

IMPACT OF COVID-19 ON THE MEDICAL DEVICE INDUSTRY

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Abstract: The main aim of this study is to review the effect caused by Covid 19 on the medical device industry and to study the challenges faced by the medical device industry in different countries such as India, the USA, European countries. In earlier May 2020, over 4.7 million people have been confirmed to be infected with the SARS-CoV-2 coronavirus, and governments are worried to get contain its spread. The high RO value (a measure of contagiousness-estimated to be between 2.0 and 3.02) of SARS-CoV-2 means that those infected copiously spread the virus and develop complications suddenly. As a result, health care systems are widespread, and the effective delivery of medical care to all patients has become challenging to the whole world. Improper seeking to early warning signals, less amount of stockpiling, lack of ease to testing kits and personal protective equipment (PPE), and country-wise variability in the approaches to testing kits, distribution of PPE, and timing and degree of social distancing measures are likely to get affect the spread of disease. As the COVID-19 pandemic continues to get imbalanced, medical device companies are finding it difficult to make précised decisions about their products, supply chains, and regulatory obligations in the advent of uncertainty. With a technique that leverages exemptions, production procedures that innovate to fill needs, and a communication plan that works across public and personal entities, which may navigate the chaos and support public health. Obligations from governing bodies and conversations with key decision-makers and regulatory authorities hold the key to the success of the medical device industry. At last, the implementation of several new regulations may be postponing as making many companies and regulatory agencies time to react to the crisis. However, there is no evidence to make this scenario be the deadline for suggestions.

Keywords: Medical device, Regulatory bodies, Surgical handling instruments.

I. Introduction:

A medical device is any device intended to be used for medical purposes. Medical devices benefit patients by helping health care providers diagnose and treat patients and helping patients overcome sickness or disease, improving their quality of life. Significant potential for hazards is inherent when employing a device for medical purposes and thus medical devices must be proved safe and effective with reasonable assurance before regulating governments allow marketing of the device in their country.

As a general rule, as the associated risk of the device increases the amount of testing required to establish safety and efficacy also increases. Further, as associated risk increases the potential benefit to the patient must also increase. Medical devices vary in both their intended use and indications to be used. Examples range from simple, low-risk devices such as tongue depressors, medical thermometers, disposable gloves, and bedpans to complex, high-risk devices that are implanted and sustain life.

One example of high-risk devices is those with embedded software like pacemakers, and which assist in the conduct of medical testing, implants, and prostheses. The design of medical devices constitutes a serious segment of the sector of biomedical engineering.

II. Medical devices according to WHO

Medical Device – Full Definition

'Medical device' means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material, or another similar or related article, intended by the manufacturer to be used, alone or together, for the citizenry, for one or more of the precise medical purposes(s) of:

1. Diagnosis, prevention, monitoring, treatment, or alleviation of disease.
2. Diagnosis, monitoring, treatment, alleviation of, or compensation for an injury.
3. Investigation, replacement, modification, or support of the anatomy or a physiological process,
4. Supporting or sustaining life,
5. Control of conception,
6. Disinfection of medical devices
7. Providing information utilizing in vitro examination of specimens derived from the human body; and does not achieve its primary intended action by pharmacological, immunological, or metabolic means, in or on the physical body, but which can be assisted in its intended function by such means.

Note: Products that can be considered to be medical devices in some jurisdictions but not in others include:

1. Disinfection substances,
2. Aids for persons with disabilities,
3. Devices incorporating animal and/or human tissues,
4. Devices for in-vitro fertilization or assisted reproduction technologies.

Medical device safety:

The optimum assurance of medical device safety has several essential elements:

- Absolute safety cannot be guaranteed
- It is a risk management issue
- It is closely aligned with device effectiveness/performance
- It must be considered throughout the lifetime of the device
- It requires shared responsibility among the stakeholders.

Risk assessment:

- The current approach to device safety is to estimate the potential of a device becoming a hazard that could result in safety problems and harm. This estimate is often referred to as the risk assessment.
- Hazard is a potential for an adverse event, a source of danger. The Risk may be a measure of the mixture of (1) the hazard; (2) the likelihood of occurrence of the adverse event; (3) the severity or overall impact.
- Risk assessment begins with risk analysis to identify all possible hazards, followed by risk evaluation to estimate the risk of each hazard.
- In general, risk assessment is based on experience, evidence, computation, or even guesswork. Risk assessment is complex because it is often influenced by personal perception and other factors like cultural background, economic conditions, and political climates.

Effectiveness/performance of medical devices:

Every device has a designed purpose. A device is clinically effective when it produces the effect intended by the manufacturer relative to the medical condition. For example, if a tool is meant for pain relief, one expects the device to truly relieve pain and would also expect the manufacturer to possess objective, scientific evidence, such as clinical trial results, that the device does relieve pain.

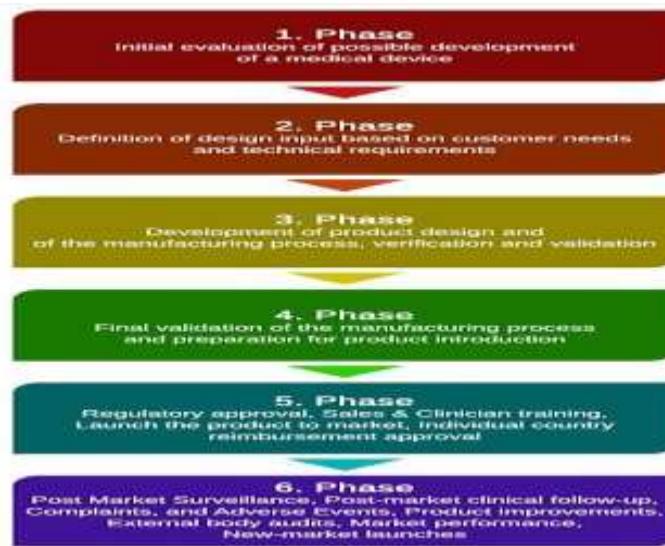
Clinical effectiveness may be a good indicator of device performance. Performance, however, may include technical functions additionally to clinical effectiveness. For example, an alarm feature might not directly contribute to clinical effectiveness but would serve other useful purposes. Furthermore, it's easier to live objectively and quantify performance than clinical effectiveness.

Performance is closely linked to safety. For example, a blood collection syringe with a blunt needle would perform badly for collecting blood and will inflict injury. A patient monitor that does not perform well could pose serious clinical safety problems to the patient. Thus, the safety and performance of medical devices are normally considered together.

The above discussion highlights the inherent risk of a medical device. It is incumbent on the medical device manufacturer to demonstrate that all possible risks associated with the device are identified and adequately addressed. The role of the regulatory agency is to make sure that the manufacturer has effectively implemented the danger management process.

Phases in the life span of a medical device:

The diagram below illustrates the major phases in the life span of a medical device from conception and development to disposal. The activity phases are simplified to form it easier to know the regulatory system. For example, the event phase includes development planning, design verification/validation, prototype testing, and clinical trials. In practice, the phases outlined below may overlap and interact.



Major phases in the life span of a medical device

It is important to acknowledge that any of those phases can affect the security and performance of a medical device. Examples of how each phase can create health hazards are described below:

1. Conception and development:

The scientific principles upon which a tool is predicted are fundamental to its safety and performance. For example, a pacemaker should deliver a small electrical impulse of a particular size and shape that simulates the natural functioning of the guts. Significant deviation from this might compromise safety and performance. The more complex the device, the higher the risk of user error. The Soundness of concept and adequacy of design, construction, and testing (including verification, validation, and clinical trials) require the scrutiny of scientific experts to make sure that style parameters and performance characteristics do not impose unwarranted risks.

2. Manufacture:

Good, functional medical devices are produced when the manufacturing process is satisfactorily managed. However, poor manufacturing management can produce inconsistency within the quality of products, such non-conforming devices can filter through the assembly line to the market, even when the prototype has been well-designed. This consideration has led to the event of excellent manufacturing practice (GMP) for drugs, biological products, and medical devices. Now, GMP is more commonly mentioned as “quality systems in manufacturing”, and these are addressed later during this guide.

3. Packaging and labeling:

Properly packaged medical devices pose little risk to individuals handling them, albeit if the medical device is biohazardous. This highlights the importance of well-designed packaging systems in delivering clean, sterile, and guarded medical devices to the purpose of use. Shipping is one of the hazards a medical device and its packaging must survive. Subtle damage can result during transportation and handling unless the entire packaging system is meant robustly and may withstand various stresses. Well-sealed packaging is important for those medical devices that have got to be maintained sterile.

Labeling is crucial in identifying the medical device and specifying instructions for its proper use. As for drugs, mislabeling medical devices can result in serious consequences for the user. Hazard warnings or cautions and clear instructions to be used are vital.

4. Advertising:

Advertisement has the potential to make expectations and powerfully influence the assumption in a medical device’s capabilities. It is important, therefore, that medical device marketing and advertising are regulated to stop the misrepresentation of a medical device and its performance. Misleading or fraudulent advertising of medical devices may increase sales. However, from the buyer’s perspective, the acquisition of an inappropriate medical device could also be a waste of money which can deprive the tolerant of more appropriate treatment and can lead to patient or user injury.

5. Sale:

The sale of medical devices by the vendor is a critical stage that leads to the device being put into actual use. If the vendor is not subject to regulation, then there is a higher risk of exposing the public to low-quality or ineffective devices.

6. Use:

Users of medical devices can have a profound effect on their safety and effective performance. Unfamiliarity with a particular technology or procedure, and therefore the use of products for clinical indications outside the scope of these laid out in the labeling,

can cause device failure even within the absence of any inherent design or manufacturing defects. Within the clinical engineering community, it is widely believed that user error underlies at least half of all medical device-related injuries and deaths. The re-use of disposable devices contrary to the manufacturer's instructions, and without proper control or precautions for minimizing associated risks, can be dangerous. The lack of or inappropriate, calibration and maintenance of medical devices can seriously jeopardize their safety and performance. These issues are often overlooked or underestimated.

7. Disposal:

Disposal of certain sorts of devices should follow specific and stringent safety rules. For example, devices that are contaminated after use (e.g. syringes) or devices that contain toxic chemicals, can present hazards to people or the environment and must be disposed of properly. It is people that manage each introduce the lifetime of a medical device, and these people should be identified and called on to participate in ensuring medical device safety.

The role of each participant/stakeholder:

The manufacturer, because the creator of the device, must make sure that it's manufactured to satisfy or exceed the specified standards of safety and performance. This includes the three phases (design/development/testing, manufacturing, packaging, and labeling) that cause a product to be ready for the market. The term "user error" is defined as an act that features a different result than that intended by the manufacturer or expected by the operator. User error may result from a mismatch between variables, for instance, the operator, device, task, or environment. By incorporating human factor engineering principles in design, and appropriate training for users, the danger of user errors is often minimized.

The vendor provides the interface between the product and the user. He/she should ensure that the products sold comply with regulatory requirements. With increasing public interest in health and a competitive marketplace, vendors should be taken care of to avoid making misleading or fraudulent claims about their products or issuing false compliance certificates. In addition, used or refurbished devices should be clearly labeled intrinsically.

Vendors should provide after-sale service. Medical devices often require specialized training from the manufacturer for proper use and service; therefore, the vendor should make training a condition to the manufacturer or importer in accepting to sell the device. In turn, vendors should take responsibility for supporting or training their customers. Participating in post-market surveillance (receiving and reporting customer complaints/ incidents) is critical for ensuring medical device safety and performance. The vendor must fulfill these obligations specified by the regulatory agency.

For example, the seller must make arrangements for processing complaint/incident reports concerning medical device safety and performance. In the case of home-use medical devices, the seller should recognize that the device being sold might find yourself within the hands of a layperson who may have special instructions for the proper use and maintenance of the device. In this situation, efforts must be made to provide non-technical instructions and to educate and help the customer.

The user should confirm that he/she has qualifications and training within the proper use of the device, and is conversant in the indications, contra-indications, and operating procedures recommended by the manufacturer. It is crucial that have gained with medical devices be shared with other users, the seller, and manufacturer to stop future problems. This is often done by reporting any incidents to a coordinating center from which warnings can be issued.

When using medical devices, users should bear in mind that the security and health of the patients are in their hands. The user has the responsibility to use the medical device just for the intended indications (or to assure that any non-indicated use of the medical device doesn't compromise the safety of the patient and other users). The user also has the responsibility to make sure proper maintenance of medical devices during active use and safe disposal of obsolete medical devices.

The public is the last word beneficiary of medical devices. They should be fully aware that each one device carries a particular risk which will help to market safety and performance through self-education and by putting "customer pressure" on manufacturers to comply with standards. Medical devices are increasingly available for home use, making the general Public the direct user. Purchasers of home-use medical devices should remember of associated risks and take the responsibility to become educated within the functions and proper operating procedures for those devices.

The government has the responsibility to oversee the efforts of manufacturers and vendors and make sure that medical devices sold or made available within the country are safe and effective. It should provide leadership in creating healthy cooperation among stakeholders in establishing policies and regulations that are fair and clear to all or any. Policies and regulations should be reviewed periodically to reply to changes in technologies by incorporating appropriate amendments.

III. Medical devices – INDIA

Definition of medical devices

By the notification of February 11, 2020, by the Ministry of Health and Family Welfare (MOH&FW), the definition of medical devices has been amended to mean – any instrument, apparatus, appliance, implant, material, or another article, whether used alone or all together, including software or an adjunct, intended by its manufacturer to be used especially for citizenry or animals by any

pharmacological or immunological or metabolic means, but which may assist in its intended function by such means for one or more of the specific purpose of:

- ❖ Diagnosis, prevention, monitoring, treatment, or alleviation of any disease or disorder;
- ❖ Diagnosis, monitoring, treatment, alleviation, or assistance for, any injury or disability;
- ❖ The Investigation, replacement or modification, or support of the anatomy or a physiological process;
- ❖ Supporting or sustaining life;
- ❖ Disinfection of medical devices; and
- ❖ Control of conception

CDSCO Classification for medical devices

The CDSCO classifications of medical devices govern alongside the regulatory approval and registration by the CDSCO is under the DCGI. Every single medical device in India pursues a regulatory framework that depends on the drug guidelines under the Drug and Cosmetics Act (1940) and medicines and Cosmetics runs under 1945.

CDSCO classification for medical devices has a set of risk classifications for numerous products planned for notification and guidelines as medical devices. The Health Ministry of India has distributed new medical devices and IVD guidelines to improve the nation's Drugs and Cosmetics Act for making viable regulations. Further CDSCO alongside state controllers is together answerable for allowing licenses of certain specific classes of basic medications, for example, blood and blood items I.V. Liquids, Vaccine, and sera.

Classification:

Medical Devices are generally supported risks; the particular risk-based classification of the medical device depends upon its intended use and purpose. CDSCO classification of medical devices features a larger group of devices, like cannulas and stents in additional specific subgroups.

- (a) **Low Risk/Class A:** Absorbent cotton wools, surgical dressing, alcohol swabs, etc.
- (b) **Low Moderate Risk/Class B:** Thermometer, BP monitoring device, disinfectants, etc.
- (c) **Moderate-High Risk/Class C:** Implants, hemodialysis catheter, etc.
- (d) **High Risk/Class D:** Angiographic guide wire, heart valve, etc.

The classification for the medical devices in these categories is based upon Part I of the First Schedule of the Rules. All notifications regarding these are often accessed through the CDSCO website apart from the none, the classification possesses to assessed by the applicant from Part I of First Schedule of the Rules.

The regulation concerning the manufacture of Class A & B devices is done through the State Licensing Authority, which is the State Drugs Controller, and for Class C & D is done through the Central Licensing Authority, which is the DCGI.

IV. INDIA'S MEDICAL DEVICE APPROVAL PROCESS

Step 1

Medical devices and IVDs are regulated by the Drug Controller General of India (DCGI) within the Central Drugs Standard Control Organization (CDSCO), apart of the Ministry of Health and Family Welfare. The regulatory framework for medical devices is predicted on the Medical Device Rules, 2017. Only a limited number of medical devices and IVDs require registration in India. A full list is often found within the CDSCO's Notice on the classification of medical devices and IVDs. This is not an exhaustive list. CDSCO doesn't maintain a top list of regulated devices, but rather subjects devices to regulation through the Drugs and Cosmetics Rules, the Medical Device Rules 2017, and subsequent Gazette Notifications, which should be reviewed before making a final determination of a device's regulatory status.

Step 2

Appoint an India Authorized Agent to interact with the CDSCO on your behalf. Your Agent must have a legitimate wholesale license (Forms 20B and 21B/21C), and be granted Power of Attorney to manage your registration and device importation in India.

Step 3

Class B, C, and D IVDs require in-country performance testing through the National Institute of Biologicals (NIB) or an accredited lab. Class D IVDs require performance testing through the National Institute of Biologicals (NIB). Class B and C IVDs require performance testing through an accredited Indian lab, though CDSCO may instead accept existing reports for such products with approvingly during a major regulatory market.

Step 4

Compile device application (Form MD-14), including manufacturing facility information, device technical information, ISO 13485 certificate, IFU, testing results (if applicable), clinical data (if applicable), proof of approval in the US, EU, Australia, Canada, or Japan, plus proof of approval in your home country (satisfied by CFS/CFG).

Step 5

File application for registration/Import License with the CDSCO and pay fees. All documents must be in English.

Step 6

The CDSCO reviews applications and should require a Technical Presentation. Approximately 25% of applications require a formal Technical Presentation. The Technical Presentation is an in-person meeting with the CDSCO to debate the merchandise in additional detail. A representative from the manufacturer (such as an engineer) is predicted to attend this meeting alongside the India Authorized Agent.

Novel devices also will undergo a Subject Expert Committee (SEC) review. Devices novel to the Indian market (new technology, material, intended use) may face additional regulatory hurdles. CDSCO may require clinical studies conducted in India before regulatory approval, or the agency may issue a restricted approval. A restricted approval could include a requirement to actively collect and submit post-market data. The SEC meeting will include local clinicians and other experts who will weigh in on the acceptability of the prevailing clinical data.

Step 7

The CDSCO issues an Import License in Form MD-15. Following the implementation of the Medical Device Rules, 2017, the processes for obtaining device registration and import licensing were combined in India. Accordingly, the CDSCO doesn't issue Registration Certificates under the Medical Device Rules, instead of issuing market authorization for foreign devices through the Import License (Form MD-15).

The License doesn't expire; however, license retention fees are due every five years.

Step 8

Once approved, only your India Authorized Agent may import products. However, you'll obtain multiple registrations for an equivalent device through different Authorized Agents.

National accreditation body

National Accreditation Board for Certification Bodies (NABCB) under the standard Council of India found out by the Ministry of Commerce and Industry, Government of India act because the national accreditation body for the needs of accrediting Notified Bodies.

NAB lays down the conformity assessment activities for accreditation of Notified Bodies and standards for such accreditation; prepares norms and procedures for accreditation of Notified Body, and audits a Notified Body periodically for assessing conformance with the Medical Devices Rules.

Notified body

For a fee, the Notified Body accredited by the NAB audit the manufacturing sites to verify conformance with the Standard Management System and other applicable standards as laid out in the principles. For now, Intertek India, TUV Rhineland (Delhi), and TUV Sud South Asia (Mumbai) are the Notified Bodies registered for the purpose.

Test license to manufacture for the aim of clinical investigation/ performance evaluation, examination, demonstration, or training

The application shall be made in Form MD-12 for the manufacture in small quantities for the aim of clinical investigation/ performance evaluation, examination, demonstration, or training. The fee for Test License is INR 500.

Clinical investigation of medical devices

In the past, investigations were necessary if the investigational medical device fell under the notified 14 categories. This has changed under the MDR and a replacement list of notified medical devices was released on All Saint's Day, 2017. The list contains 351 medical devices under 29 categories (table 1) and 247 IVDs under 21 categories (Table 2).

No sponsor is allowed to conduct any clinical investigation without approval from CDSCO and the institutional ethics committee. An application to conduct a pilot or pivotal clinical investigation is made in Form MD-22 or MD-24 for IVD by the Sponsor/ CRO alongside information laid out in the Seventh Schedule of MDR and submitted also. For the pivotal study, data emerging from the pilot clinical investigation is required to be submitted as well. The clinical investigation should be initiated by enrolling the first participant within a period of a year from the date of grant of permission, failing which prior permission from CDSCO shall be required to initiate a clinical investigation.

Medical devices requiring clinical investigation but claiming substantial equivalence to a predicate device also require CDSCO approval. Clinical investigation/ performance shall be conducted by the approved clinical investigation/ performance plan (study protocol) and CDSCO-Good Clinical Practices guidelines. All study-related document templates are listed in table 4 for investigator brochure, table 5 for clinical investigation plan, table 6 for case report form, table 7 for reporting a serious adverse event, table 8 for consent document, table 9 for investigator undertaking, and table 10 for the clinical investigation report.

The sponsor as specified under rule 122DAB of the Drugs and Cosmetics Rules, 1945 should provide medical management or compensation within the event of death causally associated with the investigational medical device, as in pharmaceutical research (Schedule Y).

The site and sponsor shall maintain all data, records, registers, and other documents for a period of seven years after completion of the clinical investigation.

In addition, the sponsor is predicted to offer source and quantity of samples which shall be used during evaluation, an outline of the device including specification of raw material and finished product, data allowing identification of the device in question, proposed instruction to be used, labels and regulatory status in other countries, in-house performance evaluation data enhance to establish stability, specificity, sensitivity, repeatability, and reproducibility. The medical device should be tested and evaluated by a Government testing laboratory that's accredited by National Accreditation Body for Testing and Calibration Laboratories (NABL).

The study should be registered with the Clinical Testing Registry of India before enrolling the primary participant. Annual status report of each clinical investigation/ performance on whether it's ongoing, completed, or terminated, shall be submitted to CDSCO by the sponsor.

The results of clinical investigation/ performance might not be required to be submitted where the investigational medical device/ IVD is approved by the regulatory authorities of either the United Kingdom, United States of America, Australia, Canada, or Japan and therefore the said device has been marketed for a minimum of two years within the above-mentioned country and CLA is satisfied with the info of safety, performance, and pharmacovigilance of the device, and there's no evidence or theoretical possibility, on the idea of existing knowledge, of any difference within the behavior and performance in Indian population, the applicant has given an undertaking in writing to conduct post-marketing clinical investigation/ performance with the target of safety and performance of such investigational medical device as per protocol approved by CLA.

The fee for application to conduct a pilot or pivotal clinical investigation is INR 100,000 and to conduct clinical performance evaluation is INR 25,000. Per rule 51(2), no fee shall be payable by any institute, organization, hospital-run, or funded by Central Government for the conduct of a clinical investigation.

Import of medical devices

An authorized agent in India having a license to manufacture or wholesale license for purchasable or distribution purchasable or distribution shall make an application for grant of import license to CDSCO through the online portal in Form MD-14.

For import or manufacture of a medical device that doesn't have predicate medical device, an application for grant of permission for such medical device after completion of its clinical investigation under Chapter VII shall be made to the CLA in Form MD-26 either by a licensed agent just in case of important or the manufacturer.

The fee for import of grade A medical device per site is USD 1000 and USD 50 per product; for class B per site is USD 2000 and USD 1000 per product, and for grade C or D per site is USD 3000 and USD 1500 per product.

The fee for import of class A or B IVD per site is USD 1000 and USD 10 per distinct product, and for grade c or D per site is USD 3000 and USD 500 per distinct product.

Fee for import license for test, evaluation, demonstration, or training for every distinct medical device is USD 100

Manufacturing

The application shall be made through the online portal of the Ministry of Health and Family Welfare in Form MD-3 for the manufacture of grade A and B (obtain marketing authorization in MD-5 for class A and MD-6 for class B); class C in MD-7 and grade D in MD-8 (obtain marketing authorization in MD-9 and MD-10) respectively.

For class A medical devices, the State Licensing Authority shall, after scrutiny of documents, grant a license to manufacture within 45 from the date of application. No audit of the manufacturing site is necessary before grant of manufacturing license. However, an audit of such manufacturing site by the registered Notified Body is administered out within 120 days from the date on which the license was granted by the State Licensing Authority.

Audit of the manufacturing site of grade B shall be carried out within 90 days from the date of application by the registered Notified Body before grant of marketing authorization.

A manufacturing license or loan license is valid in perpetuity, subject to payment of license retention fee before completion of the period of five years from the date of its issue, unless, it is suspended or canceled by State/ Central Licensing Authority.

The fee (and renewal) for manufacturing grade A or B medical device per site is INR 5000 and INR 500 per product, and for class C or D per site is INR 50,000 and INR 1000 per product.

Post-marketing

The permission holder of Form MD-27 shall inform the date of launch of the medical device within the market to the CLA and shall submit Periodic Safety Update Report from the date of launch within the market and such report shall be submitted every six months for the first two years followed by submission of the said report annually for the twice more successive years.

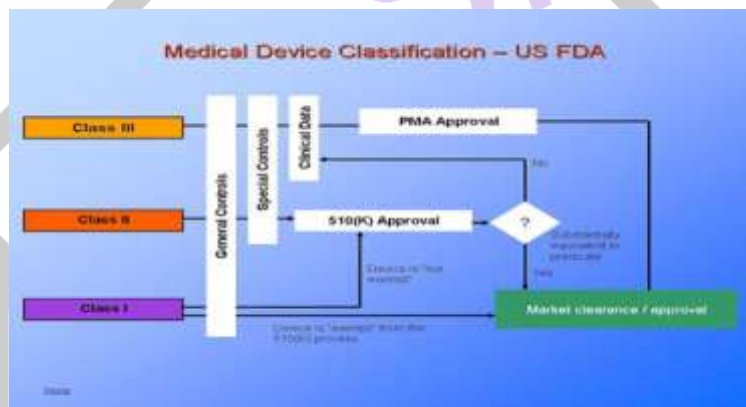
Export of medical devices

Where a manufacturer intends to export any medical device, manufactured in India, and for that purpose, requests a certificate within the nature of free sale certificate or a certificate about quality, safety, and performance concerning that medical device as required by the authority concerned of the importing country, such person, may apply to CLA for the purpose along with a fee as specified.

V. Medical devices – USA

Introduction

In the United States, medical devices are regulated by the Food & Drug Administration or FDA. The specific branch within the FDA is the Center for Devices & Radiological Health (CDRH). The mission of CDRH is to protect and promote public health. In other words, ensure medical devices are safe.



Classification:

In the U.S., medical devices are either Class I, Class II, or Class III. The FDA CDRH classification is predicated totally on the risk the medical device poses.

(a) Class I medical devices are generally deemed low risk

(b) Class II are of moderate risk

Class III medical devices are seen because of the highest risk.

The types of controls required to depend on your product's classification. Classification is directly associated with the intended use and indications to be used. The distinction between these terms may be a bit confusing.

- **Intended Use** is the general purpose of the medical device or its function (what you "claim" the medical device does).

- **Indications to be used** describe the disease or condition the medical device will diagnose, treat, prevent, cure, or mitigate, including an outline of the target patient population.

1. The United States "Export Certificate" Section 801I(2) grants permission for the export of unapproved medical devices which are not equivalent to devices cleared for marketing in the USA after the firm has submitted to the FDA proof of the safety of the device and obtained a letter from the foreign government granting permission to import the device.

2. The US "Certificate of Exportability" Section 801I(1) certifies the export of devices that are not approved for use within the USA, distribution of which would be considered adulterated or misbranded under U.S. law because they lack marketing permission, U.S. labeling, and/or aren't being manufactured under QS Regulation. These devices must be equivalent in design and intended use

to class I and II medical devices already granted marketing permission by FDA labeled for export and must be in compliance with the wants of the purchaser and the laws of the foreign country.

3. The United States “Certificate of Exportability” Section 802 certifies the export of unapproved devices which are manufactured in compliance with the wants of the QS Regulation or equivalent FDA recognized international standard and which are authorized for marketing during a “tier one” country. Tier one countries included those within the European Union, the European Economic Area, Australia, Canada, Israel, Japan, New Zealand, and South Africa.

4. The US “Certificate to Foreign Government” is issued for devices that are legally marketed in the U.S. and in compliance with the Food, Drug & Cosmetic Act. FDA – medical devices approval pathway.

FDA medical device approval process step-by-step guide

Process 1

Decide the classification of your device by examining the FDA classification database using relevant search terms, or by distinguishing another device with the equivalent planned use and innovation. Grant special attention to the three-letter Product Code and seven-digit Regulation Number associated with the predicate devices you the order can't be resolved, use 513(g) to appeal classification from the FDA

Process 2

Most Class I devices need to consent to the QSR (GMPs), apart from Part 820. For Class II and III devices, execute the Quality Management System (QMS) which meets the FDA Quality System Regulation (QSR) found in 21 CFR Part 820. Innovative Class II, and everyone Class III, devices will probably require clinical investigations. Get “Pre-Submission (Pre-Sub)” input from the FDA.

Process 3

If the clinical examination is going to be required, they ought to apply for an Investigational Device Exemption (IDE). Develop clinical trial agreements and conduct studies. Non-significant risk studies could be performed with IRB approval.

Process 4

For Class II devices, plan and submit 510(k) Premarket Notification application and pay the related charge. For Class III devices, prepare and submit the Premarket Approval (PMA) application. Pay PMA submission expense.

Process 5

For Class III devices, FDA conducts facility investigations of each major supplier related to the planning and production of your device. All parties must be according to FDA QSR.

Process 6

For the Class II devices, the FDA issues a 510(k)-clearance letter and posts it online. And for Class III devices, the FDA issues a PMA approval letter and posts it online.

Process 7

As of now, you ought to be fully consistent with QSRs. The FDA will not examine Class I or II device manufacturers for compliance before device registration but does conduct unplanned inspections and can issue a Form 483 for non-compliance.

Process 8

If you have no local presence in the US, name an FDA US Agent representative as a local point of contact with the FDA.

Process 9

List your device and register your company utilizing FURLS framework on the FDA website as per 21 CFR Part 807. Pay charges for Establishment Registration and Listing which must be renewed per annum.

Process 10

You are currently able to move your gadget to the US. Your organization and device registration status are going to be recorded on the FDA website. Your approval doesn't lapse as long as no changes are made to the device design, intended use, and so on.

VI. Medical devices - EUROPE

Introduction

Medical devices can't be placed on the European market without conforming to the strict safety requirements of the European Union; one among these requirements is that the affixation of the CE conformity mark.

Legislation

Collectively referred to as the Medical Device Directive (MDD), this core legal framework consists of three directives that regulate the security and marketing of medical devices in Europe and came into effect in the 1990s. The three directives are the:

- (a) Active Implantable Medical Device Directive (AIMDD 90/385/EE)
- (b) Medical Device Directive (MDD 93/42/EEC)
- (c) In Vitro Diagnostic Medical Device Directive (IVDMDD 98/79/EC)

Classification:

All medical devices are placed into one of four graduated categories, using the classification rules listed in Directive 93/42/EEC Annexure IX. It is considered more feasible, economically and justifiably, to categorize medical devices instead of all of them being subject to rigorous conformity assessment procedures.

The categories are -

- (a) Class I (including Is & I'm)
- (b) Class IIa and IIb and
- (c) Class III ranked as the highest.

The higher the classification the greater the extent of assessment required by NBs.

Legislation

The European regulatory framework ensures the security and efficacy of medical devices and facilitates patients’ access to devices within the European market. To keep up with advances in science and technology, 2 new Regulations are replacing the three existing Directives within the coming years (until 2022).

Medical devices within the EU are currently regulated by 3 Directives:

- Council Directive 90/385/EEC on Active Implantable Medical Devices (AIMDD) (1990)
- Council Directive 93/42/EEC on Medical Devices (MDD) (1993)
- Directive 98/79/EC of the European Parliament and of the Council on in vitro Diagnostic Medical Devices (IVDMD)
- On 5 April 2017, 2 new Regulations on medical devices and in vitro diagnostic medical devices establishing a modernized and more robust EU legislative framework to ensure better protection of public health and patient safety were adopted.
- ✓ They entered into force on 25 May 2017 and will progressively replace the existing directives after a transition period.
- ❖ Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC
- ❖ Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU
- ❖ With patient health and safety as a guiding principle, the Council and the Parliament adopted on 23 April 2020 Regulation 2020/561 amending Regulation (EU) 2017/745 on medical devices regarding application dates of certain of its provisions. This Regulation postpones the date of application for many Medical Devices Regulation provisions by one year – until 26 May 2021. This postponement takes the pressure off national authorities, notified bodies, manufacturers, and other actors so they can focus fully on urgent priorities related to the coronavirus crisis.
- ❖ The IVDR Regulation (EU) 2017/746) corresponding date of application remains the same.

Sectorial challenges:

As a sector experiencing continuous and rapid development, ensuring a sustainable set of regulations that guarantees safety but also innovation may pose certain challenges at national, European, and international levels.

- Public health systems

EU public health systems got to adapt to face new and emerging needs, which needs the event of a shared understanding of healthcare goals to beat inequalities and look after an aging society

- ★ Access to healthcare

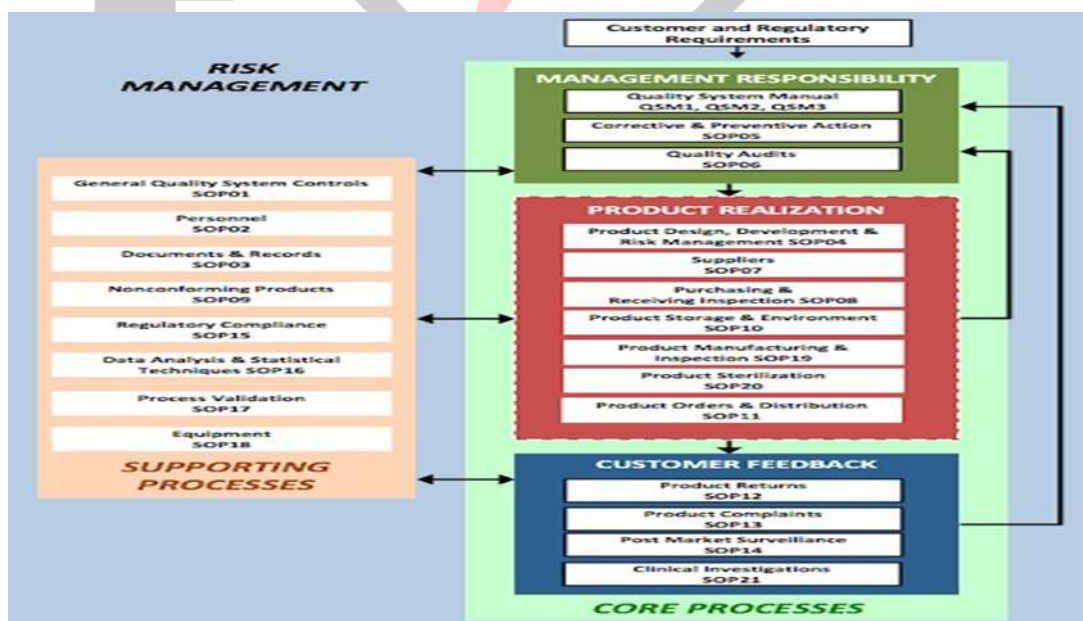
As the access to healthcare are often costly, both to the patient and to the national health systems, the EU must make sure that patients recover access to medical devices at affordable prices

- ★ Sustaining innovation

to foster innovation, it is necessary to adapt research and development to emerging scientific and technological progress and to move towards a circular and green economy, whilst maintaining competitiveness.

What is the European Commission doing?

Enhancing competitiveness while ensuring the security and performance of medical devices may be a key objective of the European Commission. To achieve this, the Commission regularly liaises with patient and industry associations to explore ways of bringing innovation to patients while helping enterprises and maintaining growth.



VII. SUMMARY AND CONCLUSIONS

In closing, I might wish to reiterate that we're in the midst of an unprecedented global health crisis. This crisis calls on the medical device industry to ensure closely with customers, patients, regulators, and public organizations for the sake of public health. The news is going to be fast-paced, and far of it will be disappointing, frustrating, and dispiriting. The key, however, is going to be for companies to specialize on how they will make the foremost contributions to regulate the spread of the virus and save lives. Short term, which may mean ramping up production to new levels; future which may mean sticking closely to regulatory guidelines to make sure that speed doesn't destroy quality, creating even more problems in the future. No matter what, medical device professionals will have an important role to play in the fight against COVID-19. Among a number of the most important changes seen under EU MDR are:

- Increased requirements for clinical evaluation
- Digital and physical labeling
- Post-market surveillance (PMS), and
- Total life cycle traceability.

There is no word yet on the In-vitro Diagnostic Medical Devices Regulation (IVDR), or the impact of this potential delay on European Notified Body audit activities.

Clinical Trial protocols are required to be changed to eliminate apparent immediate hazards to participants such as changing in-person visits to virtual visits, elimination of study visits/procedures that do not impact the integrity of the study or participant safety, incorporation of screening questions to identify potential COVID-19 exposure.

Other challenges posed by sponsors of clinical trials include:

- [1] Delays in study initiation activities resulting from the inability to perform site selection/initiation visits and/or clinical vendor qualification visits, and subsequent downstream delays in patient enrolment,
- [2] Protocol adherence issues arising from an inability to comply with visit schedules, study procedures, drug administration, and monitoring procedures,
- [3] Delays in clinical material distribution and import/export delays due to limited manufacturing and operations staff, limited or reprioritized hospitals staff, and travel bans,
- [4] In some cases, suspension of all patient activities for trials, sites, or studies that do not have active patients being treated,
- [5] Cancellation or postponement (indefinitely, in some cases) of major scientific and professional conferences and meetings, and KOL, investigator, and scientific advisory board meetings.

REFERENCES:

- [1] <https://www.greenlight.guru/blog/medical-device-regulatory-classification#:~:text=In%20the%20U.S.%2C%20medical%20devices,seen%20as%20the%20highest%20risk.>
- [2] [https://morulaa.com/cdsc/medical-devices-rules-2017-classification-of-medical-devices/#:~:text=Medical%20devices%20under%20the%20new,Class%20C%20\(moderate%20high%20risk\)](https://morulaa.com/cdsc/medical-devices-rules-2017-classification-of-medical-devices/#:~:text=Medical%20devices%20under%20the%20new,Class%20C%20(moderate%20high%20risk))
- [3] MEDICAL DEVICE REGULATIONS - WHO | World Health Organization: https://www.google.com/url?sa=t&source=web&rct=j&url=https://www.who.int/medical_devices/publications/en/MD_Regulations.pdf&ved=2ahUKEwjC6KeXwoDwAhUNbn0KHUc6COWQFjABegQIAxAG&usq=AOvVaw1jksCHyoLkbnPtzgoUH7Uk&shid=1618498965085
- [4] United States of America: Food and Drug Administration: www.fda.gov/default.htm
Corresponding medical device-related information site: www.fda.gov/cdrh/index.html. (This site also offers "Device Advice" – www.fda.gov/cdrh/devadvice/ – a self-service site for medical device and radiation product information) The FDA enforcement report site: www.fda.gov/opacom/Enforce.html also offers useful information for import control.
- [5] European Union: http://europa.eu.int/comm/enterprise/medical_devices/index.htm
- [6] The EU Member States with a different linguistic regime:
- [7] France: www.afssaps.sante.fr/
- [8] Germany: www.bfarm.de/de/index.php
- [9] Spain: www.msc.es/farmacia/home.htm
- [10] U.S. Food and Drug Administration. Classification of Products as Drugs and Devices and Additional Product Classification Issues. Available at: <http://www.fda.gov/RegulatoryInformation/Guidances/ucm258946.htm>. Accessed March 4, 2016.
- [11] U.S. Food and Drug Administration. Soft Tissue Fillers (Dermal Fillers). Available at: <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/CosmeticDevices/WrinkleFillers/default.htm>. Accessed March 4, 2016.
- [12] U.S. Food and Drug Administration. Device—Not a Device. Available at: <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051521.htm>. Accessed March 4, 2016.
- [13] Kaplan AV, Baim DS, Smith JJ, et al. medical device development: from prototype to regulatory approval. *Circulation* 2004; 109:3068–72.

- [14] U.S. Food and Drug Administration. CFR-Code of Federal Regulations Title 21 vol. 8. Sec 880.5240. Medical adhesive tape and an adhesive bandage. Available at: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?FR!4880.5240>. Accessed March 4, 2016.
- [15] U.S. Food and Drug Administration. CFR-Code of Federal Regulations Title 21 vol. 8. Sec 878.5020 Nonabsorbable polyamide surgical suture. Available at: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?FR!4878.5020>. Accessed March 4, 2016.
- [16] https://ec.europa.eu/info/sites/info/files/list-covid-19-essential-medical-devices_en.pdf

