"QUALITY, SAFETY, EFFICACY AND REGULATORY PROSPECTS OF MEDICAL DEVICE IN UNITED STATES AND EUROPE"

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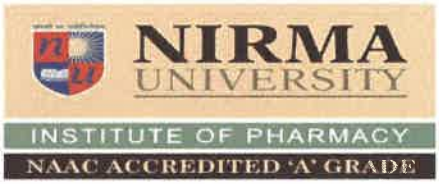

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CERTIFICATE

This is to certify that Project Work (BP812PW) entitled ***"QUALITY, SAFETY, EFFICACY AND REGULATORY PROSPECTS OF MEDICAL DEVICE IN US AND EUROPE"*** *is the bonafide work carried out by* ***THAKORE DEVANSHI*** *(18BPH013),* ***TRIVEDI KARTIK*** *(18BPH032),* ***RATHOD MAHARSHSINH*** *(18BPH044),* ***PATEL RIYA*** *(18BPH079), B.Pharm semester VIII under my guidance and supervision in the Institute of Pharmacy, Nirma University, Ahmedabad during the academic year 2021-2022 . This work is up to my satisfaction.*

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CERTIFICATE OF SIMILARITY OF WORK

This is to undertake that the B.Pharm. Project work (BP812PW) entitled ***"QUALITY, SAFETY, EFFICACY AND REGULATORY PROSPECTS OF MEDICAL DEVICE IN UNITED STATES AND EUROPE"*** *Submitted by* ***THAKORE DEVANSHI*** *(18BPH013),* ***TRIVEDI KARTIK*** *(18BPH032),* ***RATHOD MAHARSHSINH*** *(18BPH044),* ***PATEL RIYA*** *(18BPH079), B.Pharm. Semester VIII is a bonafide review/research work carried out by us at the Institute of Pharmacy, Nirma University under the guidance of "Name of a Guide and Co-guide". We are aware about the rules and regulations of Plagiarism policy of Nirma University, Ahmedabad. According to that, the review/research work carried out by us is not reported anywhere as per best of our Knowledge.*

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DECLARATION

We, ***THAKORE DEVANSHI*** *(18BPH013),* ***TRIVEDI KARTIK*** *(18BPH032),* ***RATHOD MAHARSHSINH*** *(18BPH044),* ***PATEL RIYA*** *(18BPH079), students of VIIIth Semester of B.Pharm at Institute of Pharmacy, Nirma University, hereby declare that our project work (BP812PW) entitled* ***"QUALITY, SAFETY, EFFICACY AND REGULATORY PROSPECTS OF MEDICAL DEVICE IN UNITED STATES AND EUROPE"*** *is a result of culmination of our sincere efforts. We declare that the submitted project is done solely by us and to the best of our knowledge, no such work is done by any other person for the award of degree or diploma or for any other means. We also declare that all the information was collected from various primary sources (journals, patents, etc.) has been duly acknowledged in this project report.*

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ABSTRACT

With the expanded rising population and economic environment, person's interest for health-care benefits has altered from looking for medical treatment after disease to keeping up dynamic wellbeing into later years. Not only medicines, but also medical devices play significant role in treatment and in maintenance of patient's health. So, it is important to regulate medical devices. Medical Gadgets are regulated by the United States Food and Drug Administration (US-FDA), in which they have special center for it, namely Center for Devices and Radiological Health Center for Devices and Radiological. Health is answerable for safeguarding as well as advancing the general wellbeing by guaranteeing 3 parameters of medical device, namely quality, safety as well as effectiveness, also guaranteeing security of radiation-discharging items, continuous development, and furnishing general society with accurate, science-based data about the device regulated. The Regulations on Medical Devices (Regulation (EU) 2017/745) and on In-Vitro Diagnostic Devices changed the European lawful system for medical device, presenting latest responsibilities regarding European Medicines Agency (EMA) and public equipped experts in the evaluation of specific classifications of medical devices. Registries will allow both an imminent appraisal of the exhibition of high-risk gadgets and a review examination when indications from different wellsprings of data propose issues. The people who do application for an advertising endorsement for another device ought to need to guarantee controllers of its quality of production, efficacy and safety prior to permitting. Medical Devices are sorted in view of their level of difficulty as well as grade of risk involved, apart from that "pre-1976" gadgets were permitted to stay available in market characterized without audit of FDA. Devices which are "post-1976" and having low difficulty and hazard that are significantly identical to an advertised "predicate" devices are cleared through the 510(k) premarket warning interaction. Indeed, almost all straightforward medical devices are demonstrated to be utilizable in practice.

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1. INTRODUCTION:

- Medical Devices assume a filling part in the finding and the board of infection, the worldwide clinical medical device has outperformed US$350 billion in yearly income. Medical device is characterized by the World Health Organization(WHO) as "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 specific medical purpose and does not achieve its primary intended action by pharmacological, immunological, or metabolic means, but which may be assisted in its intended function by such means Current definitions and regulatory classifications of medical devices are complex and designed primarily for regulators.

- The United States (US) and the European Union (EU), two of the main world business sectors for medical device, present unfathomably various ways to deal with endorsing gadgets for use in patients. (Kramer DB, 2012) In the US, roughly 66% of all recently promoted gadgets are excluded from formal assessment by the US Food and Drug Administration (US-FDA), including most generally safe (Class I) gadgets, most moderate-risk gadgets (Class II) and a few high-risk gadgets (Class III) are cleared by the FDA through the "510(k)" pathway, in view of significant proportionality to recently supported gadgets, without requiring clinical preliminaries. In the EU, medical device exposed to the PMA interaction in the US might be supported that is, in truth a Conformite' Europe'enne (CE) mark — by nearby associations called Notified Bodies in view of more restricted premarket testing simply showing that the gadgets function as expected in a way where the advantages offset the dangers.

- The advancement of medical device is an intricate issue according to the point of view of its multi-partners, including: the public authority, administrative organizations, insurance agency, patients, doctors, medical services experts, hospitals" organization, industry the board, designers and makers. In wellbeing associations, the quality confirmation programs need a certified clinical innovation the executives. The administration of the presentation control of medical devices is turning out to be more unmistakable as the quantity of medical device increments. Along these lines, explicit exercises are expected to deal with the presentation tests for the medical device wellbeing. The Medical Device User Fee and Modernization Act (MDUFMA) of 2002 gave the FDA extra assets to audit gadgets, alongside administrative changes planned to build the proficiency of the survey cycle.

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- In this review article, we propose a more-clear meaning of a medical device, upheld by grouping, as well as fundamentally survey of latest administrative cycles. We have noted inconsistencies from various administrative definitions to all necessary guidelines, which are beneficial from harmonization. We focus on guidelines proclaimed not only via Food and Drug Administration (FDA) but also via European Medicines Agency (EMA). In addition, we additionally included quality, wellbeing and viability boundaries expected for medical device. The accompanying segments of paper covers quality, wellbeing, adequacy and administrative possibilities of medical devices.

2. WHAT IS MEDICAL DEVICE?

- As per World Health Organization, medical device is any instrument, mechanical get together, execute, machine, contraption, insert, reagent for in vitro use, programming, material, or other tantamount or related article, arranged by the producer to be used, alone or in mix, for individuals, for no less than one unequivocal clinical explanation and doesn't achieve its fundamental expected movement by pharmacological, immunological, or metabolic means, but which may be helped its normal limit by such means Current definitions and regulatory portrayals of clinical gadgets are convoluted and arranged chiefly for regulators.

- We characterize a clinical gadget as a creation planned and fabricated for use in medical services, and not exclusively therapeutic or dietary. We order clinical gadgets in light of the locales of purpose, the time size of purpose, and whether they are remotely controlled. (Organization, 2019)

3. DEFINITIONS OF MEDICAL DEVICE:

- Given the variety of sorts of clinical gadgets, administrative definitions have been outlined to be comprehensive, and go a long-ways past what are generally considered gadgets.

3.1 As per US:

- In the USA, the medical devices are defined as per FDA as;
  - "An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part or accessory which is: recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
  - intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
  - intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes" (Administration., 2019)

3.2 Definition of Medical devices as per EU:

- The EMA characterizes "medical device" via its utilization, single or in blend, in individuals, for at least one of the accompanying explicit clinical purposes: (The Medical Devices Regulations 2002, n.d.)
  - determination, avoidance, checking, forecast, anticipation, treatment, or lightening of illness;
  - analysis, checking, treatment, or easing of or remuneration for a physical issue or incapacity;
  - examination, substitution, or adjustment of the life structures, or of a physiological or obsessive cycle or state;
  - giving data through in vitro assessment of examples got from the human body, which includes blood, organ and tissue gifts

- Below listed two types of products are also considered as medical devices:

(i) devices for the control or support of conception;

(ii) products specifically intended for the cleaning, disinfection, or sterilization

4. REGULATION AND CLASSIFICATION OF MEDICAL DEVICES:

4.1 As per US:

- The 1976 Medical Device Amendments (MDA) gave the FDA the essential power to control medical devices and to prove "sensible confirmation of security and adequacy" prior to permitting makers to showcase their findings. The 1976 MDA guideline have been revived with Medical Device User Fee and Modernization Act (MDUFMA) of 2002, which spread out help client costs for application studies and set forth unambiguous execution aims of the association. The FDA dispenses gadgets into one out of three authoritative categories taking into account device's arranged use (Table 1), whether it is meddlesome or implantable, also the bet introduced by gadget to the client.

- Hardships in grouping devices emerge from their assortment as well as purposes. For example, the FDA's Global Unique Device Identification Database (GUDID) records over 2.2 million things and it is developing everyday by an expected 2500. Medical devices are characterized and managed by their intricacy and level of hazard to general society. This arrangement conspire decides the necessities for advertising a device in the United States. The utilization of expression "showcased" is deliberate as the FDA doesn't manage an act of medication but instead the deal, conveyance, and advancement of clinical items.

- There are 3 FDA administrative groupings of clinical gadgets: Class I, Class II, and Class III. (Administration U. F., n.d.)The orders are given out by the bet the clinical gadget represents to the patient and the level of regulatory control the FDA chooses is supposed to honestly publicize the gadget. As the portrayal level forms, the bet to the patient and the degree of FDA regulatory control increase. The groupings of clinical gadget that were displayed in the US as of May 28, 1976, the date of section of the Medical Device Amendments, were organized by FDA and were permitted to remain accessible. New clinical gadget entering the market after May 28, 1976, are organized through assessment with honestly exhibited clinical contraptions in regards to anticipated use and mechanical characteristics. Without even a hint of a sensible commensurate contraption,

conventionally implied as the "predicate," the gadget is thus situated into the most essential authoritative class (Class III, portrayed further) until FDA renames the gadget using a bet-based approach (if legitimate).

- Class I gives minimal level of managerial control and is anticipated gadget for which there is sufficient information to assume that security and suitability can reasonably be ensured by General Controls alone. General Controls are described in the Medical Device Amendments and integrate execution master for misbranding, pollution, enlistment and posting, contraption prohibiting, buyer cautioning and survey, thing reporting, premarket notice, and extraordinary gathering practices. Class I gadget present immaterial conceivable naughtiness to the client and are consistently essential in plan and have a foundation set apart by safe use. Occasions of Class I gadgets consolidate manual cautious instruments, for instance, supports and retractors, hand-worked urological tables, and manual biopsy forceps.

- Clinical gadgets alloted as Class II are devices for which General Controls alone are not satisfactory to reasonably ensure prosperity and suitability, yet rather for which there is sufficient information to spread out Special Controls to give this certification. Along these lines, despite General Controls, these gadgets are reliant upon something like one Special Controls. Remarkable Controls integrate the going with: novel naming essentials, required execution standards, both International and United States, post-market perception, and FDA bearing record. Examples of Class II gadgets consolidate urinary catheters, cryotherapy systems, x-bar structures, brachytherapy seed additions, and PC helped (mechanized) cautious structure.

- Class III clinical gadgets address the most bet, and, along these lines, are subject to the almost all extreme regulatory controls. For Class III clinical gadgets, satisfactory information isn't open to ensure security and suitability using General and Special Controls. Taking everything into account, despite General Controls, these devices require FDA overview and underwriting of a premarket support (PMA) application before publicizing. Class III gadgets backing or backing human life, are basic in hindering incapacity of human prosperity, or present a potential unreasonable bet of infection or injury to the patient. Delineation of Class III gadgets that require a PMA are transurethral microwave thermotherapy (TUMT) structures for the innocuous prostatic hyperplasia (BPH), inflatable penile additions for erectile brokenness, and centered energy focused ultrasound systems for uterine fibroid expulsion.

Classification	Premarketing Essentiality	Approval Time	Examples
Class I	Dependent upon the most un-administrative control, mostly all Class I gadgets are excluded from premarket warning or potentially great producing rehearses guideline, albeit some general controls apply (eg, gadget enrollment and posting, marking guidelines).	Varies	Manual careful instruments, for example, clasps and retractors, hand-worked urological tables, and manual biopsy forceps
Class II	It is necessary for almost all Class II are devices to pass premarket notification 510(k) necessities. In uncommon cases, clinical investigations are expected for a 510(k) accommodation. What's more, these gadgets might be dependent upon other unique controls, for example, unique marking prerequisites and required post market reconnaissance.	6 to 12 months.	Urinary catheters, cryotherapy frameworks, x-beam frameworks, brachytherapy seed inserts, and PC helped (automated) careful framework
Class III	These gadgets have the most rigid necessities. Commonly, the data is lacking to	More than 12 months	Transurethral microwave thermotherapy, inflatable penile implants and extreme focus centered ultrasound frameworks

	guarantee wellbeing and viability exclusively through broad or unique controls. In this way, a premarket application (PMA) is expected for Class III gadgets, which incorporates proof from forthcoming, randomized control preliminaries.		

Table 1: Regulation requirements of medical device as per US-FDA

4.1.1 Marketing Pathway of 510(k)

- Devices approved under 510(k) pathway are considered having optimum safety and efficacy and elevated compatibility as per the US FDA. (Administration U. F., 21CFR 807 Sub part E., n.d.) Most of the Class 2 and class 1 devices are required to go through the marketing review process of 510(k). Advancement of the new devices by this process can be seen as recent trends.

- The marketing company has to claim the safety and efficacy of their device, for this they have to made a comparison of their new device with already approved device. This reference device should...
  a) marketed in the US before 1976 so that is PMA is not needed
  b) reformulated from any device from any class
  c) undergone through the marketing process which is having much similar aspects as 510(k) pathway.

- Proposed medical device is considered new when it has the equal intended use and technical aspects as the reference device. Data submitted to the FDA can arise need of clarification of many safety and efficacy problems is the device is having same intended use but functions through different technology. (Food Drug and Cosmetic Act 21 U.S.C. Section-513(i).)

- Clinical investigations are rarely needed for proving the similarity of the medical device. If the device matches the expected criteria of the FDA, then, producer receive a letter which permits the sale of medical device in the USA.

There are 2 examples of medical devices that has gone through 510(k) pathway:

- The advancements in the class 2 medical device named Brachytherapy seed plant results in very different and effective device then its origin era of 1976. These advancements are declined size of the pallets, needles and modification in dosimetry methods, because of these modifications its use in cancer therapy becomes more effective, especially in prostate cancer therapy.

- Trend of robotic surgical system is enhancing nowadays. These systems are generally computer assisted in nature and they are classified as class 2 medical devices. (Computer-Assisted(Robotic)SurgicalSystems., n.d.). A classic example of this robotic advancement is seen in laparoscopic clinical instruments which were used manually before but now they are computer assisted, which does not cause alteration of the intended function but made enhancement in the effectiveness of the therapy.

4.1.2 Pre-market approval process:

- The separate evaluation of class 3 medical devices for its safety and efficacy is being done by US-FDA's regulated process called PMA process. (Administration U. F., n.d.). Main function of this process is to validate that the medical device is matching with its intended use in safe manner. PMA can consider as a proof of safety and efficacy of the clinical device. In case of drugs the proof of safety is given by intense study and at least 2 blinded randomized clinical trials, but in case of medical devices only the practical evidences which sounds scientific are sufficient for assuring the safety and efficacy. This evidence includes controlled trials, case studies which are well documented and scientifically sound reports. Personal reports and random experience which do not have enough scientific approach are not considered as a proof of safety. (FDA, n.d.) (Administration U. F., n.d.)

- The process of PMA for a device is given with an appropriate example in the following paragraph:

- Treatment of benign prostatic hyperplasia is done by Transurethral microwave thermotherapy but it was not official in US. Hence, no other device was available to use as reference evidence for 510(k) process. Apart from this, it includes use of microwave therapy which can cause lesions surrounding the prostate gland because of excessive heat. The approval was initiated under PMA process thus, it needed adequate safety evidences which proves the effectiveness and safety of the

TUMT device. Device of this treatment was approved under de novo act of FD & C which is discussed in upcoming topic.

4.1.3 Approval process of De novo:

- The new device which requests de novo is classified as class 3 without concerning the risk level as per the Food, drug and cosmetic act, section 513-f/1. The assembly, in 1997 has approved the modernization act for FDA, which introduced a new path of marketing of medical devices which possess lower risk, thus falls under class 3. The pathway named as de novo which has recent amendment of 2012 by FDA through safety and Innovation act. (Evaluation of automatic class III designation (de novo) summaries, n.d.).

- Devices which are new in market and do not possess any threat to human life is eligible for the de novo process. The additional requirements needed to be satisfied for de novo process are as follows:

  - The level of the risk must be mild to medium, not very high so that it can match the legislator requirements as per US FDA act of FD & C.
  - The risk benefit ratio has to be identified adequately so that it can be controlled efficiently.
  - The device satisfies these conditions then the FDA accepts de novo request by generating class 1 or phase 2 regulations. (New Section 513(f)(2) - Evaluation of automatic class III designation, guidance for industry and CDRH staff, n.d.). The upcoming devices which come after new device can get approval through the 510(k) pathway as there is already a reference device of similarity.

- The incident of a device entering in the market by de novo process is given here: For inspecting the GI track, capsule camara is used which was not in market before 1976. Hence the first device was introduced in market by de novo process as there were no other supporting evidence of safety to be proven for 510(k) pathway. The safety and effectiveness of the device was determined by clinical investigations. Finally, this product was introduced in the market by de novo pathway and subsequent devices are approved by 510(k) pathway till now.

4.1.4 IDE application:

- An investigational device exemption (IDE) application is a petition for initiation of clinical research on an investigational device with "significant" risk in the U.S.

(Administration U. F., U.S. Department of Health and Human Service, n.d.) The IDE absolves specific regulatory prerequisite and permits an investigational medical device to be transported legitimately to clinical review destinations and is the primary vehicle by which clinical proof might be gathered to help a future advertising application. The reason for an IDE is to guarantee the welfare as well as safety of human test subjects. The IDE ought to incorporate the clinical protocol, informed consent, investigational labelling and risk examination. Medical Devices having "significant" risk will need an IDE endorsement not only by the FDA but also by an institutional survey board (IRB) endorsement, while utilization of investigational device without critical risk will only require IRB approval only. The below listed attributes of a medical device denote critical risk. (Administration U. F., U.S. Department of Health and Human Service, n.d.)

- It is planned as an implant and presents significant risk to the welfare, safety and health of a patient;
- It is indicated or addressed to be for a utilization in supporting human life and presents a potential for significant risk to the welfare, safety and health of a patient;
- It is for a utilization critical in curing, diagnosing, treating or moderating illness or in any case in prevention of any hindrance of human wellbeing and presents a significant risk to the welfare, safety and health of a patient; or
- It in any case presents a significant risk to the welfare, safety and health of a patient;

- For instance, latest medical devices are utilized to remove prostatic tissue in the therapy of confined prostate malignant growth might present significant risk of injury, and that's why commonly require presenting an IDE application to FDA for examination inside the U.S.

4.2 As per Europe:

- Until the 1990s, every part state had its own way to deal with managing devices. To manage an assorted and complex market and advance the "interior market" in Europe, new guidelines, known as the New Approach Directives, were presented by the European Council that characterized the "Fundamental Requirements" to

- guarantee devices' security and performance.12 These prerequisites apply to all nations. Accordingly, on the off chance that a gadget meets the prerequisites and gets a CE mark in one country, it tends to be advertised in all part states. A CE mark affirms that a gadget is protected and works as indicated by the expected reason depicted by the maker. Under these mandates, gadgets are arranged into four classes as per the level of chance related with their planned use (Table 3).

- Like in the US, Europe's evidence requirements for market endorsement rise with the degree of peril related with device. Creators of for the most part safe gadgets (Class I) are required solely to self-articulate congruity with the Necessary Requirements to public "Prepared Authority," like the Medicines and Healthcare Products Regulatory Agency (MHRA) in the Europe. More moderate-and high-risk gadgets (Classes IIa, IIb, and III) require a mix of nonclinical and clinical data on the gadget being assessed. (Table 2) If open, information for an indistinguishable gadget right now accessible may be submitted. Though clinical examinations are all around referenced for high-risk Class III gadgets, the verification essentials are dark, not open for everybody, and nonbinding for creators and audit require not be randomized. For producers affirming resemblance to an ongoing thing, a close to composing review routinely takes care of business.

- Makers of the gadgets select and pay one of around 80 for-benefit, private "Told Bodies" to assess their gadget as well as to get a CE mark. Award of a CE mark relies upon an appraisal of execution (that a device limits as expected) and safety and not practicality (clinical benefit). At the point when a gadget is free, makers are supposed to report all veritable unpleasant events to the Competent Authorities. In UK, this information is assembled into a central informational collection, the European Databank on Medical Devices (Eudamed). Despite wariness information, Eudamed contains data on makers; supports gave, adjusted, suspended, eliminated, or dismissed; and clinical assessments. The usage of Eudamed has been mandatory start around 2011. post market focuses also may be expected in case a gadget's medium-or long stretch security and execution are not aware from past utilization of the gadget or when other post market perception activities would give inadequate data to address bets.

➢ Medical devices, including all clinical gadget programming, are characterized by their gamble level (see Chapter 5 in Regulation (EU 2017/745)), (Majety RPD, 2021)and the regulatory requirements increase with the risk level.

➢ The European Union Medical Device Regulation (EU-MDR) assigns 4 medical device groupings:

- I Class
- IIA Class
- IIB Class
- III Class

➢ I CLASS DEVICES:

- As per EU, medical device under I Class have the least number of risk.
- Most of the time, the maker can self-insist Class I gadgets except the relationship of an exhorted body.
- Example includes products like bandages, glasses and stethoscopes.
- Regardless, there are 3 more sub-orders inside Class I clinical gadgets that have an imperceptibly more seen risk and do require the consideration of a told body before the maker can join the CE checking.
- I Class medical device are classified into following three types:
  i. **Class I(S):** should be introduced sterile.
  ii. **Class I(M):** has an estimating highlight.
  iii. **Class I(R):** reusable careful instrument.

➢ IIA CLASS DEVICES:

- IIA Class devices are viewed as moderate-risk gadgets by the Medical Device Regulation.
- This suggests that unlike a Class I gadget, the maker ought to get a otification of congruity from an educated body following its closeness examination.
- Examples: hearing aids, catheters and short-term contact lenses.

➢ IIB CLASS MEDICAL DEVICES:

- IIb class devices are viewed as medium-to high-gamble with gadgets under the MDR, and hence their CE course likewise requires association of an advised body.
- Examples: insulin pens, incubators, ventilators and long-term contact lenses.

➢ III CLASS MEDICAL DEVICES:

- Particularly like the FDA portrayal structure, Class III gadgets are considered to be high-risk and are subject to the most intense essentials, including clinical appraisal of the gadgets.
- Example includes devices like pacemakers, prosthetic heart valves, careful lattice, bosom inserts, and different gadgets that require super durable observing all through their lifetimes.

Class	Premarket Essentiality	Approval Time	Examples
Class I	Producers are permitted to announce congruity with the Essential Necessities.	No requirement of approval	stethoscopes, bandages, or glasses.
Class IIa	As a rule, makers are expected to present a dossier of pertinent supporting writing (nonclinical and clinical) to prove wellbeing as well as execution. In spite of the fact that there is general container European information guidelines, proof prerequisites are genuinely liquid, contingent upon what is put together by the producer and needed or suggested by the pertinent Advised Body.	1-3 Months	Catheters, portable hearing assistants, or momentary contact focal points
Class IIb	The gadgets incorporate those representing a generally more gamble to the human body, for example, innovations like dialyzers, respirators, and muscular inserts. Medium gamble		Hatcheries, ventilators, long haul contact focal points and insulin pens.
Class III	Clinical investigations for the most part are suggested for high-risk		Pacemakers, prosthetic heart valves, careful

	gadgets, yet almost all are nonrandomized as well as single arm (zeroed in on showing wellbeing). Necessities are to some degree unclear for European nations also, factor across Notified Bodies.		network, bosom inserts, also, different gadgets that require long-lasting Checking all through their lifetimes

Table 2: Regulation requirements of medical device as per EU

5. QUALITY STANDARDS OF MEDICAL DEVICES:

- As per the idea of connection between human framework and medical devices, biocompatibility data measures are finished by relating GB/T 16886 principles (ISO 10993 series). For efficacy study of electrical wares, various tentative trials are done for relevant parameters, like bending as well as torsion, electronic ability and transmission rate, beginning along-with parts of actual devices. The autatic assets of adaptable electrical wares as well as wearable gadgets in view of not only these materials, but also matching with human body are tested.
- The mechanical properties of adaptable electronic materials and wearable contraptions in light of wares, along-with the matching to the human body are inspected.
- Asper GB 9706 principles (IEC 60601 series), the electronic security of wearable hardware are tried as indicated by the expected use. As per YY 0505-2012 (IEC 60601-1-2:2004), the electromagnetic similarity of adaptable electric wares and wearable gadgets ought to be tried.
- Medical devices are suppose to demonstrate recognition with ISO 13488 and 13485 principles. These principles give prerequisites to effective execution of a frequently improving quality management process for design plotting and production of medical devices.
- ISO 13488 and 13485 standards supplement ISO 9002 and 9001 respectively. The ISO 9000 principle gives structure to the execution, documentation, improvement and support of a quality administration framework to industry. ISO 13485 and 13488 gives a guidance about exceptional prerequisites of medical device industry.

- The preliminary work of the ISO 9000 series principles is to check that method regarding design and configuration, assembling and installation of products is carried out and sufficiently documented to guarantee about weather all staff-members are aware with the roll of their job or not on the overall quality of the product.
- ISO guidelines spread out a chain of liability regarding the resources of assets to the quality administration framework, item acknowledgment, quality framework estimation, examination, quality framework development and the association between the association and the customer.
- ISO 13485 indicates extra prerequisites for medical device makers incorporating:

  (1) Arrangement of training of staff-members who should work in exceptional circumstances or are expected to utilize new instruments;

  (2) Risk appraisals are necessary at whatever point when configuration changes are implied after the plan has been frozen;

  (3) Acquisition records of parts as well as wares from outer resources should be kept up with you;

  (4) Modified gadgets must be recognized and differentiate them from variant medical devices;

  (5) Sanitization cycles as well as settings should be observed, restricted and reported

  (6) Natural variables of bundling as well as stockpiling that might be inconvenient to presentation of devices should be reported

5.1 Design for "X" (DfX):

- DfX techniques are carry out to ensure accomplishing explicit goals, for instance the simplicity of gathering or assembling a medical device. In addition, the usage of DfX techniques is recognized by Clarkson and Alexander (Alexander K. a., 2000) as a decent plan practice for device rehabilitation. These methodologies are prescribed along-with simultaneous designing way to deal with all the while work on the item and its assembling processes during the planning and designing stage.
- The significance of express DfX thoughts for medical gadgets is affected by the target of creating protected and compelling medical gadgets, along-with Good Manufacturing Practices characterized by FDA.
- Relying on the scope of an item, the plan and advancement could be revolved around a couple of basics; where the plan might be sought after with the

- accompanying targets: assembly, manufacturing, quality, variety, dismantling and maintainability. (Chiu, 2011)
- The DfX for medical devices are shown in (Figure 1) is characterized as a synergistic utilization of numerous DfX ideas: Manufacturing, Validation, Reliability, Usability, and Quality.

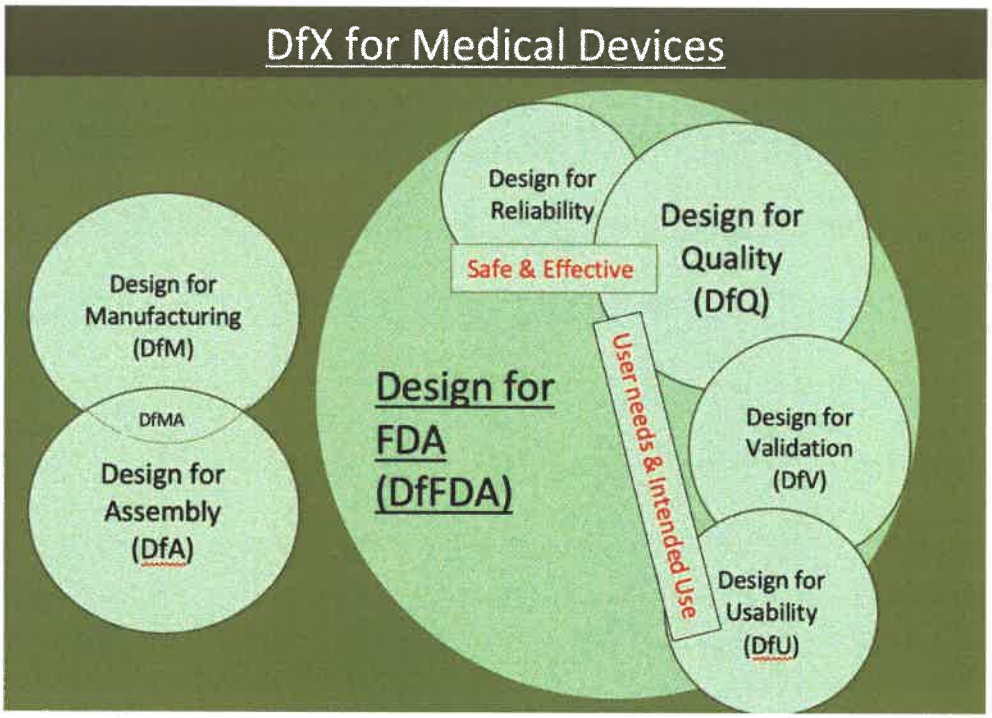

Figure 1: Design for X allotted to Medical Devices

5.1.1 Design for Manufacturing (DgM) and Design for Assembly (DgA):

- DfM initially seen in the device advancement process in line up with idea of device and model improvement relying on the kind of the device. (Pietzsch, 2009) The DfM approach described by Pietzsch incorporated the arrangement for installations, tooling and machines to fabricate the medical device.
- DfA is considered as a component of the idea age to limit the quantity of parts and gathering tasks, and to have straightforwardness to collect math. While Pietzsch began the DfM at the theoretical stage, Clarkson and Alexander proposed DfM after a point by point configuration has been set up, with the gole to remove non-useful parts and decrease utilitarian. (Alexander K. a., 2000)

5.1.2 Design for Reliability (DfR):

- The DfR method is exceptionally connected with US-FDA's targets for creating protected as well as successful clinical devices. Then Weininger et al. (Weininger, 2010) contended that "dependability and security are significant traits deciding viability", having connections and interdependencies between the wellbeing, adequacy and unwavering quality of medical devices.

- Fries (Fries, 1997) characterized different instruments to accomplish dependable gadget determinations; which contained quality capacity arrangement (QFD), human elements, risks and the utilization of measurements overall.

- Weininger et al. (Weininger, 2010) explained 8 elements of DfR:

  1) Plan sensible item necessities and requirements,
  2) Discuss the item life-cycle,
  3) Selection of t parts with the imperative degree of quality,
  4) Recognize potential disappointment functions, destinations as well as components,
  5) Plan regarding use and ability of the item,
  6) Cross-check the dependability of the item in the normal climate,
  7) All assembling and gathering processes should have imperative ability, and
  8) Use shut circle the board for item life-cycle utilization.

- In general, DfR assumes a significant part specifically in guideline of life-adherence devices, whose disappointment addresses what is going on to the clients.

5.1.3 Design for Validation (DfV):

- Plan approval incorporates the confirmation of the plan as it helps in development and in evaluation to guarantee fulfillment of client requirements and congruity with it's expected use (Alexander K. a., 2000) (Alexander K. a., 2002)

- The DFV V-model created by Alexander and Clarkson incorporates the gadget configuration, yet grows to the interaction plan and creation improvement. Their methodology is planned to advance an all the more supportive of dynamic utilization of approval exercises at each phase of the improvement interaction, as can be outlined from the chart. They likewise characterized six plan strategies that urge fashioners to be all the more favorable to dynamic and think ahead while seeking after the clinical gadget improvement procedure.

- These strategies include:

  (1) Catching certain and unequivocal prerequisites,
  (2) Verification of prerequisites,
  (3) Utilization of an approach which is based on risk,
  (4) Taking into account the impacts of re-plan on prerequisites,
  (5) Concerning about the impacts of medical device improvement on process prerequisites,
  (6) Concerning impacts of interaction re-plan on device prerequisites. (Alexander K. a., 2002)

5.1.4 Design for Quality (DfQ):

- Targets of DFQ incorporate gathering client necessities, having sufficient heartiness to limit the impact of changes in the item's assembling or climate, and having the option to work on the item's dependability, execution and innovation ceaselessly (Kuo, 2001)

- Nagle (Nagle, 1992) given a draft of techniques which are utilize to plan quality of devices, also including conversations about the device improvement cycle, dependability issues, adaptation to non-critical failure.

- The quality capacity organization (QFD) and all-out quality administration (TQM) strategies are portrayed as the two for the most part involved techniques to integrate quality in the medical device plan. Kuo et al. (Kuo, 2001) distinguished QFD as a significant procedure for the execution of DFQ, as it guarantees the proper moving of client prerequisites into important specialized determinations and fills in as an instrument for benchmarking while performing client investigation and ceaseless improvement exercises.

- On the other side, TQM is an interaction approach focused on improvement, containing the quality in plan might be accomplished because of the cycle. (Nagle, 1992)

5.1.5 Design for Usability (DfU):

- With regards to medical devices, DfU ought to be utilized to further develop the device plan and to stay away from use mistakes that could bring about tolerant wounds or passings.

- DfU incorporates preparation of medical devices more straightforward to utilize it, while device approval of guaranteeing satisfaction of customer requirements and the rightness of plan utilized. (Alexander K. a., 2002) The dynamic

- contribution of the users in the medical device advancement cycle can likewise bring about higher convenience of the device and further work on human execution.

5.2 User-Centered Design Approach:

- Client Centered approach are the most well-known approach that been utilized in planning medical device beside information driven plan because of coordinated and more solid in planning process. (Leune, 1998) It additionally adds to consumer loyalty while utilizing the item since it fits the necessities of client.
- In earlier years, the attention on planning medical device have expanded because of popularity in such region. In connection of a medical device plan epitome, most creators have center more around device plan, human blunder, convenience and patient wellbeing in their applied plan.

- The job of medical device in understanding security occurrence have been explored in 2007 by the United Kingdom's National Patient Safety Agency. Taking a gander at all passing and serious occurrences announced by them, the reason for the episode is fundamentally the plan of the medical device that isn't protected to be utilized (J. L. Martin D. J., 2012)

- Ergonomic or well known as human component have contribute fundamentally in medical device wellbeing have featured commitment which will further developing security in medical services discipline particularly on plan. (Diego, 2009) (J. L. Martin B. J., 2008)

- Research made by Kianfar have utilized Quality capacity arrangement (QFD) strategy to Reliability-Centered Maintenance (RCM) to further develop RCM ability in saving the elements of the plants. Their goal is basically to save the capacity of plant with least asset. By adding such strategy to the RCM have recapture more productivity (Kianfar, 2010)

- Self-administration drives progressively depend on the utilization of advancements to work with the course of care in the home.

- These innovations range from medical devices, for example, glucose screens to thorough PC intervened telemedicine frameworks that offer intelligent help as well as World Wide Web access. (J. Zhang, 2003)

5.3 Performance Analysis for Medical Devices:

- In a research of Mana Sezdi, overall 542 medical devices were examined, there were 6 different types of medical devices examined at Istanbul University. (Sezdi, 2010)

- The medical devices which were analyzed were defibrillators, infant incubators, physiological monitoring systems, electrosurgical units, anesthesia units, ventilators. The distribution can be observed in table 3.

Sr No.	Name of medical device	Number of medical devices used in study
1	Anesthesia	53
2	Defibrillator	52
3	Electrosurgery	59
4	Physiologic Monitor	245
5	Infant incubator	34
6	Ventilator	99

Table 3: Breaking up of medical devices which were tested

- The functional trial of these medical device were executed and deciphered by the Inspection and Preventive Maintenance System (IPM) techniques, these were created by Emergency Care Research Institute (ECRI) can be seen in Table 4.

Device Under Test	Performance Tests
Infant Incubators	Baby probe test
	Temperature test
	Humidity test
	Energy test
	ECG arrythmia test
	Synchronized discharge test
	Charge time test
	ECG amplitude test
Physiological Monitor	IBP static pressure test
	NIBP alarm test
	NIBP cuff leakage test
	NIBP cuff pressure test
	NIBP performance test
	ECG alarm test
	ECG frequency test

	ECG pulse test (BPM)
	sPO2 performance test
	IBP alarm test
	sPO2 alarm test
	IBP dynamic pressure
Ventilators	Flow test
	O2 concentration test
	Peak pressure test
	Expiratory time test
	Frequency test
	Tidal volume test
Anesthesia Units	Minute volume test
	Gas concentration test
	Flow test
	O2 concentration test
	I:E ratio test
	Inspiratory time test
	Tidal volume test
Electrosurgical Units	REM alarm test
	Bipolar power test
	Cutting power test

Table 4: Performance analysis test with name of medical devices

- In investigation, they found out medical device disappointments were distinguished inside 21% out of total 542 medical devices from various branches of Istanbul University. Out of total 542 devices, 115 were endorsed as "Failed" while 427 were endorsed as "Passed". When the "Failed" devices were dissected by the mistakes, a few specialized issues were noticed. The defects can be seen in Table 5.

Infant Incubator	34	28	No problem	100
		1	Not working	101
		2	Display Error	103
		1	Over Heat	102
		1	Baby Probe Error	104

		1	Broken Cover	105
Defibrillator	52	43	No problem	200
		1	Not working	201
		2	Low/High Energy	202
		1	BPM Error	206
		1	Lead Error	204
		2	Low Battery	203
		1	Paddle Error	205
		1	Synchronization Error	207
Ventilator	99	87	No problem	300
		1	Not working	301
		2	Pressure Check Error	304
		1	Flow Sensor Error	306
		1	Connection Leakage	308
		1	Power Circuit Error	302
		1	O2 Sensor Error	305
		4	Volume Check Error	303
		1	Dirty Filter	307
Anesthesia Unit	53	30	No problem	400
		1	Not working	401
		2	Dirty Filter	407
		1	Volume Check Error	403
		12	Gas Concentration Error	409
		2	O2 Sensor Error	405
		2	Power Circuit Error	402
		1	Pressure Check Error	404

		1	Connection Leakage	408
		1	Flow Sensor Error	406
Electrosurgical Unit	59	45	No problem	500
		1	Not working	501
		1	Alarm Error	509
		1	High/Low Cut Power	503
		3	Patient Return Elect. Error	508
		2	High/Low Bipolar Power	505
		2	Power Circuit Error	502
		1	Footswitching Error	507
		1	Broken Pencil Electrode	506
		1	High/Low Coag. Power	504
Physiological Monitor	245	194	No problem	600
		4	Not working	601
		3	High/Low O2 Saturation	608
		2	ECG Pulse Meas. Error	603
		17	NIBP Error	606
		7	Power Circuit Error	602
		4	IBP Error	604

Table 5: Errors and technical problems in analyzed medical devices

- This research represents approaches for using the medical device's concerns to further develop the quality affirmation rehearses. The main end is utilization of plenteous data about the issues of all device causes the plunged on medical device disappointments and causes the basic rising on the medicinal support.

6. EFFICACY AND SAFETY EVALUATION OF MEDICAL DEVICES:

- It needs not be forgotten that protection reviews and normal overall performance evaluations cannot be separated from each special truly. The improvement of bendy electronics calls for a stability of various residences, especially flexibility, flexibility, durability. It is very difficult to find a gadget with all the characteristics. In some case the compatibility has to be determined for improvement of the function of the device which has not been used in the human body. Changed life style with adequate biocompatibility is the crucial factor to make any medical device, for instance the use of nanomaterial is extensively accepted in the composition of new generation devices. A classic example of nanotechnology is use of silver nanowire which have optimum conductivity for electronic devices. But to identify a compatible mixing of technologies which fulfill the needs of the optimum performance with utmost safety is not a easy task. As discussed, that silver nanowire is very useful in medical devices, but its toxicity is also a major concern to be studied as it can mix with body fluids and can cause metal toxicity by oxidation and ion leaching.
- The guidelines for biocompatibility test of medical devices given in ISO 10993 and GB-T 16886 suggests that it must be monitored one and before conducting the compatibility tests the adequate physical as well as chemical characteristics of should be obtained. The medical devices which come in contact with skin should be tested for topical irritation, cytotoxicity and biocompatibility.

- With electronic devices, that can affect vulnerable or implanted parts of the body, a consistent biocompatibility test should be performed depending on the type of connective tissue and the duration of the contact.

- Many chemicals are associated with composition of medical devices; thus, the safety measures should be taken under consideration for these chemicals. Their biocompatibility and interaction of one chemical with another chemical should be checked. It becomes very important for medical devices which remains in contact with human for longer duration of time.

- Primarily based totally on the recommendations provided in ISO 10993-1, studies issues for biocompatibility studies are provided in table 6 with precise recommendations for medical devices.

Biocompatibility task	In-vivo assay	In-vitro assay	Environmental conditions	Limitation	Accepted Std. reference
Cytotoxicity	cytotoxicity test called Balb/c 3T3	cytotoxic assay performed by using cell cultures(L929)	Time – 24h Room temp.	Cell culture proliferation ≥70 %;	ISO 10993-5:2009
Sense stimulation	Cell colony preparation from guinea pig			Testing of sense stimulation in the skin of guinea pig – responding to testing material	ISO 10993-10:2010
	(LLNA^c)		Mixture of polar (acetone) and non-polar (olive oil)		
Itching	Skin of rabbit is used			Detection of redness and edema	ISO 10993-10:2010
Haemocompatibility	Haemolysis, Complement activation	Thrombogenicity: dog/sheep	dressing Total blood or plasma, depends on testing	Haemolysis: determined absorbance of blood	ISO 10993-4:2017
Pyrogenicity	Single dose testing		Additional solvents	Elevated temperature	ISO 10993

Systemic toxicity	Single dose testing		Vehicles administered Using parenteral route, vehicle is administered	Pathology and physiology, biochemistry of the body , physique observation	

Table 6: Research concerns of biocompatibility tests (Kuan Chen)

- Despite the fact that in most clinical wearables, which may be expected to come into contact with skin, cytotoxicity, sensitivity, and irritability ought to be considered, there are nonetheless some issues that want to be addressed. as an example, some wearable clinical gadgets use flexible virtual gadgets designed to display human life parameters inside the course of sports sports / workout, eg walking and swimming, representing places of work complete of sweat and water. because of this, researchers need to take into account this wet art work surroundings and adjust experimental conditions, which incorporates cultural media, to mimic the real going for walks regions of a tested wearable medical tool.

6.1 Risk Management as safety model for medical devices:

- Clinical devices need to be safe and green in advance than it could be offered, but there had been events of undesirable events, even deaths, because of sudden layout errors. Biomedical engineers need to lessen possible dangers to customers and customers Apprehension and observation of the risk management is an important engineering expertise that every biological engineer should have. Risk management is the implementation of control guidelines, methods of identifying, analyzing, controlling and monitoring danger. In this newsletter, i will in quick describe a few not unusual steps you may take to assume failure, make merchandise more secure, and decrease debt amounts.
- Regulatory agencies have additionally identified the significance of danger management. The FDA tool fantastic tips and EC's medical device Directive require hazard control. There are also international requirements for hazard management. one of the most beneficial is "AAMI / ISO 14971 - risk control - software of chance management to scientific device" (Bartoo)

- Global standard, "ANSI / AAMI / ISO 14971: 2007 Medical Devices-Application of risk management to medical device", states the procedure for a manufacturer to identify hazards clinging with medical equipment, for evaluating and assessing concerned risks, for manipulating the risks, and guiding the effectiveness of manipulating means.

- The given figure 2 illustrates the risk management process: (Vaishali Hegde, 2011)

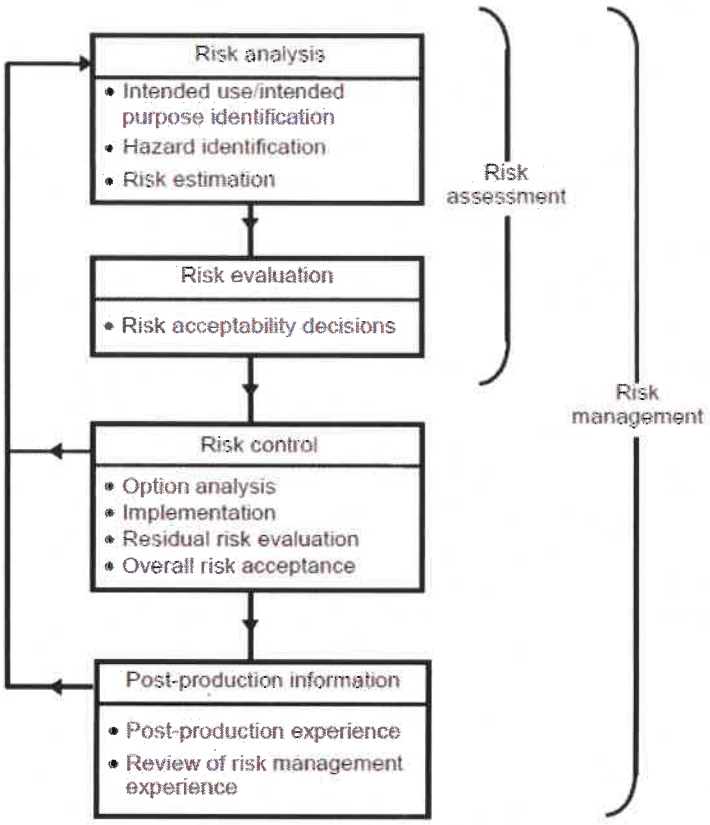

Figure 2: Flow of risk management process

- Risk Analysis
  - Centered utilization and identification of factors concerning to medical protection for a specific device or assumed accessory, the producer have to specify the supposed use or reason and any explicit mild misuse. The producer will note every indicator which could make contributions to the

safety of the medical device and, wherein appropriate, its boundaries. One manner to do this is to ask a series of questions about the design, use, and very last disposal of a scientific tool. A questionnaire that can assist the scholar in identifying all the possible risks of the diagnostic tool is furnished in Appendix A. identification of regarded or foreseeable risks

- A list of acknowledged or perceived dangers related to the medical device in each common and defective instances will be compiled by producer. Dangers that are known already might be diagnosed.

➢ Counting the risk of each hazard

- By applying the adequate utilization of data that is available, each hazard should be identified and error measured. Gadgets which are applied for quality classification and chances of occurring of risk or difficulty extent will be added in a disaster management report.

➢ Evaluation of Risk

- By application of the guidance set out in the risk management plan, minimization of risk must be done for every identified hazard. The risk management file contains the outcomes of this risk assessment.

➢ Control of Risk

- For lessening the risk, the procedure given by the risk management concept must be followed. It can justify the reduction of the risk concerning every individual hazard fairly.

➢ Analysis of available options

- At acceptable range, the risk is eliminated by the manufacturer by applying the adequate measures to manage the risk. The management of risk comprised of an approach which allows use of more than one crucial aspect from the following list:

  a) optimum safety as outcome of design;

  b) the production process or medical devices itself contains safety means;

  c) Information about the security.

➢ Risk control measure implementation

- Use of risk management rating which is selected in prior levels of process is being done by the manufacturer. The references, that are applied to control the risk are recorded in risk management file along with the verification outcomes that are obtained for the efficacy of the applied risk management measures.

- Remaining risk evaluation
  - After the implementation of the risk management measures, risk that remaining will be assessed implementing the aspects set out in the risk management plan and output of this assessment is noted in the risk management file. Different risk management approaches are applied if criteria do not match and if it matches, then all the crucial information the residual risk should be included in the appropriate document.
  - If further controlling of the risk is not effective or the residual risk is be accepted by risk management system, then the marketing firm must gat and scrutinize the reference bibliography which exhibits the benefits of medical devices for intended use and must claim that the benefits outweigh the risk. If the producer fails to claim this then it means that associated risks remain as such which is not accepted. All the data should be entered in risk management file.
  - Other concerning risks are identified by risk management approaches and if there is any of them, they are included in risk management file.
- Risk evaluation completeness
  - Assessment of known risk is ensured by manufacturer and recorded in RMF.
- Evaluation of residual risk
  - Acceptability of the risk caused by any medical device is determined after starting and validating the approaches of risk management. If the risks are unaccepted then the supporting literature on uses and benefits of device is being collected to prove that benefits are way sounder then risks. Failure in proving this causes unacceptability of the device.
- Risk management report
  - Risk management report includes all the results of risk management process. Risk profile by analysis, assessment, implementation of the risk is provided in this report. Acceptability of the risks are also mentioned in this report and it is integral potion of risk management file.

6.2 Risk management Case Study: (Vaishali Hegde, 2011)

- Risk management system applied for production of Continuous Positive Airway Pressure (CPAP) is given as per ISO14971.
- What is CPAP and OSA device?

- Contraction and reflection of muscle of respiratory tract cases Obstructive sleep apnea (OSA) resulting frequent waking from sleep because respiratory tract get collapsed. Prevention of air from entering to the lung may be caused by oversized tongue or either reduced muscle control or presence of extra muscle. This results in drowsiness because of rapid decrease in oxygen level in blood. The treatment is done by CPAP- which flows the pressured air through nasal track so breathing is possible which results in a comfortable sleep.

➢ Risk Management Program and it's steps (Table 8) (ISO14971, n.d.)
➢ The entire program is based on ISO14971.
➢ The initiation of program includes written planning of risk management that can cause the extension of life of the product from compounding and designing to user. Following steps are included in the plan:

➢ Identifying acceptable risks
• The usefulness of the risk management plans is identified.
• Responsibilities and power are assigned among the staff members
• Required analysis of risk management
• Crosschecking the functions of risk management
• Collection of reviews of the product as well as post production information

➢ Risk Acceptability Criteria

Guidelines of acceptability of any device is not given in ISO14971, hence the producer himself should build the criteria as per the type of the medical device. The process of formulating the risk acceptability process is given in the table 7 following by definitions, terms regarding to acceptability.

Recurrence	**Resulted hazards**				
	Catastrophic	***Severe***	***Moderate***	***Mild***	***Ignorable***
Frequent	5	5	4	3	2
Probable	5	4	3	3	2
Occasional	4	3	3	2	1
Unlikely	3	3	1	1	1
Remote	3	2	1	1	1

Table 7: Criteria for acceptability of risk

➢ Criteria for acceptability of risk:
1 - Even with no holding and manipulating measures the risk can be accepted
2 - After identification of risk, application of control measures is being

done by project team
3 - The approval from upper hierarchy is taken for risk identification depending on the risk-benefit ratio

• injury is described as physical or life-threatening harm, or harm to belongings or the environment.

• disaster - demise or severe damage despite the presence of any consumer intervention or every other

• intense - demise or serious harm, when intervention of the user or everybody else fails

• Moderate - treatment does not paintings for long and the consumer and anyone else can; recurrent injuries

• Mild - Minor accidents; first resource or health practitioner's office visit
Negligible - treatment isn't working, however the user is

- Definitions of recurrence incidents:
  - Occasional – If the abnormality occurs over 100 times during the use of the device for a year.
  - Probable – If the abnormality occurs 100-500 times during the use of device for a month.
  - Frequent – If the abnormality occurs once or more than one time per day it is called frequent
    - Unlikely – When functioning may alter and cause harm but it is not happening or not anticipated to happen
    - Remote – If fault in the functioning can be seen 100 times or less during the entire span of usage.

  Note: charges of incidence are primarily based on having as a minimum a million units getting used in the discipline. faulty quotes can be extrapolated primarily based on subject population at the time, to equate to a population of 1 million units.

1	Identify product use, requirement and uniqueness	Necessities and foreseeing	Documents required for product	Analysis of immediate risks
2	Clearing the doubts related to risk management of device, which are mentioned in ISO 14971	Designing the entire system	Questions and doubts form ISO 14971 IEC 62366 to identify misuse of the device	Information on Benefits and misuse of the device
3	Finding risk and harm and causative factors of it	Designing the entire system	Doing functional failure analysis by performing dFMEA and Fault tree analysis	Scrutinization of hazards and immediate risk identification
4	Bibliographic data for device similar to the CPAP	Designing the entire system	Database platform provided by FDA	Reasons of failure of products similar to CPAP
5	Providing risk level for each hazard	Designing the entire system	Committee of experts	Judging of the severity of risk
6	Implementation of the controls	Designing the entire system	Medical engineers	Identification of control measures
7	Analysis of device failure	Designing the entire system	dFMEA	Cause and prevention of failure
8	Overseeing the control measures	Designing the entire system	Validation and verification	Adequate implementation of control measure
9	Controlling the risk related to manufacturing, supply and service	Designing the entire system	Supply chain management	Qualified equipment and methods

10	Adjustment and verification of controlling features	Verification	Final tests and reports	Verification table of controlling features

Table 7: – Different tasks performed during the risk management of the project (ISO14971, n.d.) (www.fda.gov "MAUDE database", n.d.) (Vaishali Hegde, 2011)

- Activities for managing the risk
  - In accordance with ISO 14971, different tasks have been performed at different stages of development of the device CPAP. Identification as well as evaluation of the risks along with assessment, manipulation of risk and safety and efficacy determination is obtained by the application of these tasks.
- Virtual tools and electronic templets used in the project
  - The risk management program was established by using IBM (DOORS) and HP (Mercury Quality) software. In addition to this basic Microsoft tools like Excel and Word is also used in the program, especially for writing assessments of the risk. Follow up of the needs to monitor the measures is done by IBM software. Validation of control measures was done by testing from HP mercury QC. SAP software contains all the records of the process as well as the final risk assessment file which is supposed to submit to FDA.

- Risk Management File
  - Analysis of the risk form initiation to detailed scrutinization and planning of risk management along with risk assessment, manipulating, controlling, cross checking is included in the risk management file. Apart from this, identification of risk after marketing of the device is added in this file. This file is substantially changed with current data. For example, finding of new risk, alteration on risk level of any hazard. This hazard risk management file is submitted to the FDA.

7. CONCLUSION:

In this review article, we propose characterizing a medical device as "A creation planned and manufactured for use in medical care, and not exclusively only in therapeutic or nourishing." Existing administrative groupings of medical device are complicated and planned fundamentally for regulators. Devices that consolidate with medicines should be expected to fulfill similar administrative guidelines as restorative items. Alongside by US medical device guideline, there is a rising harmonization of global principles between EU medical device directives and US-FDA necessities. This paper propels the current literature tending to the FDA guidelines and DfX by giving a particular outline of the guidelines and proposing another DfX idea. DfX techniques which are relevant to medical device, while DfFDA rules are created with a premise on the design of the guidelines, basic elements recognized for improvement and contemporary issues as the difficulties with advancement. This article exhibits that a couple of specific biomedical applications could help us to keep away from the medical device failures. The performance analysis of medical device can help to prevent the large issues. In addition, risk analysis and risk management of medical device is also necessary to prevent harm/ negative effect to patient.

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