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Review Article

A Study of Regulatory Requirement for Registration Process for Breast Implant Medical Devices as per European Medicinal Agency

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Abstract

One of the key causes of the breast implant market is the rising prevalence of breast cancer around the world. Breast cancer has surpassed lung cancer as the most commonly diagnosed cancer worldwide, according to GLOBOCAN 2020. According to the World Health Organization, around 2.3 million women will be diagnosed with breast cancer in 2020, with 685,000 of them dying. In addition, over the last five years, over 7.8 million women have been diagnosed with breast cancer. Breast cancer was found to be so common in Asian women that it accounted for 22.9 percent of all cancer cases in women in 2020. The increased inclination and knowledge of women globally toward breast augmentation is another factor that is predicted to promote the market's growth.

Keywords: Plastic Surgery; Breast Augmentation; Recombinant Surgery; Implants

Introduction

Medical devices

Medical Devices are defined as any instrument, apparatus, appliance, software, material, or other article, whether used alone or in combination with or without software, that is used for human beings for the diagnosis, prevention, treatment, or alleviation of disease, as defined by the Medical Devices Directive 93/42 EEC [1].

Medical Devices are Classified taking into account the intended purpose of the Devices and Their inherent risks. Classification shall be Carried out in accordance with Annex VIII.

Medical equipment are classified according to the European Union's classification system [2].

Classification	Risk	Description	Examples
Class I	Low	The vast majority of non-invasive gadgets that do not interact with the human body.	Hospital beds, bed pans Sterile plasters
Class IIa	Medium	It is generally intrusive but confined to natural orifices, and it becomes a class	Thermometers, weighing scales,
		IIb if it is dangerous to a patient.	Diagnostic equipment
Class IIb	Medium	The majority of surgically invasive/active devices can only be partially implanted in the body.	Infusion Pump, Ventilators, Surgical lasers
Class III	High	A device that is either directly connected to the Central Nervous System or includes a medical substance.	Many implants: vascular Neurological, replacement heart valves, silicone gelfilled breast implants.

Table 1

Implants

Medical implants are devices or tissues that are implanted either inside or outside the body. Many implants are prostheses, or artificial body components that are meant to replace missing bodily parts. Other implants help organs and tissues by delivering medication, monitoring biological functioning, or providing assistance [3]. The various types of implants are described as below.

- Implantable cardioverter defibrillators
- Artificial Hips
- Heart pacemakers
- Breast implant
- Coronary Stents
- Ear Tubes

The Various type of breast implants [4]

- Saline breast implants
- Structured saline breast implants
- Silicone breast implants
- Gummy bear breast implants
- Round breast implants
- Smooth breast implants
- Textured breast implants.

Construction of breast implants [6]

Saline filled breast implants

Silicone rubber shell made of polysiloxane(s), such as polydimethylsiloxane and polydiphenylsiloxane, is inflated to the required size using sterile isotonic saline in a saline-filled breast implant. The shell surface, shape, profile, volume, and thickness of saline-filled breast implants can all vary.

The sterile saline used as a filler material should meet USP criteria for Normal Physiological Saline (injection grade), which has a concentration of 0.15M and a pH of 7.2-7.4 and a concentration of 0.15M.

Silicone gel-filled breast implant

Silicone gel-filled breast implant consists of a silicone rubber shell consisting of polysiloxane(s), such as polydimethylsiloxane and polydiphenylsiloxane, that is filled with a predetermined amount of silicone gel. The shell surface, shape, profile, volume, and thickness of silicone gel-filled breast implants may vary.

The authorized design for silicone gel-filled breast implants is now a fixed volume implant with a single lumen carrying a fixed amount of silicone gel that can be curved or spherical, textured or smooth, and filled with silicone gel of different viscosities.

Comparison of saline and silicone breast implants [10]

Silicone Breast Implant	Saline Breast Implant
Silicone Breast implant are approved by the FDA in 2006	Saline Breast implant are approved by the FDA in 2000
Silicone Breast Implants was gel filled inside and outer surface is Silicone shell	Saline Breast Implants was saline filled with silicone shell
Silicone implant has lower Chance of rippling and Natural Feel and appearance	Saline Implants are Inserted empty and allowing for More discreet incisions
If the Silicone implants are rupture removal Silicone is Typical required	Saline Implants rupture occur the saline water was Absorbed in the body and its Causes harmlessly by the body

Table 2

Figure 1

Figure of saline implants and silicone implants use of breast implants [9]

A mammoplasty surgery is used to insert breast implant devices for three reasons.

- Replacement of breast tissues that have been destroyed by trauma (blunt, piercing, blast), disease (breast cancer), or failed anatomic development (tuberous breast deformity).
- Revision and reconstruction: the outcome of a previous breast reconstruction operation is revised (corrected).
- Major augmentation: to improve the size, shape, and feel of the breasts aesthetically.

Risk of breast implant [8]

Some of the complications and adverse outcomes of breast implants include:

- Implant Complication
- Additional Surgeries
- Capsular Contracture
- Rupture and Deflation
- Breast Implant associated-anaplastic large cell lymphoma (BIA-ALCL)
- Connective Tissue Disease
- Systemic Symptoms
- Breastfeeding
- Effect on Children

Introduction to European Union [11,12]

The European Union is the legally recognized successor to the European Community. The EU is a legal entity that consists of an economic and political union of Member States. The European Council is made up of the 27 EU member states' heads of state or government, as well as the President of the European Council (who chairs its meetings) and the President of the European Commission.

In 2012, Austria, Belgium, Bulgaria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom were all members of the European Union.

Pathway for registration of drug [13]

Presently different countries must follow different regulatory requirements for sanction of new drug. Marketing Authorization Application (MAA) a single regulatory approach is valid to various countries is almost a difficult task. Therefore, it is essential to have knowledge about regulatory requirement for MAA of each country.

There are mainly four procedure in European countries for marketing

- Centralized Procedure
- Decentralized Procedure
- Mutual Recognition Procedure
- National Authorization Procedure

Challenges and opportunities for breast implant

Global breast implant market [15]

Type (Silicone Implants, Form-stable Implants, Saline Implants, and Structured Saline Implants), Application (Reconstructive Surgery, and Cosmetic Surgery), End User (Hospitals, Cosmetology Clinics, and Other End Users), and Geography are the segments that make up the Breast Implant Market (North America, Europe, Asia-Pacific, Middle East and Africa, and South America). During the forecast period, the breast implant market is expected to grow at a CAGR of 5.3 percent (2022-2027).

Demand for breast implant in EU [14]

By 2027, the European breast implant market is estimated to have grown from US$ 381.67 million in 2019 to US$ 537.25 million. From 2020 to 2027, the market is expected to develop at a CAGR of 4.6 percent.

In Europe, breast augmentation is the most popular cosmetic operation. Women, on the other hand, are most concerned about their safety when it comes to getting breast implants. As a result, organisations have taken a number of steps to increase the safety of breast implants.

Market opportunities for breast implant in EU [16]

Silicone breast implants are a popular choice among women considering a breast augmentation operation because they appear firmer and more attractive than saline implants. Breast implants are available in a variety of sizes and forms, ranging from low profile to high profile. Round breast implants are the most common and continue to be the most popular choice among women who

have their breasts augmented. Various Company Engaged in Manufacturing of Breast Implant.

- Allergan
- Mentor Worldwide LLC
- GC Aesthetics Plc
- Sientra, Inc
- Groupe Sebbin SAS
- Polytech Health and Aesthetics GmbH
- Establishment Labs S.A
- Hans Biomed Co, Ltd
- Cereplas.

European regulatory framework [17]

Medical devices and *in vitro* diagnostic medical devices play a critical role in saving lives by delivering cutting-edge healthcare solutions for disease diagnosis, prevention, monitoring, prediction, prognosis, treatment, and relief. The European regulatory framework assures the safety and effectiveness of medical devices while also making it easier for patients to obtain them on the European market. Two new Regulations will replace the three existing Directives in the future years to keep up with breakthroughs in science and technology. With approximately 500 000 types of medical equipment and *in vitro* medical devices on the market, the European Union (EU) boasts a competitive and inventive medical devices sector.

Four directives presently govern medical devices and *in vitro* medical devices on the EU market:

- Directive 90/385/EEC on Active Implantable Medical Devices (AIMDD)
- Directive 93/42/EEC on Medical Devices (MDD)
- Directive 98/79/EC on *in vitro* Diagnostic Medical Devices (IVDMD)
- Directive 2007/47/EC amending Council Directive 90/385/EEC relating to active implantable medical devices and Council Directive 93/42/EEC concerning medical devices
- CE Marking [20,21].

Many products traded on the European Economic Area's expanded Single Market bear the letters 'CE' (EEA). They indicate that products supplied in the European Economic Area have been evaluated to ensure that they fulfil stringent safety, health, and environmental protection standards. The letters CE (as a logo) on commercial products indicate that the producer or importer certifies that the product complies with European health, safety, and environmental protection regulations. It's not a certification mark or a quality indication. The CE marking is needed for goods sold in the European Economic Area (EEA), although it can also be seen on products made to EEA standards that are sold elsewhere.

Steps required for CE marking [21]

The CE Marking Process involve following the Steps:

- Identify the Applicable Directives
- Identify the Applicable Requirement of the Directive
- Identify an appropriate Route of Conformity
- Assessment of the Products conformity
- Compile the Technical File
- Make a Declaration and Affix the CE Mark

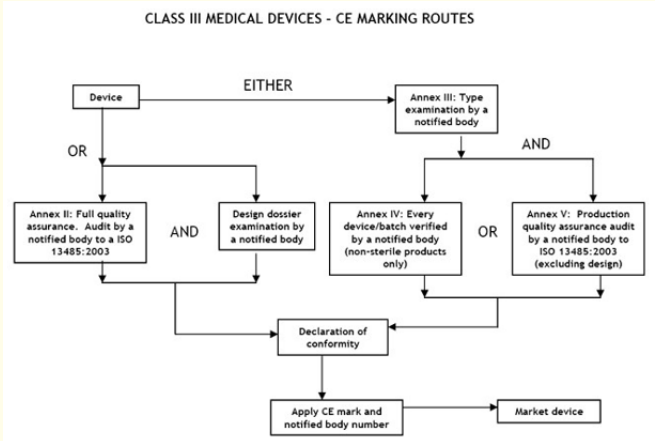

Figure 2: Flow Chart for the Conformity Assessment procedure provided for in Directive 93/42/EEC on Medical Devices.

Possible registration pathway for registration of breast implant

The Commercial Distribution of The Breast Implant Included the Preparation of Technical File and According to The Summary Technical Document of The Global Harmonization of Task Force.

The Below is Document and Data Required for The Submission in the Technical Fie Documentation they are Mentioned as Below.

Steps for class III medical devices compliance

- Classification: Ensure the Devices is a Class III Medical Devices
- Choose Conformity Assessment Route
- Compile the Technical File
- Obtain The Certification from a Notified Body
- Declaration of Conformity
- Appoint an Authorized Representative
- Vigilance and Post market Surveillance.

Case studies of breast implant

Title: US FDA breast implant post approval studies

Objective

To analyze the long-term safety and efficacy outcomes of patients with breast implants Summary Background Data: The safety of silicone breast implants is still being studied. Despite the high number of patients with breast implants studied in major post approval studies (LPAS) by the US Food and Drug Administration, this database has not been properly analyses or reported.

Methods

This is a cohort study with multiple sites. LPAS prospectively monitors long-term implant related outcomes and systemic hazards for silicone/saline implants implanted for primary/revision augmentation/reconstruction from two manufacturers (Allergan and Mentor). The researchers compare systemic harms, self-harm, and reproductive consequences to normative data. In the short and long term, implant-related problems are analysed by implant composition and operational indication.

Results

The LPAS data covers 99,993 patients, with silicone implants accounting for 56 percent of primary augmentation implants. Long-term magnetic resonance imaging monitoring accounts for less than 5% of all cases. Silicone implants are linked to greater frequencies of Sjogren syndrome (SIR8.14), scleroderma (SIR 7.00), rheumatoid arthritis (SIR 5.96), stillbirth (SIR4.50), and melanoma (SIR4.50) when compared to normative data (SIR3.71). A single instance of BI-ALCL has been recorded. There is no link between the two. In the short term, saline causes more rupture (2.5 percent vs. 0.5 percent, P 0.001), and silicone causes more capsular contracture (5.0 percent vs. 2.8 percent, P 0.001). The reoperation rate for primary augmentation is 11.7 percent at 7 years, and 25 percent for primary/revision reconstruction. Capsular contracture (III/IV) is the most prevalent reason for augmentation reoperation, occurring in 7.2 percent of primary augmentations and 12.7 percent of primary reconstructions.

Conclusion

Breast augmentation is a very popular cosmetic procedure, and based on current trends, it is likely that its popularity will continue to rise. More than 34% of American women are unhappy with their breast size or shape and are considering augmentation.

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