be proved.

Furthermore, according to Article (2) of Ministerial Decision No. 109/2008, the application for the pre-qualification of companies of medical devices shall be submitted by its agent or its representative to the concerned Directorate on the form prepared. All required documents should either be in English or Arabic language.

The following documents and certificates shall be attested by the concerned authorities in the C.O.O and the Embassy of the Sultanate of Oman:

1. LoA
2. Company registration certificate;
3. GMP Certificate, Good Quality Certificate such as: (ISO 9001-2000), (EN 46001), (ISO 13485) certificates.
4. A certificate for products made from plasma and blood derivatives. This certificate is required to ensure that these items are free of any component that causes any of the different types of hepatitis viruses, HI viruses and other infective viruses.
5. Supportive certificates, scientific researches and clinical studies for surgical implants manufactured by orthopedics and spine surgery devices companies,
6. A statement of the products, their trade and scientific names and catalog numbers,
7. A statement of the company capital, the date of its establishment, its type, number of the technical staff, their qualifications in addition to the details of activities of company,
8. A statement of the company branches and their activities,
9. The status of Devices distribution and
10. Samples of original packing with the product name, the name of the manufacturing company, its logo, batch number, and date of manufacture, expiry date, catalogue number, storage conditions and the product catalogue.

C. Pre-Owned Medical Devices

The import of used or refurbished medical equipment has no restrictions, but the MOH does not buy them. The Ministry of Health is the main buyer of medical equipment in Oman. As a matter of practice, the MOH does not purchase used or refurbished medical equipment. Normally, when the ministry decides to purchase equipment, it

contacts regular suppliers and requests the latest equipment; in some cases, such purchases are conducted through tenders. Generally, equipment is purchased along with a minimum five-year maintenance contract.[60]

4.1.5 Kuwait

A. Medical Devices Regulation

Kuwait is a member of AHWP. Medical Devices are registered as products ONLY within the Nonclassified Products Unit of the MOH Food & Drug Control Department. The registration procedure requires submitting an application form and other relevant document through a local representative.[72,73]

B. Required documentation

Documents and materials required for registration of non-classified products and Medical Devices as per ministerial decree 201/99 are[74]:

1. The application form,
2. Legalized by the Kuwait Embassy: the manufacturing license and the GMP certificate, the FSC from the C.O.O,
3. The status of registration of the product in the C.O.O.,
4. The letter of Authorization (LoA) be legalized by the Arab Chamber of Commerce and the Kuwait Embassy,
5. The list of countries where the product is registered with registration dates and numbers,
6. The Certificate of Analysis (CoA) of the finished product.
7. In addition, if the committee requests for more information of that particular product those requests have to be complied with.

Following technical documentations have to be included:

8. Information of the product on the outer and inner packs. Samples should be in English or Arabic language and satisfy the requirements of the Ministry of Commerce of the State of Kuwait. The information should include the name, composition, uses, batch number, manufacturing date, expiry date and the storage conditions as well as indication.
9. Safety and efficacy studies from approved international authorities (and/or clinical studies if applicable).

C. Pre-Owned Medical Devices

It is strictly forbidden to import pre-owned medical Devices into Kuwait. Kuwait's public health institutions do not buy used or refurbished medical Devices. All tenders call for new Devices and equipment. Used or refurbished equipment does not have a market in Kuwait.

4.1.6 Bahrain

A. Medical Devices Regulation

The Ministry of Health (MOH) is responsible for the oversight and regulation of the healthcare industry within Bahrain. Medical Devices regulation in Bahrain is directed by the Pharmaceutical Product Regulatory Office (PPRO) of the National Health Regulatory Authority (NHRA). Pharmaceutical products for which the principle intended action is pharmacological, metabolic or immunological are regulated as medicines or health products; whereas where the principle intended action is physical or mechanical then the product is regulated as a medical Device.[76,77]

All medical equipment should comply with one of the international standards such as the CE mark or USA FDA standards and be approved through the NHRA Medical Devices engineering department. Before a pharmaceutical product can be placed on the market in the Kingdom of Bahrain, an application must be made for a license to the

NHRA. Such applications should contain the data necessary to support the quality, safety and efficacy for the product. These data are reviewed by the NHRA and a conclusion is reached based upon the likely balance of the benefits versus risks associated with the product. This license must be granted prior to the product being placed on the market.

According to the Law no. (18) of 1997, pharmaceutical product Importation and distribution must be done through an authorized pharmacy only (local agent). The local agent must inform the NHRA of any agreements made with new pharmaceutical companies for review and approval before starting the licensing process.[78]

5. SUMMARY & CONCLUSION

5.1. Summary – Integration of Medical Devices regulation in MENA region

During the development and registration process, several parties need to interact with each other. Local authorized representatives or agents play a key role in medical Devices registration in all MENA countries. They are required as per the regulations and they help to overcome barriers for foreign companies, like language issues and the know-how of local requirements and processes as well. Often websites and local regulations are only available in local language (mostly Arabic) and local agents can benefit from participation in local regulatory or industry networks.

As the requirements for Medical Devices are not homogeneous throughout the MENA countries, different types of dossiers will have to be prepared. The technical documentation will cover the requirements of the majority of countries, however not internationally named as ‘design dossier’ or STED.

Beside the technical documentation, the main requirements are usually GMP or QM-System certificates, a FSC from the Country of Origin, a Letter of Authorization, EC certificates, and Declaration of Conformity, a Certificate of Analysis the finished product, a statement about the status of Devices distribution, a local application form and country specific declarations.

The FSC is a key document in the registration process of Medical Devices in most MENA countries, which must be legalized by the chamber of commerce and the embassy of the foreign importing country in C.O.O. (see Annexes II, III and IV)). Annex II-IV illustrate which countries need a FSC for submission and which countries do not required a FSC. The Devices needs to be classified very early in the development process in order to determine the path forward.

Medical Devices in general usually are divided into three groups as in the USA (class I, II and III) or four groups as in the EU (class I, IIa, IIb and III) or according to the GHTF guidelines (class A, B, C and D). The main MENA countries accept both EU and FDA definitions. In vitro diagnostic Devices are seen as a separate group and the classification of these products vary a lot.

Good manufacturing practice is required in all countries (Annex II-IV). An ISO 13485 certificate is in most countries the way to demonstrate compliance with the quality system requirements.

In some countries like Egypt, an ISO 13485 certificate - issued by EU notified bodies or USA/Australian bodies - might be enough to demonstrate compliance with the quality requirements but it must be approved by the local certification body.

The requirements for the risk management report for Medical Devices vary depending on the classification of the Devices e.g. Iran requires risk assessment for class C and D Medical Devices, while the UAE only asks the risk assessment for class III Medical Devices.

Clinical studies are required mostly for high risk Medical Devices. Most MENA countries require clinical evaluation and not clinical trials.

Labeling requirements are generally the same. The language shall be adjusted to the country where the product is sold. Instructions for use are not always necessary depending on the class of the Devices. Class I Devices and sometimes class II Devices (depending on the classification system) do not always require instructions for use if the Devices can be used safely without it.

In some countries of the MENA region such as UAE, Jordan and Kuwait the importation of pre - owned Medical Devices is strictly forbidden, while in other countries such as Yemen and Morocco there are no restrictions on the importation of used equipment.

The entry of pre-owned Devices in other countries such as KSA and Qatar is allowed, but the Ministry of Health and government hospitals keep away from purchasing such equipment. Main requirements for registration are a local representative, a Certificate of Free Sale from the C.O.O, an import license from the competent authority in the importing country and the registration of the company and the product in the importing country.

The use of quality management systems and risk management systems within development, manufacturing, quality control and post market surveillance of the Medical Devices in question are required in most countries, except for medical Devices class I. Certificates of ISO 13485 and ISO 9001 are required or recommended.

5.2. CONCLUSION

Some countries have similar requirements for registration of medical Devices and are striving to harmonize with the IMDRF guidelines, in others the MD regulation is still in its infancy.

Although the US are 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.

In the authors opinion the fundamental demand to be solve in the future is the approximation of the existing individual regulations in these countries to promote a uniform commercial basis, because the relatively small amount of population in each country bears not relationship to the costs generated by such individual requirements (different in almost each country).

At least documents to be prepared for EU or USA, such as technical documentation with risk analysis, clinical evaluation, etc., can also be used for a registration of products in MENA countries, however only in English language.

6.0. REFERENCES

1. Achieving business excellence and competitiveness in the MENA region, Business Excellence and Competitiveness in MENA, 2008 (18.06.2014)
2. Regulatory Collaboration Principles In GCC States (GCC-DR), ICDRA 2010 Singapore, 27 Nov – 4 Dec 2010 (18.06.2014)
3. http://www.who.int/medicines/areas/quality_safety/regulation_legislation/PL2_2.pdf
4. Challenges and Opportunities—The Population of the Middle East and North Africa, Population BULLETIN, 2007; 62(2): (10.06.2014).
5. The Healthcare Industry in the MENA Region and Its Policy Implications for Korea-MENA Healthcare Cooperation, World economy, April 30, 2014; 4(18): (08.06.2014).
6. Medical Devices Market GCC. March 2010 osec.ch (25.05.2014).
7. MENA Healthcare Sector Report - Al Masah Capital (16.06.2014) http://almasahcapital.com/uploads/report/pdf/report_22.pdf
8. 2014 global health care outlook, Shared challenges, shared opportunities (18.05.2014) https://www2.deloitte.com/content/dam/Deloitte/global/Documents/Life-Sciences-HealthCare/dttl-lshc-2014-global-health-care-sector-report.pdf
9. World Healthcare Outlook, Economist Intelligence Unit, August 14, 2013 (08.06.2014)
10. Global Medical Devices market outperforms drug market growth. Madison, WTN News, Rosen M (2008). (http://wistechnology.com/articles/4790/, accessed 10 July 2012). (08.06.2014)
11. Medical Devices Industry. Villeurbanne, Report Linker, 2012 (28.06.2014) http://www.reportlinker.com/ci02249/Medical-Devices.html, accessed 10 July 2012).
12. Middle East and North Africa markets hold huge potential for medical technology industry http://medtechviews.eu/article/middle-east-and-north-africa-markets-hold-huge-potentialmedical-technology-industry (18.06.2014)
13. The world medical markets fact book 2011. Chichester, Espicom Business Intelligence, 2011. (01.12.2014)
14. Local Production and Technology Transfer to Increase Access to Medical Devices, World Health Organization,(18.06.2014)http://www.who.int/medical_Devices/1240EHT_final.pdf (18.06.2014)
15. The European Medical Technology Industry in Figures, (01.12.2014) http://www.eucomed.org/uploads/Modules/Publications/the_emti_in_fig_broch_12_pages_ v09_pbp.pdf
16. Espicom, Eucomed calculations. Average growth rate over 2008-2013 years. Manufacturer prices. Medical Devices and Imaging excluding in vitro diagnostics. Europe refers to EU (excluding Cyprus, Luxembourg, Malta) + Norway, Switzerland. (01.12.2014)
17. Medical Devices Middle East Market Analysis Reports, 2014 (01. 09.2014) http://www.espicom.com/middleeast/mdma/
18. Espicom, Eucomed calculations. Manufacturer prices. Medical Devices and Imaging excluding in vitro diagnostics. Europe refers to EU (excluding Cyprus, Luxembourg and Malta) + Norway, Switzerland. (01.12.2014)
19. Regulatory strategy for an efficient launch of medical Devices – a distinct focus on BRICS and MIST countries, Master of Drug Regulatory Affairs, Melanie Rosslan, 2014 PMRA, PIPER Page 63.

20. How to place human medical Devices on the market? An overview and critical examination of the regulatory requirements in Germany versus those in the United States, , Master of Drug Regulatory Affairs, Marlene Schulzensohn, 2013.
21. A model regulatory program for Medical Devices: An international guide. Washington, DC: PAHO, 2001. (18.05.2014).
22. Regulation of medical Devices outside the European Union, Version of Record - Apr 1, 2012 (24.05.2014) http://jrs.sagepub.com/content/105/suppl_1/S12.full.pdf+html
23. Medical Devices regulations global overview and guiding principles (24.05.2014) http://www.who.int/topics/medical_Devices/en/ (last accessed March 9, 2012)