

ARTIFICIAL HEART VALVES

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BMEN 5800 SECTION 001 - TOPICS IN BIOMEDICAL ENGINEERING

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May 10, 2023

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1. Introduction:

Artificial heart valve is a medical device used in case of replacing faulty valve through diagnosing dysfunctional contexts involved within the human heart. In this case, ***bioprosthetic artificial heart valves*** have been recognized as one of the potential artificial heart valve devices marketed for treating damaged heart valves due to heart disease. This bioprosthetic heart valve is considered to be one of the potential contexts associated with the determination of functioning property. Bioprosthetic heart valves in the market and regulatory consideration have been defined as the condition through the regulatory landscape. Implication of the regulatory prospect is involved with the area of defining marketing authorization conditions.

2. Purpose and scope:

The purpose of using ***bioprosthetic artificial heart valves*** is related to the condition of treating Minimally Invasive Surgery (MIS) and Open Surgery to reduce the risk of cardiovascular complications. Bioprosthetic heart valve is considered to be a specific treatment procedure to reduce the risk of congenital disorders resulting in valve dysfunction (Frankel & Nguyen, 2021). In this study, the major purpose and scope of this report is associated with the clear demonstration of regulatory strategy defining the condition for improving the overall health prospect. In this case, developing understanding for the clinical trial under the sponsorship of regulators can provide marketing approval through highlighting the safety and security of utilizing such devices in case of a medical system.

Regulatory strategy is correlated with FDA (Food and Drug Administration, USA) to complete the investigation through considering a potential group of population involved with the context of implementing a bioprosthetic heart valve. Implication of safety and security screening for the marketing approval is addressed through the FDA-oriented regulatory strategy such as Food and Drug Administration Modernization Act of 1997, Cures Act in 2016, and the Food and Drug Administration Safety and Innovation Act of 2012 (Mack & Adams, 2020). Pre-marketing approval based on the consideration of FDA approval has been defined through the implication of regulatory strategy in medical device approval. Device safety and security through post-marketing activity has been provided through FDA in lowering burdensome among the patient group. In collaboration with FDA, Center for Device and Radiological Health (CDRH) have provided proficiency in promoting the medical device innovation according to the regulatory science derivation in patient confidence development by marketing in the U.S. through regulatory pathways (fda.gov, 2023).

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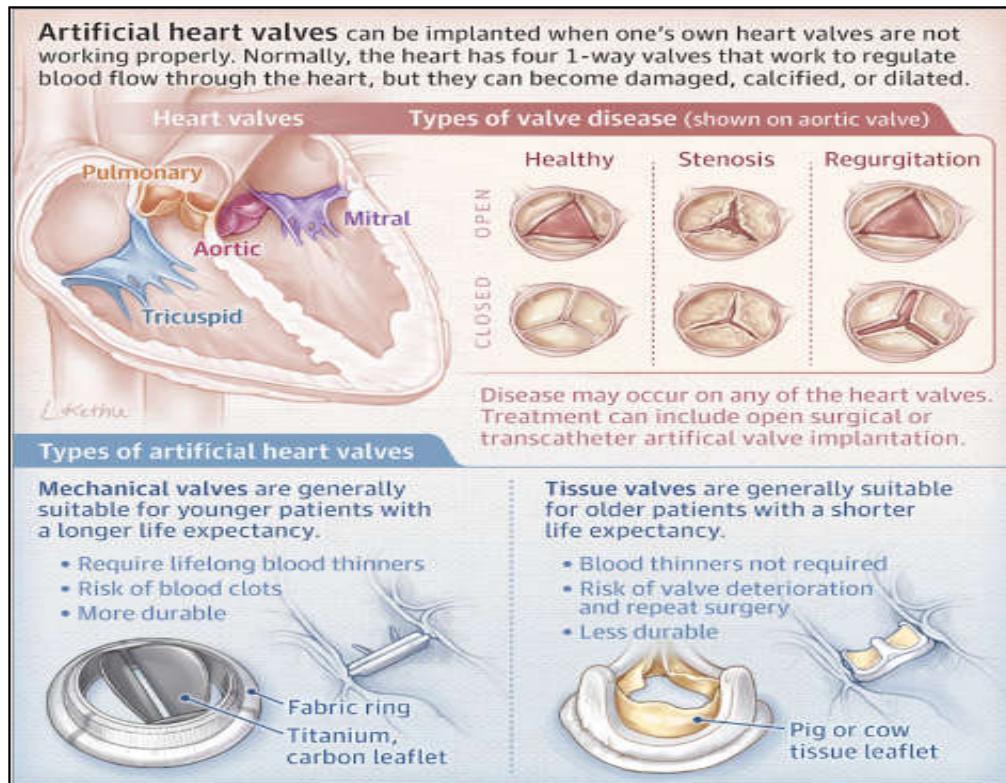


Figure 1: Artificial heart valve and their operation

(Source: Frankel & Nguyen, 2021)

3. Background:

Implication of the first artificial heart valve is derived by Dr. Charles Hufnagel in 1952, operated in a long-run success of the artificial valve transplant. Thus successful trials are responsible for turning the advanced medical department to grow for the strategy to support the artificial organ development. A silicone elastomer ball stored in the metal cage of an artificial heart valve allows blood to flow appropriately through the increasing blood pressure. Development of the bioprosthetic heart valve development has reflected the condition of structural valve development to achieve the improved modality of the heart valve replacement condition inside a human being (Mathew & Kanmanthareddy, 2019). Implanting artificial heart valves is associated with the aspects of limiting the use of anticoagulation in this case of valve replacement. In the case of bioprosthetic heart valves, high risk of mortality has been observed due to the limited chances of grafting in surgery of valve replacement (Ryu & Tran, 2022). A condition of the complicated outcome has been derived through the structural valve deterioration involved with different age groups. Effectiveness of the bioprosthetic artificial heart valve has provided the implication of successful surgery in bringing the healthy outcome for patients with the complicated heart disease.

4. Technical characteristics and real world need:

Components of bioprosthetic artificial heart valves (BHV) are involved with the bovine pericardium preserved with glutaraldehyde or porcine heart valves used for treating the valve replacement in case of degenerative valve functionality. Technical characteristics of BHV are associated with the superior hemodynamic properties included with the reduced thrombogenic nature (Kostyunin *et al.* 2020). In case of defining real-world need, BHV is involved with the treatment for structural valve degeneration including the complication in grafting procedure as an immunogenic response. According to this prospect, BHV is responsible for attempting to treat the degenerative nature of the valve degeneration associated with heart valve dysfunctionality. As per the view of Mathew & Kanmanthareddy, (2019) application of the BHV is involved with the technical component development such as biological durability, improved optimal hemodynamics, optimal delivery process along with the elimination of biological reaction to the artificial heart valve implanted to a patient.

5. Critical attributes of device:

Critical attributes of the artificial valve have been associated with the components involved with the medical condition of treating valvular disorders. Majority of the population across the globe has raised the consciousness involved with the bioprosthetic heart valve involved with the treatment of valve dysfunction. There are different types of BHV available in the medical field such as **Stented, Percutaneous, and Stentless bioprosthetic heart valve**. Stented bioprosthetic valve is associated with the designs of anatomy of the native aortic valve made up of porcine heart valves involved with 3 porcine aortic valves cross-linked with glutaraldehyde. Stented bioprosthetic valves are related to the critical attributes mounted on the area of polymer supporting stent or metallic stent. A Whole porcine aortic valves or bovine pericardium fabrication have been used for the stentless bioprosthetic heart valve development. Symptomatic aortic stenosis involved with the high operative risk has been responsible for considering percutaneous heart valves. Percutaneous transfemoral approach is involved with the implantation procedure of the artificial heart valve. Implication of the symptomatic aortic stenosis is associated with the context of fabricated consideration of the bioprosthetic heart valve. **Carpentier-Edwards valves** are associated with the derivation Porcine models of artificial grafting of the heart valve implantation in case of the valvular disorders. Glutaraldehyde has been associated with the consideration of bovine pericardium preservation for the context of critical component involvement for the bioprosthetic heart valve.

6. Clinical and performance data available:

In the USA, clinical and performance data availability has been manifested through the authentic websites and databases involved with the identification of safety and security of the medical devices in the concerned market. In the case of the medical device market, regulatory requirements and implication actions have been considered by ***The European Medical Device Regulation (EU-MDR)***. Emergence of the Post Market Surveillance (PMS) is responsible for defining the consideration for ***Post Market Clinical Follow-up (PMCF)*** that helps to demonstrate the effectiveness of searching for the clinical and performance data involved with a medical device. Addressing the specific records throughout the product life cycle has been considered through the proactive accessibility of the safety and security of the medical devices in the current market through the PMFC surveys. It is effective to imply the PMFC surveys according to the collection of randomized control trials including the collection of evidence provided through the PMFC survey evaluation in case of understanding the market of medical devices. The PMFC survey consists of the GDPR complaints including the EU regulations associated with the consideration of effective policy development through the consideration of performance data availability.

Moreover, government-based medical device databases are considered through the effectiveness of post marketing activities related to the context of safety and security determination through the post-marketing survey of the medical devices. Medical device databases through FDA are involved with the consideration of information for 522 postmarket surveillance based on the device information and the manufacturer details (fda.gov, 2022). For instance, ***Devices@FDA*** is involved with the derivation of the clear and rigid information provided for the medical device oriented information. Multiple databases are used by Devices@FDA such as 510(k)s involved with pre marketing information including pre marketed approval (PMA) (fda.gov, 2022). ***Humanitarian Device Exemption (HDE) Class III medical devices*** are provided through the implication of clinical and performance data in the FDA approved databases. Unique Device Identifiers (UDI) of the medical devices are submitted to the FDA databases to promote the identification information involved with the medical devices. Moreover, summary and medical device transcripts are related to the determination of historical information regarding the medical devices through CDRH. ***Code of Federal Regulations (CFR) Title 21 - Food and Drugs*** from FDA has provided the context of recent revision of the government approved information regarding the medical devices. De novo classification order

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has been associated with the consideration of route to classify the order of the considered devices.

7. Overview of regulation:

Medical devices such as bioprosthetic heart valve consideration and marketing approach can be supported by the approval derived through the area of assurance developed by the identification of safety and security through regulatory controls of FDA. **The Federal Food, Drug, and Cosmetic Act (FD&C Act)** is responsible for marketing approvals of the medical devices in the USA market followed by the implication of **Title 21- Code of Federal Regulations (21 CFR) Parts 1-58, 800-1299** to support the regulatory pathways (fda.gov, 2022). Multiple steps are associated with the regulatory pathways promoted by the marketing approval of medical devices through the FDA approval procedure. **510(k) premarketing notification, medical device classification by De Novo, Exempt, PMA, Humanitarian Use Exemption (HDE), Product Development Protocol (PDP) and Biologics License Application (BLA)** are classification of different steps involved with the procedure of marketing regulation of the medical devices.

Premarketing approval or PMA of the medical device are involved with the procedure of marketing the device in US market through multiple steps such as, **Step 1: Classification of device and regulatory control identification, Step 2: Premarket submission, step 3: Submitting premarket application in FDA, Step 4: Registration and device licensing through regulatory controls.** In case of device classification by FDA, section 201(h) of the Federal Food, Drug and Cosmetic (FD&C) Act helped in determination of medical devices. Categorizing the medical device in class I, II, and III and their premarketing approval submission type follows different regulatory pathways.

Class	Risk	Potential Harm	Regulatory Controls	Submission Type or Exemption
I	Lowest	Present minimal potential for harm	General	510(k) 510(k) Exempt
II	Moderate	Higher risk than class I devices	General and Special (if available)	510(k) 510(k) Exempt
III	Highest	Sustain or support life, are implanted, or present potential unreasonable risk of illness or injury	General and PMA	PMA

Figure 2: Classification of medical devices and their submission types based on different regulations (Source: fda.gov, 2022)

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21 CFR parts 1000-1050 regulation is assembled with the radiation-emitting electronic product to specify the safety and security of the medical device while making it available to the US market. "Substantially equivalent" is provided by the premarketing approach of the 510(k) contexts through identifying the safety and security of the medical devices. According to 510(k), class I and most class II medical devices are exempted from the list based on the evaluation of the predictive devices through the limitations of exemption based on **21 CFR xxx.9**. A premarket submission is promoted through the PMA submission based on the class III medical devices. Device Advice Premarket Approval (PMA) has been promoted through the accumulation of the relevant evidence provided for the medical device. **Evaluation of Automatic Class III Designation (De Novo Process) Summaries and FD&C Act, section 513(f)(2)** are considered through the De Novo submission process for the medical device approval and regulatory controls. **Humanitarian Use Device (HUD)** is considered through the process of HDE application submission for the class III medical devices intended to identify the safety and security of the devices.

Design Controls under the Quality System Regulation (21 CFR 820.30) is considered for the context of identifying the safety and security of the Class II and class III devices. Good **Laboratory Practices (GLPs) in 21 CFR 58** is involved with the non-clinical testing procedure in the medical devices that are considered for the pre medical approval considered for the health and security through the regulation. However, according to the FDA regulation, voluntary **Accreditation Scheme for Conformity Assessment (ASCA) Program** has been suggested by FDA to adopt the manufacturers to support the condition of premedical approval for safety and security of the medical devices.

8. Regulatory analysis:

Controlling, monitoring and regulatory control of the medical devices are considered through the involvement of CDRH regulations promoted by the FDA. In this case, regulation of the medical and non-medical procedures related to the manufacturing of the medical devices are controlled and monitored for the safety and security of the end users through CDRH regulations. Meanwhile, classification of the medical devices according to the severity and risk has been considered through the Class I, II, and III devices. In this condition, CDRH regulation and control has been increased by the class I to class III devices according to the activities (fda.gov, 2020). It is reported that class II medical devices are required to pass through the premarketing notification through the 510(k) submission procedure followed by exempt of the class I devices

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from premarketing notifications. **21 CFR Part 807-Establishment Registration** is required to comply with the manufacturer of the medical devices across the country (Jagadeeswaran *et al.* 2022). Manufacturers of the medical devices are required to follow **21 CFR Part 807** to accomplish the procedure of medical device listing prospects through the identification of the efficient strategy to advance the regulatory strategies. However, application of **21 CFR Part 807 Subpart E** is responsible for highlighting the premarketing notification through the 510(k) which delivers a letter regarding the substantial equivalent involved with the procedure of premarketing approval. **Fee and Modernization Act of 2002** has been involved with the charging of an efficient fee related to the procedure of premarketing approval submission to receive the substantial equivalent to market the device in the USA. **21 CFR Part 814** implication has been involved with the derivation of efficient procedure to accumulate the PMA approach to provide the substantial equivalent to the Class III or high risk-oriented devices to treat an injury or a disease (Kanti *et al.* 2022). Clinical study and evidence collection on the safety and security of the medical devices and their usage has been defined through the implication of **21 CFR Part 812** to provide investigational device exemption (IDE). Manufacturing of the medical device including the quality control, packaging, purchasing, storing, and installing of a medical device in the US market has been accumulated through the implementation of the regulation **21 CFR Part 820** under **Quality System Regulation (QS regulation)**.

9. Analysis of predicate device:

Predicate device is considered to be the approved medical device running in the US market through the 510(k) submission addressed through a comparative analysis involved with the new medical devices seeking approval in the current market. 510(k) provides opportunity to identify clear information and evidence regarding the medical devices marketed in the US medical field to provide support to the new medical devices. 510(k) databases are used to search for the details and information involved with the medical devices progressed through the implication of the **Product Code Classification Database** (fda.gov, 2018). CFR regulation, product code, and identification details regarding a predicate device has been promoted through the 510(k) databases. However, **21 CFR 888.1100, arthroscopy** has also been considered through the FDA approval system promoted by the 510(k) submission type. Analysis of the predicate device is involved with the regulation considered in the FDA regulation through indicating the multiple implication of the procedure such as identification of device name, types, manufactures, and post amendment details involved with the 510(k) database (Zhu *et al.* 2020). Generic category of the predicate device within the FDA has been identified through the implication of substantial

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equivalence of the medical devices related to the context of utilizing “Procode”. The 510(k) database in this case is responsible for defining the condition of technological characteristics identification for the predicate medical devices to alleviate the searching procedure for the medical device approval.

10. Regulatory strategy:

Implication of the 510(k) regulatory system is involved with the context of the premarketing notification submission process approached through the new medical device in the US market. Consideration of the reference sources to define the safer use of the medical device in case of any injury or health complication has been directed through the predicate device analysis by FDA. **FDA's Special and Abbreviated 510 (k) programs** have considered the regulatory strategy development for the draft submission for the medical device approval in the concerned market of the US medical field (Darrow *et al.* 2021). Implication of **The Medical Device Amendments (MDA) (Pub. L. 94-295)** is responsible for considering the (FD&C) Act to classify the medical devices in further demonstration of the risk involvement in the marketing approach.

11. Recommended next step:

Recommended steps for the marketing approval for medical devices for bioprosthetic heart valves can be associated with the identification and differential category demonstration of the similar devices through the 510(k) premarketing notification. Technological advancement and their implication should be considered through the identification of predicate devices existing in the US market. **Section 513(a)(1) of the FD&C Act (21 U.S.C. § 360c(a)(1))** needs to be considered to understand the classification of the particular medical device (Hagie *et al.* 2019). Need and requirement for the medical use of the device can be considered through the next step of FDA approval through defining the indication for usage. Validity, reliability, and accessibility of the medical device should be considered through the implication of 510(k) notification on predicate medicines in the next recommended step.

12. Additional action:

FDA's 21 CFR 820, Quality System Requirements, including the procedure for Device licensing and US establishment registration listing is required for the additional action attempted by the medical device in this case. Implication of **ISO 13485:2016** will be efficient to address the quality control requirements (Jalnasow, 2019).

13. Conclusion:

Marketing of the medical device is required for the consideration for screening and approving the safety through the regulatory body of the US through FDA. Bioprosthetic heart valve, to treat the valvular disorder can be progressed through FDA based regulatory bodies to support the safety and quality of the medical device.

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