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Regulations for the Approval Manufacture, Import and Marketing of Medical Devices in India and Regulated Markets

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ABSTRACT

Medical devices are evolved from medical technology. Medical devices need to be of adequate quality and safety to bring public health benefits without harming patients, health care workers or the community. Countries and jurisdictions have different policies and plans in relation to the personal and population-based health care goals within their societies. Each country has their own specific regulations for medical devices, to access better health care for the public. Thus, regulations mandate that all devices whether imported or locally produced, meet international norms and standards. The term “Medical Devices” includes everything from highly sophisticated computerized medical equipment down to simple wooden tongue depressors. The intended primary mode of action of a medical device on the human body, in contrast with that of medicinal products, is not metabolic, immunological, or pharmacological.

INTRODUCTION

Medicine is the science and art of healing. It encompasses a variety of health care practices evolved to maintain and restore health by the prevention and treatment of illness[1]. Innovations in medical technology - starting from the ancients and till date – have produced numerous appliances and instruments that have been essential in diagnosis, treatment, prevention and rehabilitation, apart from pharmaceuticals. Modern medicine requires and utilizes numerous such instruments that can be used to uplift the health standards. Medical devices are evolved from medical technology. Medical devices need to be of adequate quality and safety to bring public health benefits without harming patients, health care workers or the community. Countries and jurisdictions have different policies and plans in relation to the personal and population-based health care goals within their societies. Each country has their own specific regulations for medical devices, to access better health care for the public. Thus, regulations mandate that all devices whether imported or locally produced, meet international norms and standards. The term "Medical Devices" includes everything from highly sophisticated computerized medical equipment down to simple wooden tongue depressors. The intended primary mode of action of a medical device on the human body, in contrast with that of medicinal products, is not metabolic, immunological, or pharmacological.

"Medical device" as per Drugs and Cosmetics Act[2] means an instrument, apparatus, appliance, implant, material or another article, whether used alone or in combination, including a software or an accessory, intended by its manufacturer to be used specially for human beings or animals which does not achieve the primary intended action in or on human body or animals by any pharmacological or immunological or metabolic means, but which may be assisted in its intended function by such means for one or more of the specific purposes of:

1. Diagnosis, prevention, monitoring, treatment or alleviation of any disease or disorder

2. Diagnosis, monitoring, treatment, alleviation or assistance for, any injury or disability

3. Investigation, replacement or modification or support of the anatomy or of a physiological process

4. Supporting or sustaining life

5. Disinfection of medical devices

6. Control of conception

The market potential for medical devices is very high when compared to pharmaceuticals. The global market for medical products and hospital supplies is over $220 billion (2009). As like pharmaceuticals, medical devices to have regulatory issues during the development of the product. The four phases of development such as research, development, regulatory and post market studies play a vital role in getting a device into the market.

The project mainly deals with the regulations for the approval, manufacture, import and marketing of medical devices in India and regulated markets. The core area will be dealing with the type of submissions to regulatory authorities, types of approvals, crucial factors involved in classification of medical devices, clinical trial related issues and comprehensive data for approvals. The project also deals with GHTF (global harmonization task force) an international body that frames guidelines for medical devices which are accepted globally. GHTF plays a major role in framing guidance documents which are accepted globally. It prevents the trade barrier and allows safe access to medical devices in different parts of the world.

Brief History:

India's market for medical devices is in the world's top twenty - in 2007 India's medical equipment market was estimated at about $1.56 billion. The market is expected to grow about 8 percent annually[8].

Medical devices[3] in India are regulated by the Central Drugs Standard Control Organization (CDSCO) and follows the regulations laid forth in the Drugs and Cosmetics Rule (1940), though with a lot of ambiguity.

Historically, medical devices were classified as drugs and were subjected to the same rules that applied to drugs. After 2005, some devices such as disposable syringes, needles, stents (cardiac & drug-eluting), catheters, canulae, intra-ocular lenses, heart valves, orthopedic implants and internal prosthetic replacements were classified as 'notified medical devices' and were mandated to be registered and regulated. All other devices (other than intra-uterine

devices – which are classified as drugs) fall under the category of non-notified medical devices for which registration is not required.

However, amendments have been made in the recent past to address the lack of standardization across the devices portfolio and the list of notified devices has expanded now to cover over 160 devices.

Several recommendations have also been made to make the regulatory framework more stringent and covering aspects such as classifying medical devices along global guidelines and directives, setting up notified bodies to conduct quality audits of manufacturing facilities, adopting international quality management standards, conducting clinical trials and evaluation of medical devices as per Global Harmonization task Force (GHtF) guidelines (as at present there is no document detailing the guidelines for conducting medical devices related trials) and finally, adopting post-market surveillance of approved devices. Due to lack of a well-documented or a robust regulatory framework such as the FDA's, indigenous device manufacturers adopt international quality standards on their own as they progress on their maturity curve. However, the level of adherence to such standards is questionable and there is a general lack of trust in the products manufactured in India.

Regulations not only affect the product development process or product quality but also affect the economics of the industry. At present, the Indian tax codes are skewed in favor of device imports. Raw materials required to manufacture devices have a higher import duty than those for imported finished devices, thereby making imports of low-price foreign devices more financially viable than indigenous manufacturing. Furthermore, the government does not provide attractive incentives for setting up manufacturing units in India thereby making the country an import-driven market than a manufacturing hub.

These are regulatory-linked issues that impediments to domestic device manufacturers, but are in favor of foreign device manufacturers who sell their products in the Indian market.

Global Market:

In 1998, the total worldwide market for medical devices was $145bn[5]. The global medical devices market has been witnessing steady growth over the years. This consistent growth is expected to continue with high demand expected across regions. The market has good growth opportunities especially from developing regions such as China and India.

America continues to be the largest contributor with more than half of the revenue coming from this region. Awareness about medical devices and healthcare has also increased among customers. Changing lifestyles have been promoting home-based healthcare in a big way. This, in turn, has been driving the global medical devices market[6].

The fast development of health care technology, the increased complexity in medical devices and their impact on the delivery of health services are central issues addressed by the health sector reform processes currently underway in nearly all countries[7]. This paves way for the regulators to formulate stringent rules that allow the manufacturer to place a better device in the market.

Development constraints:

Based on the Brief history, still all authorities under development by revising specific guidelines to streamline the process of approval and have a control on medical devices

- Recently CDSCO has prepared draft Notification viz. Medical Device Rules, 2016 for regulating manufacturing/import/sale/clinical investigation and other related matters concerning medical devices, requirement of QMS for medical devices
- Archaic regulatory standards
- Inadequate quality standards and non-compliance tarnish images of Indian made products
- High import dependency
- Unfavorable duty structure whereby devices manufactured in India become more expensive than low priced imported ones
- Lack of tax incentives to promote indigenous manufacturing
- Meagre government funding to promote innovation
- Lack of local talent

Safety and Risk Management:

Safety can only be considered in only relative terms. All devices carry a certain degree of risk that could cause problems in specific circumstances. Many medical device problems cannot

be known until extensive market experience is gained. For example, an implantable device may fail in a manner that was not predictable at the time of implantation; the failure could be caused by conditions unique to certain patients. For non-implant devices, component failure can also happen in an unpredictable random manner. The best approach to device safety is to estimate the potential of a device becoming a hazard that could cause safety problems. This approach is called Risk assessment of Medical devices[4]. In practice, the risk assessment of medical device is based on the experience of health care professionals. The main aim of health regulatory authority is to improve the safety and reliability of medical devices used by millions of population worldwide.

2. Importance of the proposed work

The main purpose for Medical Device registration is to have complete assessment of documents provided by the applicant to regulatory authorities, ensuring quality, safety, and efficacy of the device in view of public health.

Medical Device registrations are different from country to country - much more complicated, never truly be “SIMILAR”.

Medical Device registrations approval requires special regulatory process & guidelines to ensure quality, safety and efficacy of the device. But still, there is a lack of clear regulatory guidance in India as the regulations vary in many countries like Taiwan, Korea, China, Brazil, Russia, etc.

To overcome the medical device registrations process hurdles, understanding the regulatory requirements in clear and to ensure compliance across the globe, this project work was initiated.

Regulatory authorities of the five countries under study:

Table 1: List of Countries under study with their Regulatory Authorities

S. No	Country	Regulatory Authority
1.	India	Central Drugs Standards Control Organization (CDSCO)
2.	United States(US)	United States Food and Drug Administration (USFDA)
3.	Canada	Health Canada
4.	Singapore	Health Sciences Authority (HSA)
5.	Brazil	Agencia Nacional de Vigilancia Sanitaria (ANVISA)

Objectives of the proposed article

The knowledge and compliance with regulatory requirement is a key to success in development and marketing of medical devices. Medical devices are now a pervasive part of modern medical care. The main objectives of this study are:

- To provide basic knowledge on framework of guidelines for approval to import, manufacture and marketing of medical devices in India and regulated markets such as United States(U.S), Canada, APAC (Singapore) and Brazil.

- Identify the challenges in Registration of Medical Devices in India and Regulated markets including the process of submission of documents, review, response to the queries and approval process.

- Functions of global harmonization task force (GHTF) and its guidance for the medical devices

MATERIALS AND METHODS

The section referring to the various components or subsection to be studied is given below;

Literature Survey:

A through effort will be put to understand the current constraints in Registration of Medical Devices, regulatory authorities' guidelines, regulators comments and difference pathways for registration. The survey covers go through of all the possible and available data's which may be either soft or hardcore material such as CD ROM, Internet, Journals, Magazines and NEWS papers etc. The review of guidance documents and guidelines from health authority resources and compiling of country specific regulations in a chronological manner is a challenging task. It requires a strategy to scope out the entire process in few steps. These steps should be analyzed in such a way that each and every regulatory aspect in the process of medical device development should be enlightened.

In order to facilitate the cumbersome process, the whole study has been divided into five different stages in which a parallel common phase runs in each stage. The five different steps in the project execution were:

Stage I – Define; Stage II – Identify; Stage III – Collect; Stage IV – Scrutinize; Stage V – Compile

The common phase which runs parallel at each stage was Assessment

Manufacturing a Notified Medical Device in:

A separate license is required for each manufacturing location and for each Notified Medical Device at such manufacturing location. Under the Act, "manufacturing" includes any process (or part) for making, altering, ornamenting, finishing, packing, labeling, breaking up or otherwise treating or adopting any drug with a view to its sale or distribution. However, "manufacturing" does not include dispensing or packing at the retail sale level.

Importing a Notified Medical Device into India:

Importing a medical device into India requires satisfaction of few additional legal requirements hands those indicated above. The import of all products in India, including medical devices, is governed

Under the provisions of the Export and Import Policy. Before importing device into India, the importer is required to obtain Importer and Exporter Code (**"IEC"**) Number from the office

of the Director General of Foreign Trade (**"DGFT"**). The IEC Number would be required to be mentioned in the documents filed with Customs for clearance of imported goods. For obtaining the IEC Number, an application in the prescribed form has to be submitted to the office of the jurisdictional Joint Director of Foreign Trade, wherein details of Bank Account Number and Permanent Account Number have to be furnished Under the Act, the activity of import of Notified Medical Devices into India requires an import license from the office of the Drugs Controller General of India. In order to get an import license, there is a mandatory requirement of registration of the medical devices sought to be imported, the name of the manufacturer and its manufacturing premises with the office of the DCGI. The registration is certified by grant of a registration certificate. An application for grant of a registration certificate may be made by the foreign manufacturer itself if it has a valid wholesale license for sale or distribution of Notified Medical Devices under the Rules or its authorized agent in India, either having a valid license under the Rules to manufacture for sale of a Notified Medical Device or having a valid wholesale license for sale or distribution of Notified Medical Devices in India. Many times, foreign manufacturers do not have an Indian subsidiary which has a wholesale license for sale or distribution of Notified Medical Devices. Hence, the manufacturers choose to appoint a third party as an authorized agent to make the application for grant of registration certificate. The authorization by a manufacturer to its agent in India must be documented by a power of attorney. Other documentation related requirements for import: Free Sale Certificate in country of origin issued by the Ministry of Health/National Regulatory Authority is a pre-requisite or Regulatory status of a medical device:

- In case of medical devices manufactured in USA, USFDA approval for manufacture and free sale

- As regards medical devices manufactured in Australia, Japan and Canada, approval for manufacture and free sale

- In case of medical devices manufactured in European Countries, CE certification along with approval for manufacture and Free Sale Certificate

- Other countries: approval for manufacture and free sale in the respective country of origin long with approval from any one of the following viz.

USFDA/TGA

Australia/Health Canada/ Ministry of Health, Labour and Welfare Japan or CE Certification is to be submitted.

Manufacture/Import of New Notified Medical Device:

A "new" medical device is a medical device which falls into the Notified Medical Device category, but which does not have a predicate Notified Medical Device registered (for import) / approved (for manufacture) in India. A "predicate" Notified Medical Device is one which is registered/approved in India and has the same indications/ intended use, material of construction and design characteristics as the device which is proposed for registration in India. Notified Medical Devices for which predicate devices are not registered in India are classified as "new" medical devices. These medical devices are referred to the Medical Device Advisory Committees (MDAC) to comment on safety, effectiveness, essentiality and desirability of proposed New Devices before the new medical device may be registered/approved. The importer/manufacturer of such new medical device may be required to furnish clinical data to satisfy the MDAC. It is noteworthy that if the new medical device is not marketed in any of the following markets *viz*. USA, Europe, Japan, Canada or Australia, then the marketing permission of such a device would depend on results of the local clinical trials conducted in India.

Export – Import Restrictions:

Imports and exports are regulated by the Foreign Trade (Development and Regulation) Act, 1992 along with the Customs Act, 1962 and the Export-Import Policy (EXIM Policy), issued by the Ministry of Commerce and Industry of the Government of India. The current EXIM policy also known as New Foreign Trade Policy covers the period 2009 – 2014. The purpose of the EXIM policy is to develop export potential, improve export performance, encourage foreign trade and create a favorable balance of payments positions.

The Indian medical device market:

The Indian medical device market is significantly smaller than other overseas markets. However, macroeconomics factors suggest a huge potential for double –digest growth in the Indian medical device sector. Upcoming developments in the regulatory and policy

framework are expected to accelerate growth of the medical devices sector at estimated 10 years CAGR of 15%.

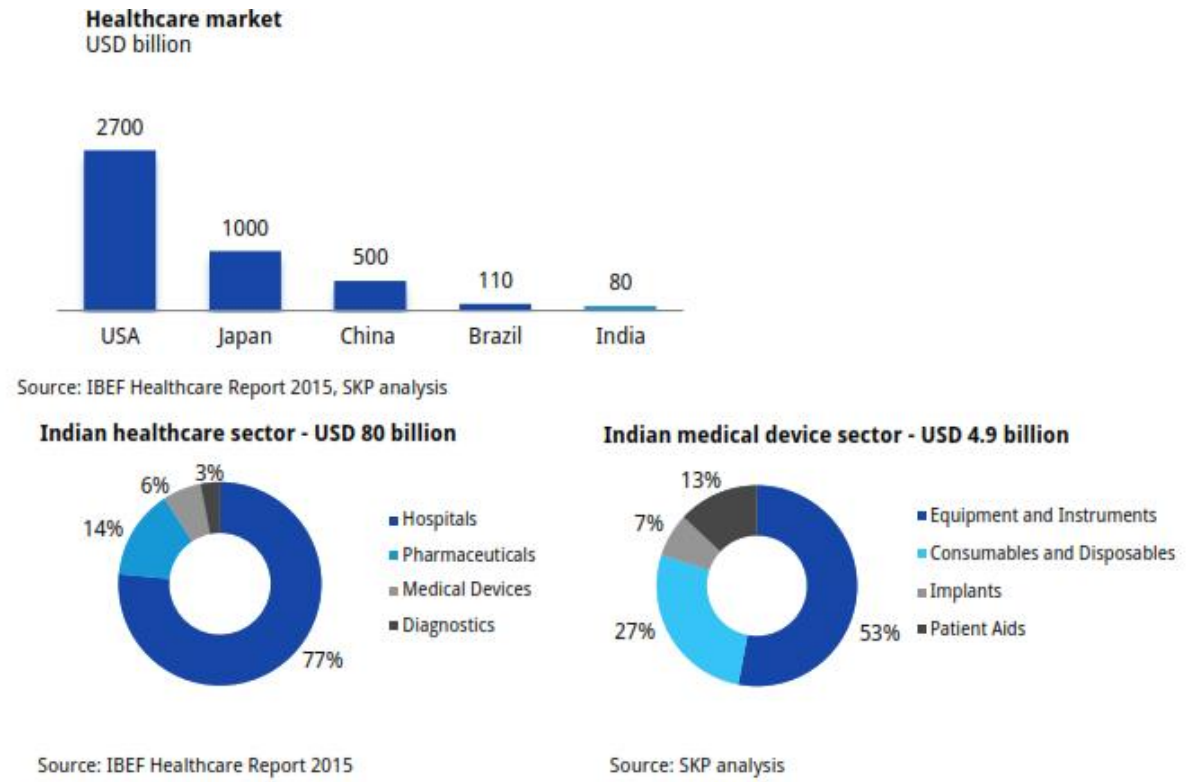

Figure 1:

Structure of Industry:

The medical device sector is characterized by import dependency and highly fragmented domestic industry. Presently, imports are preferred over domestic manufacturing mainly due to the inverted duly structure and lack of favorable policy and regulatory framework.

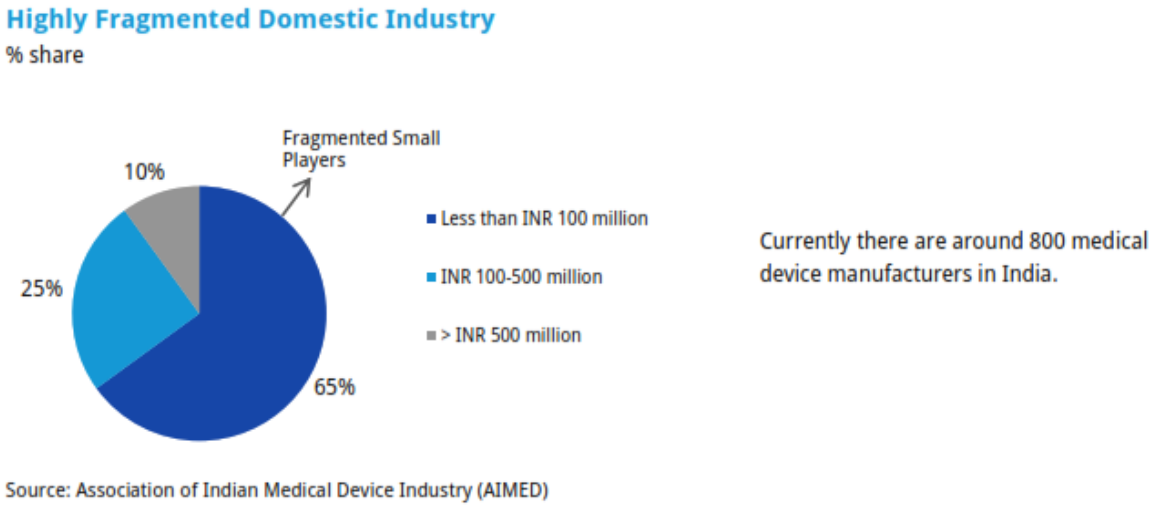

Figure 2:

Medical Device clusters in India

Over the years, various medical device clusters have emerged across India. States have down strength from the availability of skilled/unskilled labor and accordingly developed state level policies. The following figure highlights the strengths of the top states with medical device clusters.

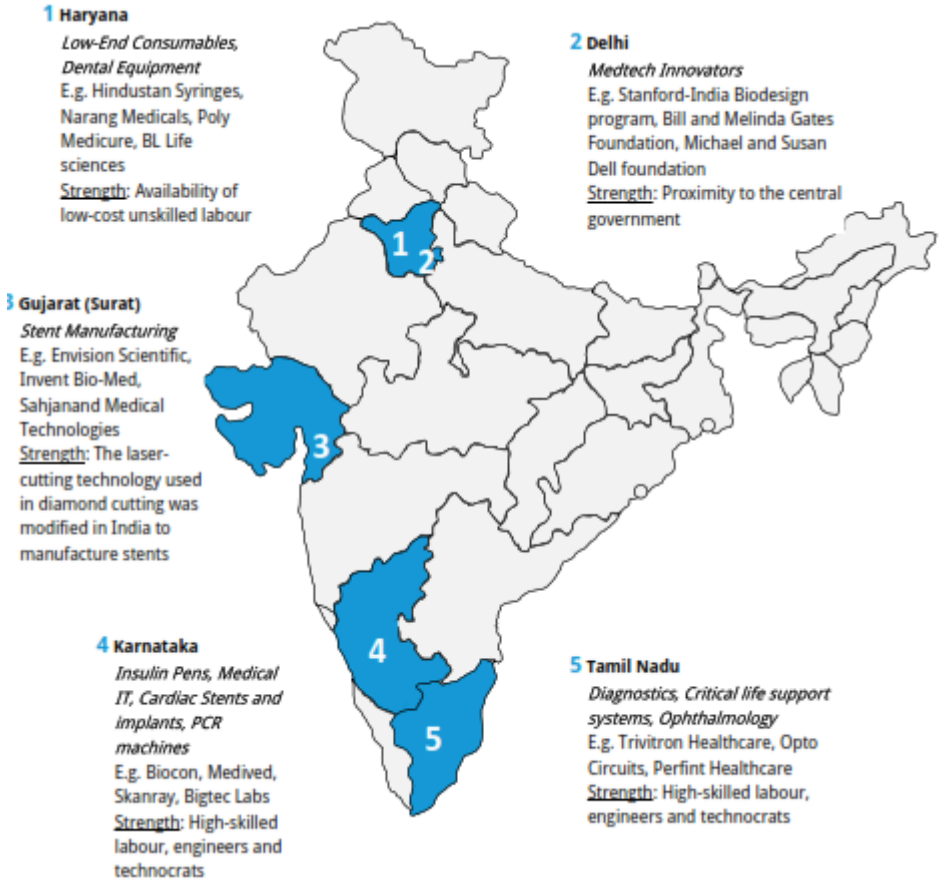

Figure 3: Medical Device clusters in India

The Shift in the Medical Device Sector after Regulatory Changes

	Structure	Conduct	Performance
Before	Nascent regulatory framework Lack of a conducive environment for technological innovations Inverted duty structure	MNCs preferred to import and be distributors Domestic companies continued to focus on low-end products and refrained from investment in R&D No investments made in manufacturing and R&D infrastructure	MNCs fetch high margins focusing on high-end products Domestic players focus on low-cost products resulting in low margins Domestic players could never build competency in R&D
	Regulatory and Policy Framework Changes		
After	Robust regulatory framework Conducive environment for technological innovations Focus on manufacturing and research in India	MNCs to manufacture in India and expand their presence across segments Domestic companies to focus on raising quality standards and technological upgradation MNCs and domestic companies to customise products for Indian needs MNCs and domestic companies to collaborate with each other through joint ventures or associations	Companies who demonstrate quality standards simultaneously with cost efficiencies to survive Difference in margins of MNCs and domestic players to gradually narrow down due to better quality products and new product developments by the domestic players

3M understands the requirements of medical device manufacturers, and we've developed a Secure Supply Chain System using RFID technology to comprehensively address these issues:

Real-Time Visibility

The 3M Secure Supply Chain System for medical devices provides tools enabling real-time visibility to inventory positions across the supply chain, including at the point of implantation or use in a clinic or hospital.

Encrypted Data

Employing RFID tags with encrypted digital signatures, combined with a unique identifier at the manufacturing site, establishes product authenticity – and that combination is decrypted and read to securely manage the inventory path of the medical device.

Value-Added Service

Plus, it helps maximize a clinic or hospital's staff time with patients, which leads to more effective and accurate patient billing potential. The system also provides tools to more efficiently track and locate product inventory by reducing or eliminating manual tracking processes, while increasing inventory turns. Medical device manufacturers also benefit by offering their customers a value-added service as an extension to their product offerings – enhancing their overall brand.

A Scalable Solution

The platform delivers a straightforward technology solution that helps provide inventory management, reduce logistical costs and increase product visibility throughout the supply chain, without requiring significant infrastructure.

Built from the Ground Up

3M's track and trace solution include all software, hardware and secure data hosting, Business Process Optimization methods help ensure that deployment is seamless, and integration services and support are part of the complete Secure Supply Chain System.

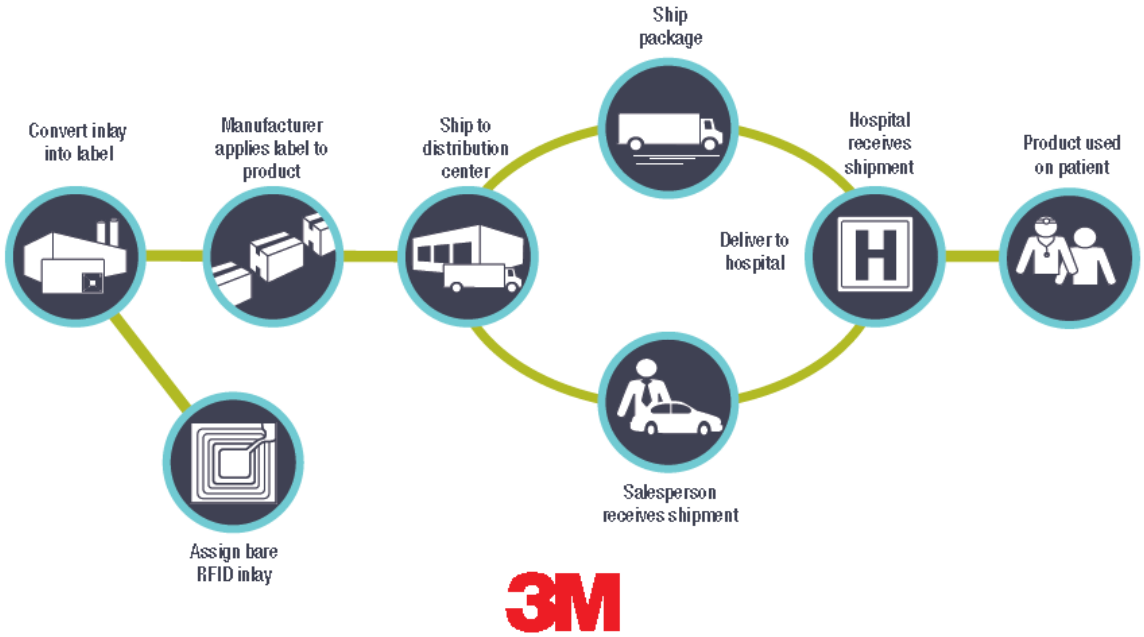

Figure 4:

United States:

Globalization presents serious challenges to the ability of the U.S. medical product 1 safety system to protect American families. Among these challenges are the growth in the number of medical products produced abroad, the increasingly complex path that medical products travel from source materials to consumers, and the greater chance for the intentional substitution of ingredients for profit (economic adulteration). FDA is implementing a comprehensive approach to medical product safety along the supply chain, similar to its approach to food safety. The ultimate goal of these efforts is to protect Americans from contamination, diversion, counterfeiting, and other risks that could harm patients. In FDA's

fiscal year (FY) 2009 appropriation, Congress directed FDA "to prepare and provide to the Committees on Appropriations a comprehensive approach to ensuring the safety of medical products from the manufacturing of raw ingredients or components to consumer use." This report addresses that directive by focusing on supply chain safety.

Supply chain safety refers to minimizing risks that arise anywhere along the supply chain continuum, from sourcing a product's raw material, ingredients and components through the product's manufacture, importation, sale and distribution. Although FDA has a significant number of efforts under way that address medical product safety issues beyond the supply chain, addressing supply chain safety presents some of the greatest challenges.

This report identifies trends and challenges that FDA faces all along the supply chain. To address them and protect public health, FDA has adopted four primary strategies:

Focus on prevention; enhance regulatory information; improve FDA's scientific and analytic capabilities; expand risk-based inspection and enforcement. This report describes these four strategies and the steps that FDA is taking to implement them.

Medical Devices Global Value Chain:

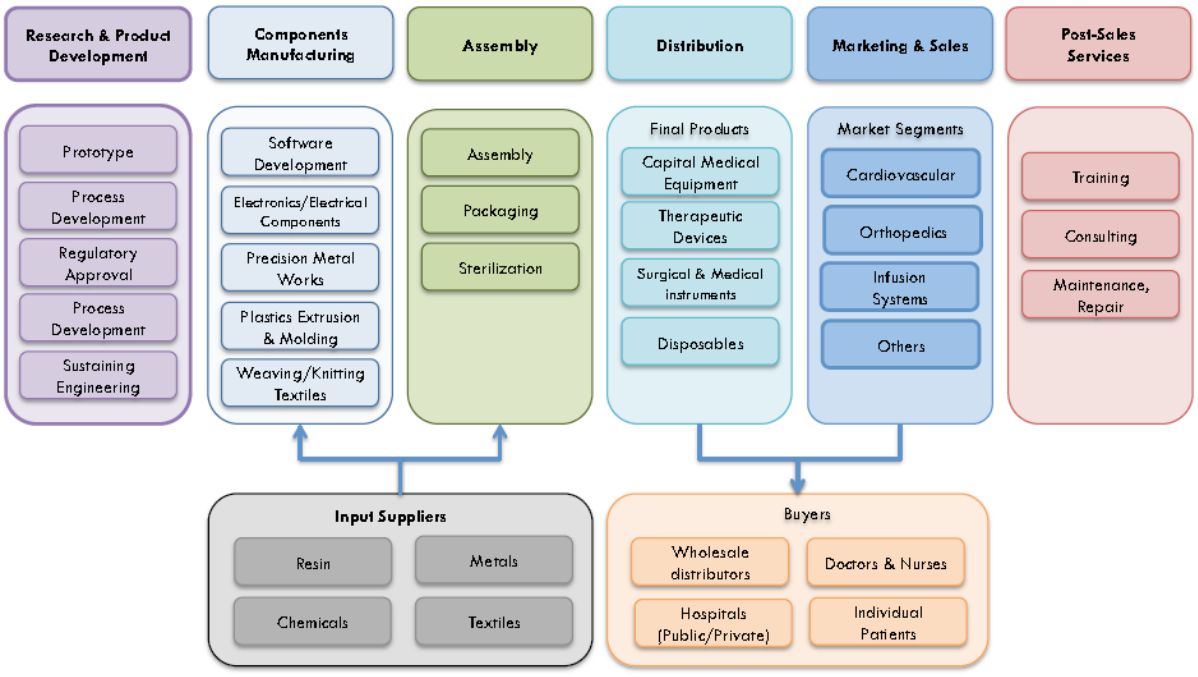

Figure 5: Medical device global value chain

Secure Solutions for Life: Medical Device Supply Chain

3M has expanded its pharmaceutical collaboration for 3M's advanced track and trace system that uses Automatic Identification (Auto ID) technology known as Radio Frequency Identification (RFID) to track medical device products as they travel from manufacturer to clinics and hospitals.

Carrying critical medical device inventory. Tracking and forecasting the purchases of high-value assets. Dealing with unforeseen logistical costs. For medical technology companies, operational challenges are a reality of doing business:

Salespeople aren't simply the main point of contact between a hospital and a medical device manufacturer. A sales representative also acts as distributor, inventory forecaster, shipper and logistics manager. Keeping products visible is another challenge, and knowledge of where this high-value asset is at any given point adds to the demand.

And then there's the time-consuming challenge of keeping inventory records accurate. Many times, up to the point of implantation, manufacturers of pacemakers, defibrillators, stents and cardiac surgical devices can only speculate where their products will end up. Plus, overstock returns, quality-control recalls, forecasting patient needs and preparing for disasters all cause logistical and operational challenges for medical device manufacturers.

There's no doubt these companies need a comprehensive, all-encompassing solution for the supply chain – one that speaks both to a myriad of operational requirements, as well as patient safety.

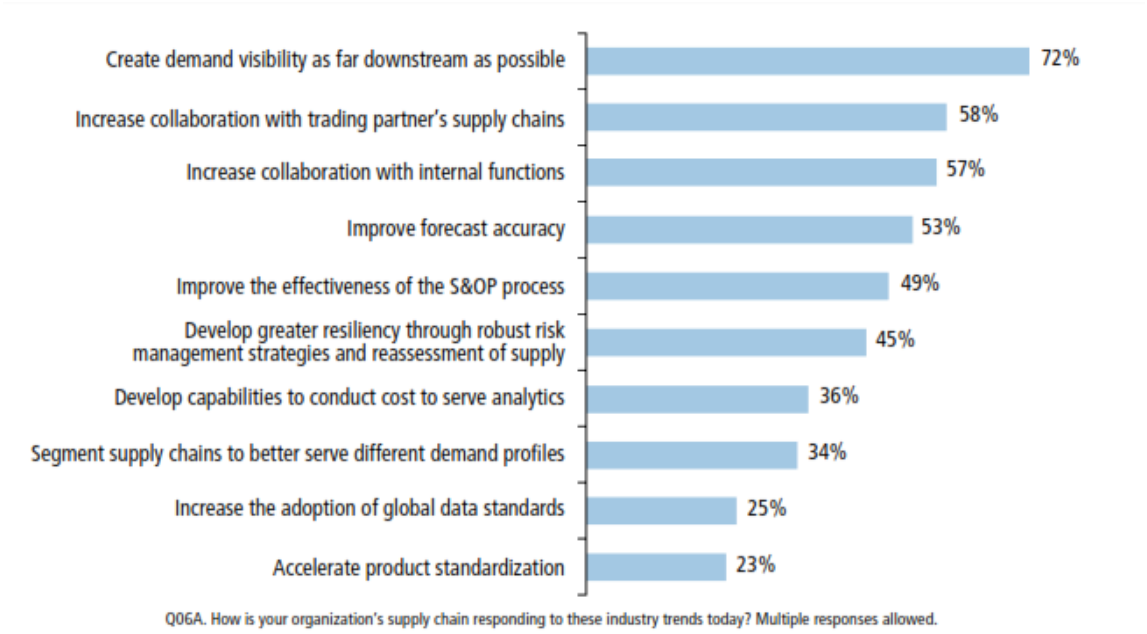

Figure 6: Increasing collaboration to improve the supply chain

Effective Supply Chain Management for Medical Device Shipments

Medical device manufacturers face a daunting challenge in today's market. In addition to understanding stringent government regulatory requirements and FDA-mandated current Good Manufacturing Practices (cGMP) designed to ensure products are safe, pure and effective, manufacturers must also bear the burden of understanding the complexities and rigors involved in moving their sensitive products through the supply chain.

With the rapid growth of the medical technology and life sciences market, the concept of supply chain management continues to change to meet the unique challenges presented when moving sensitive medical device products. There are a number of variable conditions that must be accounted for to ensure on-time delivery and protection of product condition and integrity from origin to destination.

While government regulations and cGMP protocols dealing with product manufacturing and packaging are cumbersome, a manufacturer can maintain complete control of the processes and protocols involved. However, once the product is shipped from the manufacturer's facility, it may be exposed to circumstances and conditions that increase the risk of loss or damage and that are, to some extent, beyond the control of the manufacturer.

Under FDA regulations and cGMP protocols, the manufacturer not only is responsible for validating the quality of the manufacturing and packaging process, but also for ensuring and

documenting that the proper level of care, custody and control is provided when moving product through the supply chain. It is imperative that the manufacturer has a firm understanding of the complexities involved in the supply chain and be able to identify potential gaps that could adversely affect the quality or integrity of the product.

Third Party Logistics (3PL) Service Providers:

A vital element of an effective supply chain management program is the choice of 3PL transportation service providers experienced in and dedicated to the handling, tracking, storage and transportation of sensitive healthcare technology products.

Given the sensitivity of healthcare products to handling damage and delays in transit, it is important to consider the use of a "closed loop" or single-source supply chain service provider that will maintain custody of the product and minimize handling throughout the transit. Furthermore, the use of a single-source supply chain service provider allows for tighter controls and monitoring of shipments throughout transit and to ensure adherence to required shipment handling and safety Standard Operating Procedures (SOP).

Standard Operating Procedures (SOP):

Manufacturers should develop a written supply chain management SOP that outlines the specific product handling and safety procedures required to be followed by 3PL service providers. This SOP should be distributed to all service providers responsible for handling and transporting the product to ensure that they are not only familiar with the handling and safety requirements, but also the sensitivities and tolerances of the particular products being shipped. The SOP should state the required carriage instructions, such as handling and storage requirements, transportation service levels, subcontracting limitations, routing, length of transit time, product temperature/humidity requirements, temperature/humidity excursion threshold limits, maximum amount of time product can be exposed to non-controlled environments during transit, etc. Based on cost, need and feasibility, security requirements for specified shipping lanes or highly valuable/sensitive products should also be considered for inclusion in the SOP. In many instances, carriers or logistics agents provide shippers with boilerplate or standardized SOP that are meant to be tailored to the particular products being shipped. Although the carrier or logistic agent's SOP may address some of the issues noted above, a more detailed manufacturer's SOP should take precedence and hold the carrier accountable for the strict adherence to its requirements. In addition, the

manufacturer/shipper's SOP can be tied to service provider contracts to strengthen the carrier's commitment to safe and on-time delivery of the shipment from origin to destination. This could be enforced further by adding language to a service provider contract holding them financially responsible in the event of loss/damage to product during transit, where it could be demonstrated that the shipping and handling SOP was not followed.

The manufacturer's supply chain management SOP should be reviewed with the 3PL service providers on a frequent basis and updated as necessary.

Periodic service reviews of all 3PL service providers should be conducted to ensure adherence to the established supply chain management SOP. As part of the service provider review program, consideration should be given to establishing a report card system that measures performance against key metrics allowing the company to effectively track and manage compliance with required SOP.

Pre-Shipment Planning:

So that all in-transit risk factors are identified and properly assessed, diligent front-end mitigation efforts should be undertaken. Those efforts include pre-shipment route planning to identify exact shipping lanes to be used, security and handling capabilities at all interchange points, road transport to and from airport of departure/arrival, anticipated climatic conditions throughout the entire transit and controlled transport and storage conditions.

Proper pre-shipment planning should also include contingency planning for maintenance of product quality and integrity in the event of unscheduled stoppages and/or delays due to government inspection and implementation of Customs-Trade Partnership Against Terrorism (C-TPAT) supply chain security programs.

Shipment Tracking:

Given the varying global regulatory requirements, there is an increased likelihood that product will be delayed in transit for government inspection and/or to settle import licensing/documentation issues. Therefore, an important element of an effective supply chain management program is tracking shipments throughout transit on a real-time basis. Real-time shipment tracking allows for early detection of any stoppages and/or delays that occur, prompt investigation of the circumstances involved and immediate implementation of

necessary corrective action to locate the product, confirm that product condition and integrity has not been compromised and arrange for through delivery to destination in a timely manner.

It is not sufficient for a manufacturer simply to track shipments from origin to destination to confirm delivery. Rather, they should document and record the tracking process on a shipment-to-shipment basis, to be able to confirm to regulators and inspection agencies that the integrity of the product was not compromised during transit.

Packaging:

Product packaging plays a critical role in ensuring that the condition and integrity of the product are maintained. The method of packing should be designed based on qualification studies that take the following factors into consideration:

- **Climatic conditions throughout the transit**
- **Modes of conveyance**
- **Transport routes (locations, contingency lanes, etc.)**
- **Duration of transit**
- **Duration and location of interchange points throughout the transit (including customs clearance)**
- **Product handling**

In addition to protecting the actual device, the condition of the primary packaging should be adequately protected to avoid suspicion that the product integrity has been compromised. Any appearance of damage, wetting and/or mishandling, *even if only cosmetic in nature*, could be cause for quarantine or rejection. Approved packaging methods should be monitored, periodically reviewed and revised as necessary in response to changes in any or all of the factors outlined above. Consideration should be given to consulting with independent third party vendors and experts capable of performing packaging qualification studies to ensure suitability of the packing method given the product being shipped, mode of conveyance and shipping lanes to be utilized.

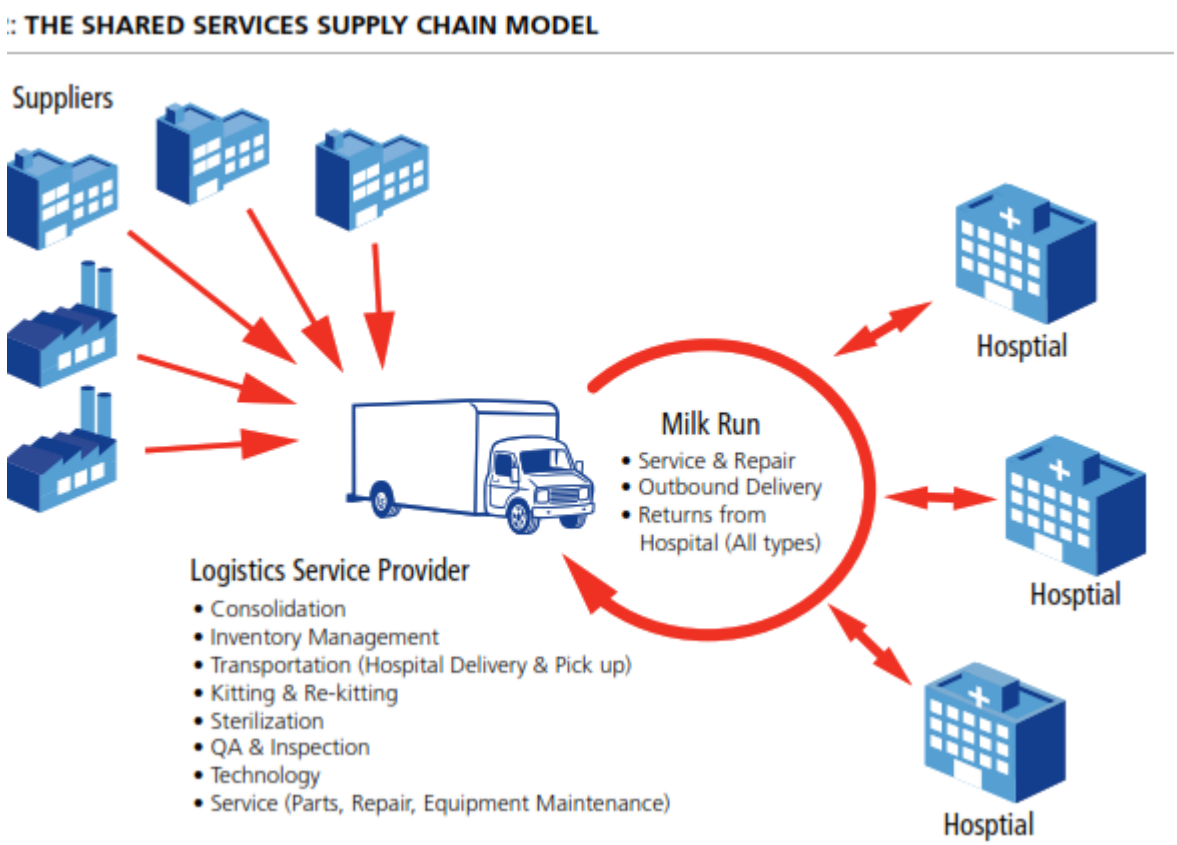

Figure 7: Shared service supply chain model

Australia:

TGA regulate medical devices:

The Therapeutic Goods Administration (TGA) regulates all medical devices that are imported into, supplied in or exported from Australia under the *Therapeutic Goods Act 1989* (the Act). Unless a specific exemption applies, medical devices must be included on the Australian Register of Therapeutic Goods (ARTG) before they can be supplied in Australia.

Importing medical devices:

Health professionals import medical devices for use in their clinical practice: Health professionals being subject to therapeutic goods regulations. Health professionals who import medical devices for use in their clinical practice are considered to be supplying the devices to the general public. Examples of importing medical devices include purchasing from overseas through the internet or from mail order catalogs or obtaining from international conferences and trade exhibits. Clinical practice really means supply of a medical device:

Yes, the term 'supply' is defined in section 3 of the Act and does include supply to mean by way of administration to, or application in the treatment of, a person. Other definitions about supply of therapeutic goods in section 3 include:

- Supply by way of sale, exchange, gift, lease, loan, hire or hire-purchase
- Supply, whether free of charge or otherwise, by way of sample or advertisement
- Supply, whether free of charge or otherwise, in the course of testing the safety or efficacy of therapeutic goods in person.

Health professionals import medical devices under the personal importation provisions:
Health professionals can import medical devices under the personal importation provisions but NOT for use in their clinical practice. The personal importation scheme can only be used to import a medical device for personal use or for the treatment of immediate family.

Under the personal importation scheme, any individual may import a three month supply of unapproved therapeutic goods into Australia in any one importation without any approval required by the TGA provided that:

The devices are for the individual's own treatment or the treatment of immediate family; the individual does not supply (sell or give) the devices to any other person; the other conditions of personal importation are met as part of the personal importation scheme.

Medical device supply chain in Japan

The Pharmaceutical Affairs Law (PAL) regulates the manufacture, marketing and distribution of pharmaceutical drugs and medical devices in Japan. Foreign manufacturers find it difficult to establish themselves because of the rules and regulations established by PAL in the country. This has led to significant M&A activity in the Japanese pharmaceutical industry. The key regulators in Japan are the MHLW and the Pharmaceuticals and Medical Devices Agency (PDMA).

Wholesaler

Japan’s drug wholesalers purchase pharmaceuticals from manufacturers for sale to medical institutions such as pharmacies, hospitals, clinics, and other customers. In addition to logistics, wholesalers have the Following important functions:

Provision of drug information: Customer support; Product promotions; Price negotiations

As of April 1, 2012, the Federation of Japan Pharmaceutical Wholesalers Association (JPWA) consists of XX member drug wholesalers (JPWA, 2011). The pharmaceutical distribution (wholesale) industry is concentrated into large four groups and has seen repeated reorganization and restructuring since the 1990s. The industry is an oligopoly, with the top four companies representing XX% of the Japanese pharmaceutical distribution market. As shown in the above figure, the pharmaceutical wholesale and distribution market grew at a rate of XX% between the fiscal year ended 2009 and the fiscal year ended 2010 to reach $XX billion, based on the sales of XX major companies. This slow growth was due to negative influence from NHI drug price revisions and the subsequent expansion of generic drugs.

Wholesale Customers

Drugs are bought from wholesalers by five types of medical institutions:

✓ Dispensing pharmacies; General pharmacies; Large hospitals; Small and medium hospitals; Clinics

A breakdown is given in the following figure:

Pharmaceutical and Medical Device Act (PMD Act) regulation

The distribution of medical devices in Japan is regulated in accordance with the Pharmaceutical and Medical Device Act (PMD Act) regulation by the Ministry of Health, Labour and Welfare (MHLW). The former regulation, Japanese Pharmaceutical Affairs Law (JPAL) was replaced by PMD Act on November 25, 2014. The revision includes third party certification systems for Class III medical devices and expansion of the responsibility of quality management system to legal manufacturers.

Because of the complexities of PMD Act and the involvement of Japanese and international governmental bodies, we can help you understand device classifications, prepare for the review process, and help you meet standards. **Pharmaceutical and Medical Devices Agency (PMDA) review process**

Under PMD Act, the Pharmaceutical and Medical Devices Agency (PMDA) review process depends on the classification of the medical device, which is generally in line with the principles outlined by the International Medical Device Regulators Forum:

Class I General Medical Devices: Pre-Market Submission (Todokede)

Devices of low risk to the human body

Approval of the product is not required, but marketing notification (Todokede) to PMDA is necessary

Class II and Class III (partially) Controlled Medical Devices: Pre-Market Certification (Ninsho)

Low risk to the human body

The majority of these devices for which certification standards have been established by MHLW are eligible for third-party review and certification by a Registered Certification Body, such as BSI. Those devices for which no applicable certification standard has been established must be submitted to PMDA for approval (Shonin) by MHLW

Class III and IV Specially Controlled Medical Devices: Pre-Market Approval (Shonin)

Medium risk to human body, high risk to human body, highly invasive to patients

MHLW approval (shonin) is required for Class III and IV devices, based on approval standards for devices for which such standards have been established, or based on review guidelines

Europe:

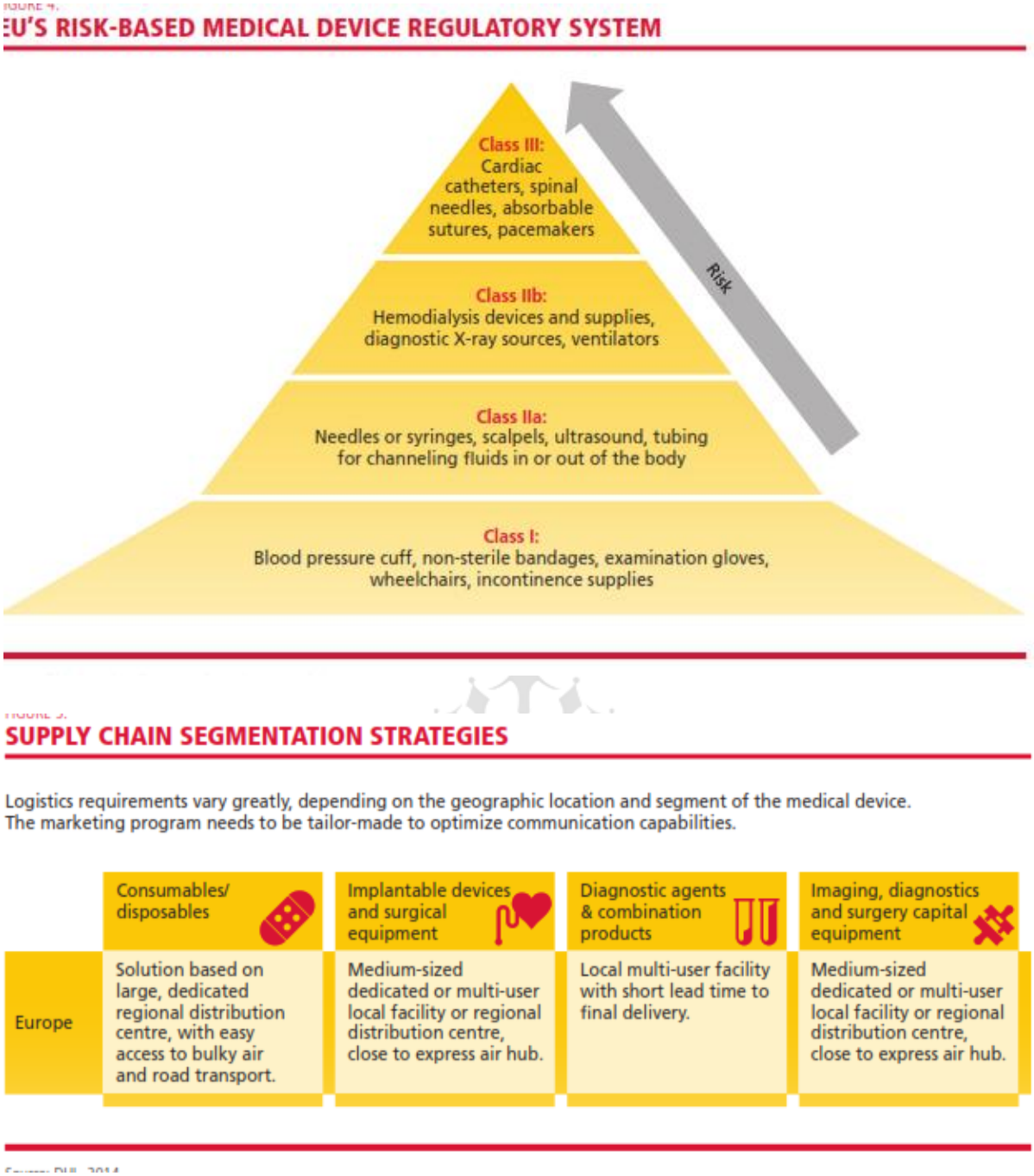

Figure 8: European risk based medical device regulatory system and supply chain segmentation strategies

THE DIRECT DISTRIBUTION MODEL

To reduce costs and increase profits, manufacturers are beginning to look at serving certain customers direct; an approach that provides an alternative to the traditional distributor-intermediary model. However, the decision between going direct versus through a distributor

is highly reliant on several factors, including attributes such as cost of product, security needs and number of final distribution points.

Moreira observes, "An increasing number of manufacturers are looking at serving more of their customers directly, rather than through distributors or agents, especially in developing Eastern European countries. There is a mutual interest between manufacturers and their customers (healthcare providers) to create these direct bonds. Hospitals can benefit from product knowledge transfer coming directly from the people who make the products. Manufacturers can collect more accurate sales and customer usage information, and get direct customer feedback about product performance and service satisfaction." By contrast, in a distributor or agent distribution model, the manufacturer has no direct connection with the end customer. As a result, it loses visibility and control over the product once it leaves the manufacturing plant. Often operations are left in the hands of providers who may not have strategic, robust capabilities, resulting in loss of control and exposing the manufacturer to various potential risks – ranging from improper instructions on usage to lack of compliance with local regulations. Furthermore, a direct model not only improves the security of the supply chain, by reducing the number By contrast, in a distributor or agent distribution model, the manufacturer has no direct connection with the end customer. As a result, it loses visibility and control over the product once it leaves the in a distributor or agent distribution model, the manufacturer has no direct connection with the end customer.

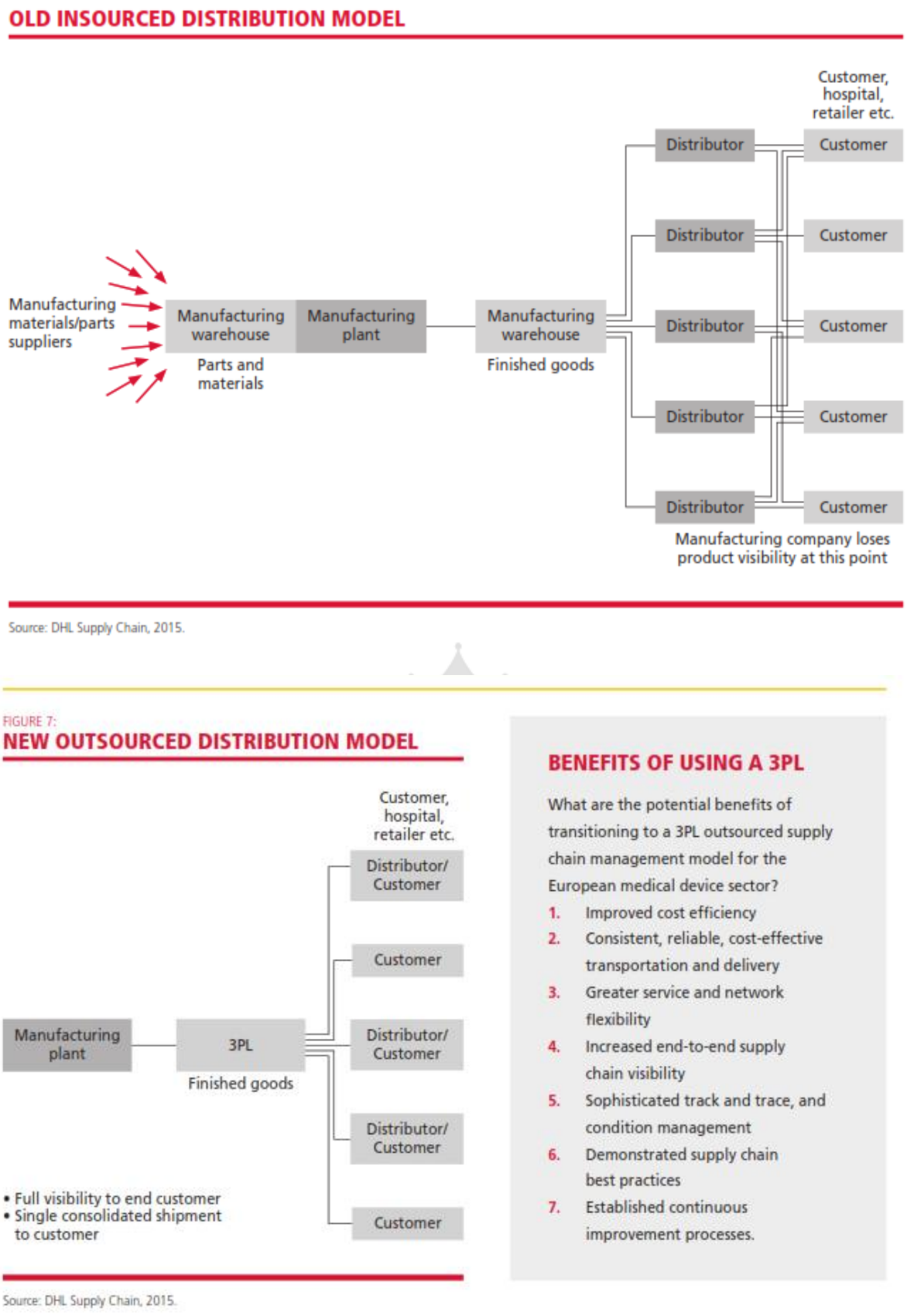

Figure 9: Old insourced and new outsourced distribution model

of intermediaries handling the product, but also reduces cost by switching from a service fee based on the cost of the product to one based on the true cost of distributing the medical device (Figure 9).

ADDING SHARED SERVICES

Another opportunity for manufacturers to reduce costs and streamline their supply comes through leveraging a shared services operating model. Medical device manufacturers typically sell to the same community of customers – e.g. hospitals, clinics and physicians' offices, resulting in individual manufacturers running parallel supply chains to service these customers. This duplication and redundancy carry a high and unnecessary cost for manufacturers and their receiving customers – one that the environment of fiscal austerity increasingly will not support.

Under a shared services solution, multiple manufacturers house their product with a single 3PL in a shared network of facilities and transportation capacity. The sharing of this transportation, distribution and warehousing systems streamlines the supply chain for manufacturers and their customers.

THE OUTSOURCING MODEL

Outsourcing the logistics activities and operations to a 3PL with expertise in managing medical device supply chains frees up the manufacturer to focus on its core business – developing and producing medical devices. It enhances flexibility by tapping into the capabilities portfolio, infrastructure and knowledge of a global 3PL – rather than trying to build and maintain those assets and processes in-house. This type of partnership provides a great benefit: it gives the manufacturer the capabilities and flexibility needed to deal with the complexities of the European market – i.e. different products, regulations, customer requirements and infrastructure. A 3PL that is already established in both the medical devices sector and the European market can provide: Tailored solutions that meet the needs of each market or country – the opposite of a one-size fits-all distribution solution Expertise in each country's government regulations, helping to ensure proper packaging, labeling and tracking of medical devices. Best practice warehousing and transportation management solutions, including state-of-the art information systems. Rapid implementation capability to support expansion into new markets and business change. By partnering with a 3PL a manufacturer can capture significant cost savings generated by a streamlined, optimized supply chain –

which is critical in meeting the rising cost pressure under which the sector operates. "The different areas of saving potential can range as high as 20 percent, depending on the solution," reports DHL's Susanne Amholt. By becoming the supply chain orchestrator, and managing the country-specific distribution operation end-to-end, the 3PL provides visibility into, and control of, product flow; coordinating deliveries, tracking those deliveries, and managing other logistics service providers and distributors – all to ensure timely, accurate and cost-effective delivery to the end customer.

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