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REGULATORY CHALLENGES IN APPROVAL OF MEDICAL DEVICES IN ICH AND SELECTED COUNTRIES, FOR BETTER REGULATORY DELIVERY

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ABSTRACT

Ensuring the availability of quality drugs and health products starts with effective management at the national level. The word "medical devices" will cover wide range of products, from simple depressors of tongue to cardiac stents. As the safety & effectiveness of medical devices is critical to human health, the products must be regulated by stringent regulations categorized on different levels of risk. The objective of this study is to identify the regulatory challenges in ICH and selected countries which include India, South Africa, Brazil, Singapore and Saudi Arabia and address them for better regulatory delivery with special emphasis on regulatory changes in these countries & the current status of global medical device harmonization. To identify the challenges faced by Medical device regulatory affair professional while filling the application for approval around the world and to address the challenges of Medical device products in emerging markets (Brazil, Singapore, Saudi Arabia and South Africa) and medical device industry stakeholders and gathered their responses and drawn. The study realized that medical device regulations around the world is very diverse and regulatory Affairs professional's primary challenge is the absence of regulatory harmonization across distinct Geographical locations. Different stakeholders from industries express that all information is not available on the website of emerging countries for filling of the complete application. Medical devices depend on computer software to carry out their tasks, the question of whether the software itself can be recommended as "medical device"? Unfortunately, software as medical device cannot be put on the market without first passing

regulatory audits to confirm that the product is safe and efficient and Association of Southeast Asian Nations [ASEAN] Is going to play a major role in harmonizing regulatory guidelines for medical devices and sensitize international best practices and provides WHO technical support to national regulatory authorities.

KEYWORDS: Harmonization, Transparency, International Medical device Regulatory Forum.

1. INTRODUCTION[1-3]

Medical devices play a decisive role in healthcare provision. For emerging nations, demand for medical devices is rising at a comparatively faster pace compared with advanced countries. Increased income, ageing, and health awareness in developing countries are key factors that support global market growth in the near future. According to the USFDA website, in 2017 and 2018 respectively about 27 and 54 new medical devices were licensed and approved by the FDA. Technological advancement and increasing demand for Innovative therapy application to address unmet healthcare needs considered to be another factor in the forecast period driving growth in the medical device industry.

All medical devices should meet accepted international quality and safety requirements. To formulate regulations for medical devices, an understanding of the various standard-setting frameworks, the mechanisms used to determine standards and their use in conformity assessment is important. So there is need to study the Regulatory challenges of medical devices in ICH and selected countries, for better regulatory delivery.

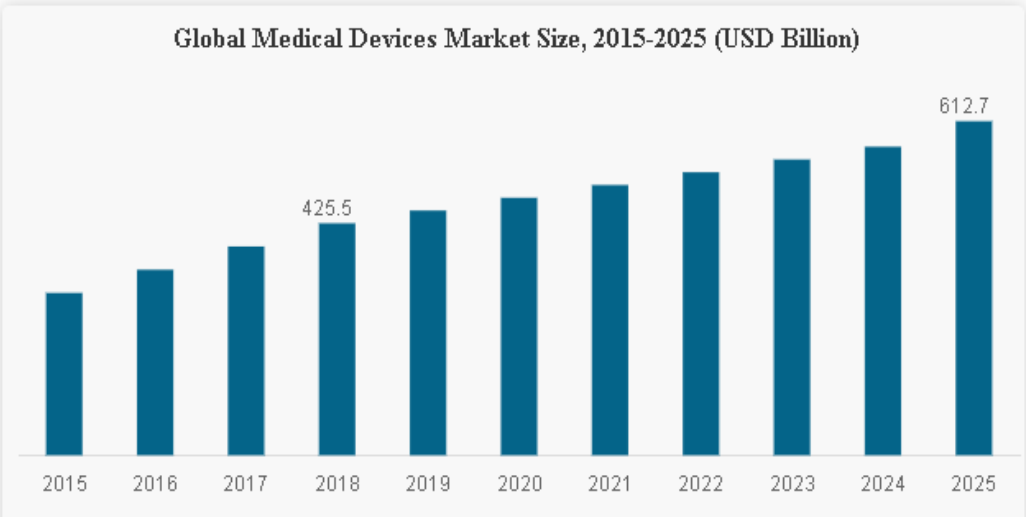


Figure 1: Global Medical Devices Market Size, 2O15-2025.

What is "Medical Device"?

Medical device" is defined as any instrument, apparatus, 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 1 or more of the specific medical purpose(s) of:

- Illness diagnosis, prevent, control, recovery/relief
- Diagnosis, diagnosis, care, accident recovery and/or compensation
- Investigating, removing, altering or endorsing anatomy or a physiologic method
- Help or support life
- Conception management
- Medical devices being disinfected

Table 1: Classification of medical device.

Classification of Medical device		
Countries	**Regulatory Agency**	**Classification**
USA	US-FDA	Class I, II, III
EUROPE	European Medicines Agency(EMA)	Class I, IIa, IIb, III
JAPAN	Pharmaceutical and Medical device Agency(PMDA)	Class I,II,III,IV
SOUTH AFRICA	South African Health Products Regulatory Authority	Class A,B,C,D
SAUDIARABIA	Saudi Food and Drug Authority(SFDA)	Class I, IIa, IIb, III
SINGAPORE	Health Science Authority	Class A,B,C,D
BRAZIL	Agência Nacional de Vigilância Sanitária (ANVISA)	Class I,II,III,IV
INDIA	Central Drug Standard Control Organization(CDSCO)	Class A,B,C,D

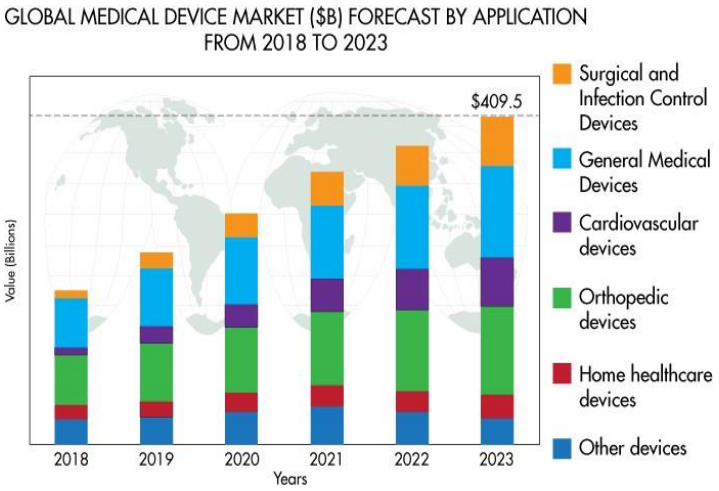


Figure 2: Global medical device market (Billion) forecast by application from 2018 to 2023.

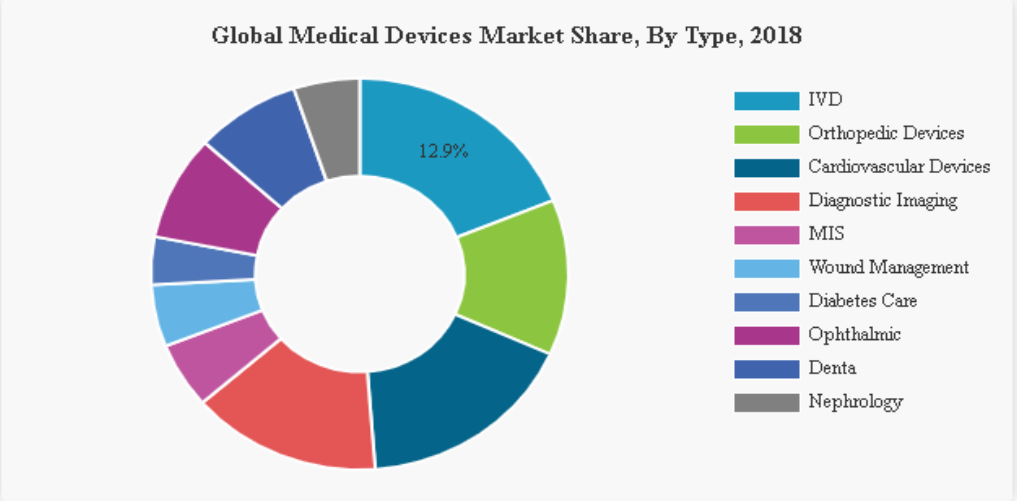


Figure 3: Global Medical Device Market Share, 2O18.

Figure 4: Standard Development Process of Medical Devices.

CLASSIFICATION AND TYPES OF MEDICAL DEVICES

It is widely accepted that there should be a method to separate medical devices intoa small number of groups, or classes, and subsequently apply different conformity assessment techniques to each class. The global adoption of a rule-based classification procedure would offer significant benefits to manufacturers, users, patients, and RAs and support global convergence of regulatory systems.

By implementing a series of principles and rules that allow a medical device to be assigned to one of four classes based on its intended use that:

- Assist a manufacturer to allocate its medical device to an appropriate class using a set of classification rules
- Allow RAs to pronounce upon matters of interpretation for a particular medical device, when required to do so. Subsequently, such classification will determine the conformity assessment procedures that will be applied to the device.

2. GOOD DISTRIBUTION PRACTICES FOR MEDICAL DEVICES[4-6]

Distribution is an important activity in the integrated supply-chain of medical device. Various people and entities are generally responsible for the product sourcing, procurement, transportation, delivery, storage, device tracking, installation, commissioning, service and maintenance, calibration, need to be appropriately managed and controlled to ensure the safety and performance of medical devices at the point of use.

Good Distribution Practices for Medical Device Principles

1. QUALITY MANAGEMENT SYSTEM
2. MANAGEMENT RESPONSIBILITY
3. RESOURCE MANAGEMENT
4. PREMISES AND FACILITIES
5. SECONDARY ASSEMBLY
6. TRACEABILITY
7. COUNTERFEIT, ADULTERATED, UNWHOLESOME OR TAMPERED MEDICAL DEVICES
8. COMPLAINT HANDLING
9. FIELD SAFETY CORRECTIVE ACTION (FSCA)

MEDICAL DEVICE PRODUCT LIFE-CYCLE

A basic product life cycle includes research, development, production, and end of life. These can certainly be expanded as needed to address a specific device design or manufacturing procedure, as well as device class, category, and classification.

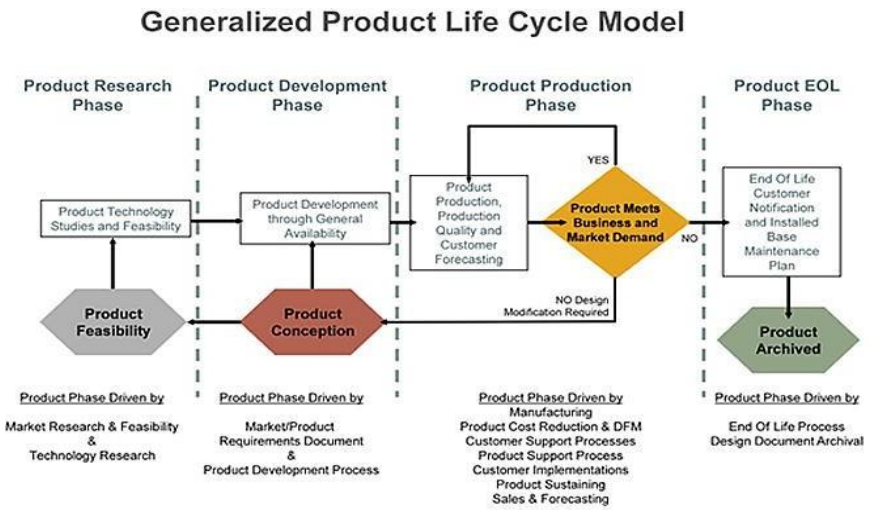
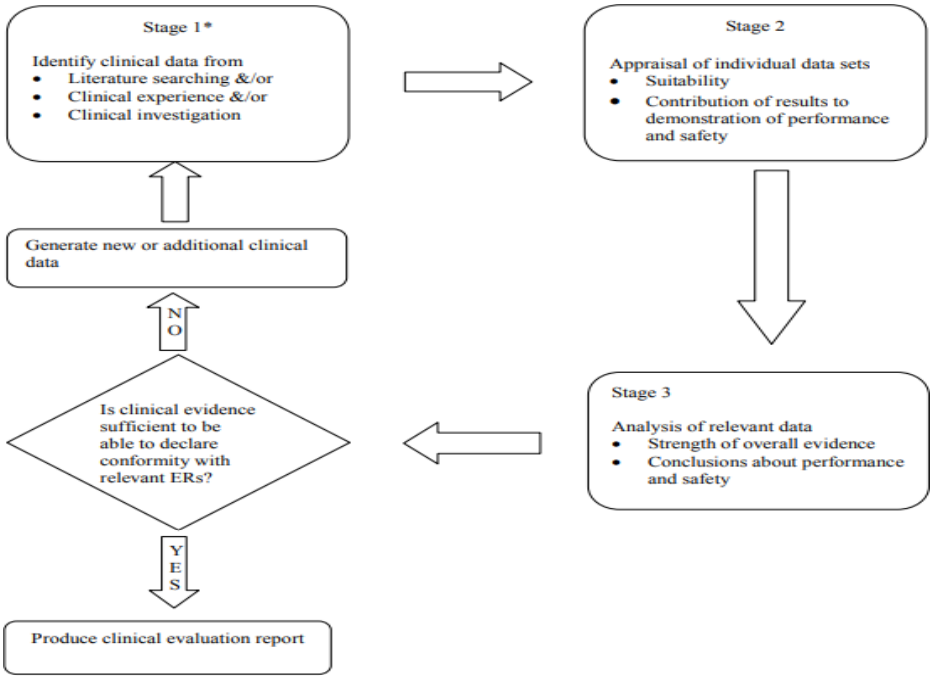


Figure 5: Medical Device Product Life Cycle.

3. CLINICAL EVALUATION PROCESS OF MEDICAL DEVICES[7]

To conduct a clinical evaluation, a manufacturer needs to:

- Identify the Essential Requirements that require support from relevant clinicaldata;
- Identify available clinical data relevant to the device and its intended use;
- Evaluate data in terms of its suitability for establishing the safety and performance of the device;
- Generate any clinical data needed to address outstanding issues;
- Bring all the clinical data together to reach conclusions about the clinical safety and performance of the device.



4. CLINICAL INVESTIGATION OF MEDICAL DEVICES FOR HUMAN SUBJECTS - GOODCLINICAL PRACTICE[8-10]

Good Clinical Practice

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.

History of ISO 14155

- ISO14155: 1996
- ISO14155: 2003 - Part1, - Part2
- ISO14155: 2009 (Revision only to annex)
- ISO14155: 2011 (harmonized with ICH GCP and other global guidelines)
- ISO14155: 201X

POST-MARKET SURVEILLANCE

Post-Market Surveillance is the collection of information on the quality, safety or performance of Medical Devices after they have been placed in the market

Subsequent to approval of an Investigational medical device, it shall be closely monitored for their clinical safety once they are marketed. The applicants shall furnish Periodic Safety Update Reports (PSURs) in order to,-

a. Report all the relevant new information from appropriate sources;
b. Relate these data to patient exposure;
c. Summarise the market authorisation status in different countries and any significant variations related to safety; and
d. Indicate whether changes will be made to product information in order to optimize the use of the product.

5. MEDICAL DEVICE REPORTING

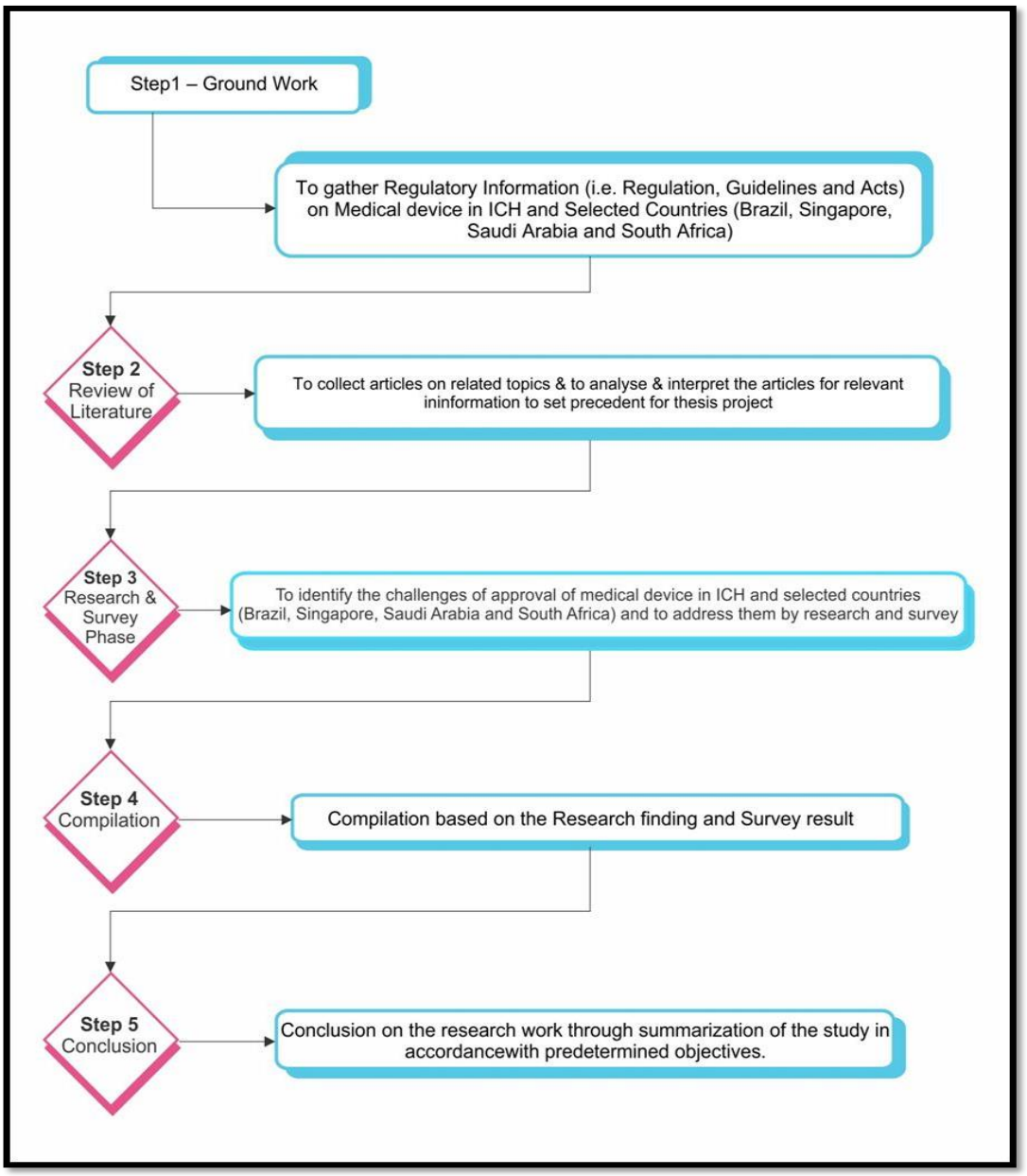
MDR is the procedure for the Food and Drug Administration to get significant medical device adverse events information from manufacturers, importers and user facilities.

Medical device adverse event/incident

- An event associated (caused or partially attributable) with the use (or misuse) of a medical device.
- An event that resulted in, or could have resulted in (had effective intervention not taken

place) serious injury, illness or death to patient, healthcare worker or other person.

- Faults that may affect the quality, timeliness and cost-effectiveness such as, problems with getting the device to operate, repeated repairs, device design and difficulty of use.



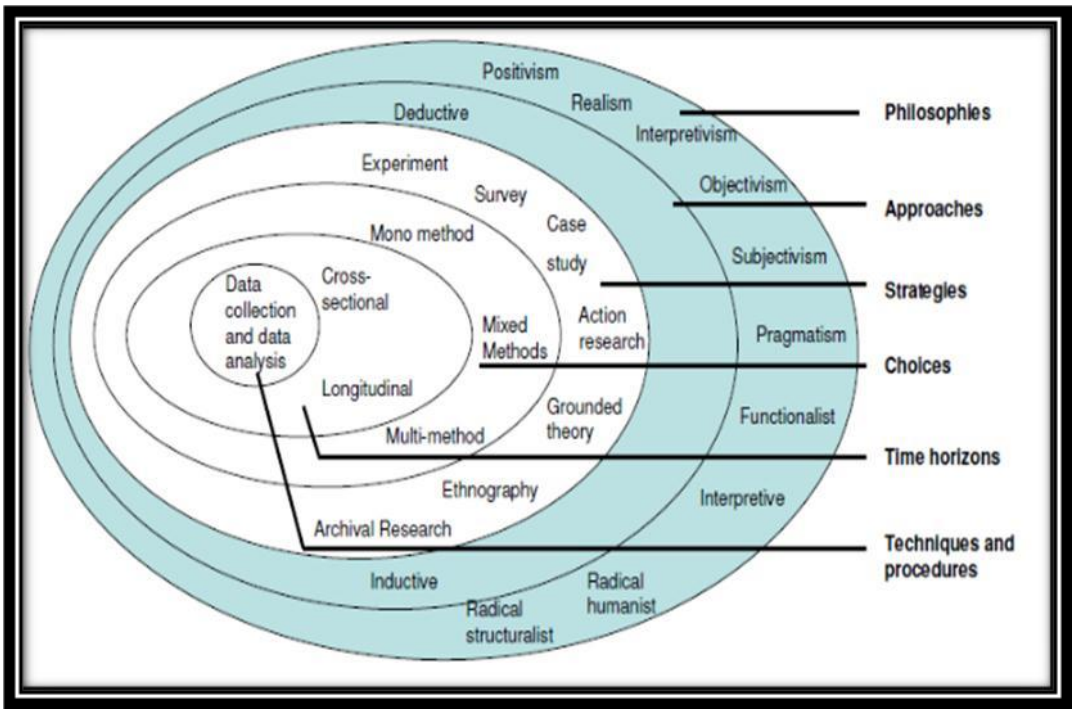
6. METHODOLOGY

Introduction

This chapter offers an extensive discussion on possible alternatives for research, strategies, time horizons, methods and information gathering procedures. The options available to the researcher are considered on the basis of the research goals, and the benefits and limitations are discussed.

Ground Work

- To identify the key regulatory agencies and regulatory websites of the selected countries
- To gather Regulatory Information on medical devices and challenges on medical devices approval.



APPROPRIATE RESEARCH METHODS

Research Philosophy

There are 4 theoretical philosophies are positivism, rationality, perception and pragmatism- according to Saunders et al. (2O12). The philosophical approach taken affects the approaches to analysis, the methodological choice and the chosen study methods (Saunders et al. 2O12). The reasoning for the methodology is given in the philosophy.

Research Approaches

According to Saunders et al. (2O12) the choice of a suitable research strategy is critical as it facilitates research design, taking into account prospective limitations. It will also assist to identify the best research approaches & decisions to solve researchissue.

Research Strategies

The method for the thesis is how to perform the work by the researcher. (Saunders et al. 2O12). Various approaches are experimental studies, research intervention, case study investigations, interviews, surveys/systematic literature review may be included. Usually,

surveys are used for exploratory & descriptive research, & encourage knowledge collection to large population.

Questionnaire Design

"The quality & reliability and response rate of the data you collect rely largely on the nature of the questions, questionnaire design & the rigor of pilot tests" (Saunders et al 2O12). Survey design is extremely significant & this part of the thesis should be given enough time. When designing the survey, the following category lists must be considered:

• Purpose of the survey
• Target audience
• Sample size
• Type of questions to be incorporated
• Method of data collection
• Data analysis

Purpose of the Survey

Literature of review had done on ICH & emerging countries which includes Brazil, South Africa, Singapore and Saudi Arabia where some of the challenges wereidentified that impact the process of regulatory approval. Some of the challenges were identified (1) Transparency of regulations of Medical device products in emerging markets (Brazil, Singapore, Saudi Arabia and South Africa), (2) No harmonization on Medical device classification (3) Evolving regulatory regulations and its impact (4) There are lack of regulators for reviewing the application submitted for the approval process.

Method of data collection

A pilot study was performed with three respondents before the survey was distributed and they were requested to give opinion on the questionnaire. They also provided suggestion and the suggestions were incorporated and got validated by them too.

Data Analysis

The study gathered quantitative information, so it needs to be processed to create it beneficial in its raw format (Saunders et al 2O12). This thesis offers graphs showing the relationships and trends in the information collected as part of the study.

Compilation

Compilation of the research work is based on the guidelines, regulation and survey results.

6. CONCLUSION

This section provided a thorough debate of the strategy adopted in philosophy and accessible study methods, strategies, time horizons methods for information collection, purpose of the study, targeted audience and limitation too. In this section author provides chosen methodology and rationalized why it is considered the most suitable.

7. REFERENCES

1. European Commission. *Guide to the implementation of directives based on the New Approach and the Global Approach.* Luxembourg: Office for Official Publications of the EC; 2000. ISBN 92–828–7500–8.
2. MDA Annual Report and Accounts 1999–2000. 2000. The Stationary Office. ISBN 0–10–556874–0.
3. MDA Business Plan 2000–2001. 2000. (available on request from MDA or on the http://www.medical-devices.gov.uk)
4. MDA Directives Bulletin No4. Conformity Assessment Procedures. 1999. available on request from MDA or on http://www.medical-devices.gov.uk.
5. Brahmaiah Bonthagarala, Regulatory Requirements for Registration of Generic Drugs in "BRICS" Countries, International Journal of Pharmaceutical Science and Health Care, ISSN 2249 – 5738, November-December, 2016; 6(6): 20-39.
6. Brahmaiah Bonthagarala, Current Regulatory Requirements for Registration of Medicines, Compilation and Submission of Dossier in Australian Therapeutic Goods Administration, International Journal of Advanced Scientific and Technical Research, ISSN 2249-9954, November-December, 2016; 6(6): 144-157.
7. Brahmaiah Bonthagarala, Comparison of Regulatory Requirements for Generic Drugs Dossier Submission in United States and Canada, International Journal of Pharmaceutical Science and Health Care, ISSN 2249 – 5738, November-December, 2016; 6(6): 1-19.
8. Brahmaiah Bonthagarala, Nanomedicine Clinical Use, Regulatory and Toxicology Issues In Europe, Journal of Drug Delivery and Therapeutics, 2019; 9(4-s): 846-848.
9. Brahmaiah Bonthagarala, A Review on global harmonization task force (GHTF) - principles of in vitro diagnostic (IVD) medical devices classification, The Pharma Innovation Journal, 2018; 7(7): 667-672. ISSN (E): 2277-7695.

10. Brahmaiah Bonthagarala, Compilation of Chemistry Manufacturing Controls In Abbreviated New Drug Application, Journal of Pharma Research, 2019; 08(08).