Singapore's GDPMDS versus ISO 13485:2003: A Comparative Analysis

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Good Distribution Practice (GDP) is a term first officially coined in the European Community Council Directive 92/25/EEC for medicinal products, and it is a subject that has been covered in guidelines by most major reference authorities.[1] In most of these cases, GDP is generally considered an extension of Good Manufacturing Practices (GMP). In US regulations and US Food and Drug Administration (FDA) guidelines, for example, there are no separate regulations or guidelines specifically for GDP, but the industry generally refers to GDP as those parts of the GMP that deal with storage and transportation of medicinal or medical device products.

In comparison, Singapore's Good Distribution Practice for Medical Devices (GDPMDS),[2] pioneered in 2008 as a result of the *Health Products Act (HPA)* of 2007, was developed to address the unique regulatory issues in a country that has a relatively small domestic market, rapid economic growth, a relatively small but targeted manufacturing sector and a proportionally large import/distribution sector (see **Table 1**).

The GDPMDS became the first of such regulations in the world that specifically addressed importers, wholesalers, distributors, and secondary assembly facilities that may otherwise not be subject to compliance with International Organization for Standardization (ISO) 13485.

The success of GDPMDS in Singapore is evident from the active participation of the local industry since its launch, and the effect is resonating in neighboring economies that have a similarly large number of importers and distributors by proportion. Malaysia, Hong Kong, and Taiwan are all in various stages of evaluating or adopting similar regulations.

RAPS has partnered with Singapore government agencies to develop and implement a new medical device regulatory affairs (MDRA) training program.

The MDRA program will help cultivate the next generation of qualified regulatory professionals in Singapore and build regulatory capacity throughout Southeast Asia.

Table 1. Comparison of the medical device industries

	Population	GDP per capita (USD)[i]	Manufacturers	Importer/Distributor
Singapore (2007 data)[ii]	4.5 Million	36,700	70	500
Canada (2005 data)[iii]	32 Million	35,000	1000	600
Switzerland (2008 data)[iv]	7.7 Million	68,500	600	500

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[i] Data from YCharts.com, accessed 22 Dec 2012.
[ii] Sethuraman, R. GHTF Guidance Implementation – The Singapore Experience, presented at the AHC Workshop on Medical Devices: Implementation of GHTF Documents in July 2011, in Seoul, Korea.
[iii] Industry Canada, Medical Device Industry Profile, http://www.ic.gc.ca/eic/site/lsg-pdsv.nsf/eng/h_hn01736.html, accessed 22 Dec 2012.
[iv] Medical Cluster, Helbling Group, and Roland Berger AG, Switzerland – a hot spot for medical technology, 2008.

This article provides an objective, comparative analysis between Singapore's current GDPMDS and ISO 13485:2003. It illustrates some of the challenges in regulating this sector, as well as some opportunities for improving industry quality and consumer welfare.

Scope and Overview of GDPMDS

The current regulations in Singapore require manufacturers to hold ISO 13485 certification, and dealers and wholesalers GDPMDS certification. A summary is shown in **Table 2.**

GDPMDS is largely based on ISO 13485. In fact, aside from added definitions and specific sections addressing disposal of devices, adulterated devices, outsourced activities and secondary assembly, much of GDPMDS is a reduced-scope or reworded version of ISO 13485. As with ISO 13485, ISO 9001 certification cannot be accepted as equivalent to GDPMDS.

A Comparative Analysis against ISO 13485:2003

Methodology

This comparison goes through ISO 13485 section by section and highlights the key differences in point forms, followed by brief discussions. Word-by-word differences that are deemed minor are not discussed, or we describe them as basically unchanged.

In general, ISO 13485 consists of eight title sections and two informative annexes; GDPMDS consists of 14 title sections and three normative annexes (see **Table 3**).

Scope, Background, Application

Key differences:
- As with ISO 13485, GDPMDS allows the organization to justify not implementing a requirement that is deemed not applicable to the medical device(s) in question.
- GDPMDS removed the paragraphs relating to design and development controls, and outsourcing ("…processes…which are not performed by the organization…").
- GDPMDS added new paragraphs applicable specifically for "suppliers of storage, warehousing, and secondary assembly and distribution services".

This section reflects the differences in scope. The GDPMDS' scope is limited to importers, distributors and secondary assemblers (defined as companies engaged in packing the medical device, which is already in its labeled primary package, into its secondary package). GDPMDS continues the spirit of ISO 13485 in allowing organizations to justify whether certain requirements are not applicable.

Normative References

Key differences:
- ISO 13485 makes reference to ISO 9000. GDPMDS does not make such references.

This section further reflects the limited scope of GDPMDS.

Terms and Definitions

Key differences:
- GDPMDS adds specific definitions on adverse effect, adverse event, certification bodies, distribution, export, field safety corrective action (FSCA), import, premises, packaging and secondary assembly.
- GDPMDS uses the term "field safety notice" in place of ISO 13485's "advisory notice."
- While ISO 13485 includes definitions of active implantable medical device, active medical device, implantable medical device, labeling and sterile medical device, GDPMDS includes a more comprehensive list of categories of devices in its Annex 2, which includes active implantable devices, anesthetic and respiratory devices, dental devices, diagnostic and therapeutic radiation devices, electro-mechanical medical devices, hospital hardware, in vitro diagnostic devices, non-active implantable devices, ophthalmic and optical devices, reusable instruments, single-use devices and technical aids for disabled persons.

The inclusion of additional definitions makes it easier for importers and distributors—many of whom may be inexperienced with postmarket surveillance and vigilance practices prior to *HPA* 2007—to comply. A list of medical device categories in Annex 2 corresponds to the available categories on a GDPMDS certificate.

Quality Management System

General Requirements

Key differences:
- GDPMDS omits the detailed texts pertaining to identifying, analyzing and monitoring processes within the organization, and retains only that "…the organization shall ensure control over such processes."

ISO 13485 uses the term "process" to refer to functions such as purchasing, receiving, quality control, manufacturing, shipping and more. Most organizations under the scope of GDPMDS have relatively simple processes, therefore the text is simplified.

Documentation Requirements

Key differences:
- General: ISO 13485 requires a quality manual; GDPMDS requires a site master file.
- General: ISO 13485 requires a separate file for each type or model of medical device; GDPMDS makes no such requirement.
- Control of Documents: GDPMDS requires documents to be controlled as with ISO 13485. However, texts related to documents of external origin, review and

Table 2. Certification requirements for companies in the medical device business in Singapore

Organization Type	ISO 13485	GDPMDS	Exempt
Manufacturer	V		
Importer		V	
Wholesaler		V	
Re-exporter			V
Imported for non-clinical use			V

Table 3. Overview of ISO 13485 and GDPMDS title sections

ISO 13485:2003	GDPMDS, Rev. 2.1
1. Scope 2. Normative references 3. Terms and definitions 4. Quality management system 5. Management responsibility 6. Resource management 7. Product realization 8. Measurement, analysis and improvement Annex A: Correspondence between ISO 13485: 2003 and ISO 13485:1996 Annex B: Explanation of differences between ISO 13485:2003 and ISO 9001:2000	1. Introduction 2. Quality management system 3. Resource management 4. Storage and stock handling 5. Traceability 6. Medical device complaints 7. Field safety and corrective action (FSCA) 8. Return of medical devices 9. Disposal of medical devices 10. Counterfeit, adulterated, unwholesome or tampered medical devices 11. Internal audits 12. Management review 13. Outsourced activities 14. Secondary assembly Annex 1: Scope of certification Annex 2: Medical device categories for inclusion in scope of certification Annex 3: Secondary assembly activities

approval by the original approving function and defined period for retaining obsolete versions are removed.

The use of the term "site master file" instead of "quality manual" suggests that the documentation burden should be less than in ISO 13485. It is also expected that importers and distributors should have fewer types of controlled records compared to manufacturers.

Management Responsibility

GDPMDS omits the entire sections on management commitment, customer focus, quality policy and planning, and retains only:
- The sections on responsibility and authority and management remain basically unchanged, but are re-categorized under the "Resource management" section in GDPMDS.
- The section on management review is basically unchanged, but is set apart in GDPMDS as its own title section, "Management review."

Importers and distributors are often small enterprises where the distinction between management and non-management is frequently irrelevant. Therefore, only the critical sections are retained in GDPMDS.

Resource Management

Key differences:
- The section on provision of resources is omitted in GDPMDS.
- The section on human resources is renamed "personnel" in GDPMDS. ISO 13485 states that, "Personnel performing work affecting product quality shall be competent," whereas GDPMDS states, "Key personnel in charge of warehouse operations shall [be competent]."
- Sections on infrastructure and work environment are entirely rewritten under "premises and facilities," which requires the organization to observe adequate premises and equipment, cleanliness and pest control.

Under GDPMDS, warehouse personnel are considered key; therefore, personnel competency is specifically required. Similarly, the storage or warehouse area is considered key. Specific statements on cleanliness and pest control borrowed from food and pharmaceutical GMP regulations allow storage and warehouse operators to respond more directly than the relatively general statements in ISO 13485.

Table 4. Summary of corresponding sections between ISO 13485 and GDPMDS.

ISO 13485:2003	GDPMDS, Rev. 2.1
1 Scope	1 INTRODUCTION
1.1 General	1.1 Purpose 1.2 Background 1.3 Scope
1.2 Application	1.4 Application
2 Normative references	None
3 Terms and definitions	1.5 Definitions Annex 2
4 Quality management system	2. Quality management system
4.1 General requirements	2.1 General requirements
4.2 Documentation requirements	2.2 Documentation requirements
4.2.1 General	2.2.1. General
4.2.2 Quality manual	2.2.2. Site Master File
4.2.3 Control of documents	2.2.3. Control Of Documents
4.2.4 Control of records	2.2.4. Control Of Records
5 Management responsibility 5.1 Management commitment 5.2 Customer focus 5.3 Quality Policy 5.4 Planning 5.4.1 Quality objectives 5.4.2 Quality management system planning 5.5 Responsibility, authority and communication	None
5.5.1 Responsibility and authority	3.1.3. Responsibility And Authority
5.5.2 Management representative	3.1.4. Management Representative
5.5.3 Internal communication	None
5.6 Management review 5.6.1 General	12. MANAGEMENT REVIEW
5.6.2 Review input	12.1. Review input
5.6.3 Review output	12.2. Review output
6 Resource management	3 Resource management
6.1 Provision of resources	None
6.2 Human resources	3.1. Personnel
6.2.1 General	3.1.1. General
6.2.2 Competence, awareness and training	3.1.2. Training
6.3 Infrastructure 6.4 Work environment	3.2. Premises And Facilities 3.2.1. General
None	3.2.2. Cleanliness
None	3.2.3. Pest Control
7 Product realization 7.1 Planning of product realization 7.2 Customer-related processes 7.2.1 Determination of requirements related to the product 7.2.2 Review of requirements related to the product 7.2.3 Customer communication 7.3 Design and development 7.3.1 Design and development planning 7.3.2 Design and development inputs 7.3.3 Design and development outputs 7.3.4 Design and development review 7.3.5 Design and development verification 7.3.6 Design and development validation 7.3.7 Control of design and development changes 7.4 Purchasing 7.4.1 Purchasing process 7.4.2 Purchasing information 7.4.3 Verification of purchased product 7.5 Production and service provision	None
7.5.1 Control of production and service provision 7.5.1.1 General requirements 7.5.1.2 Control of production and service provision — Specific requirements 7.5.1.2.1 Cleanliness of product and contamination control	

ISO 13485:2003	GDPMDS, Rev. 2.1
7.5.1.2.2 Installation activities	4.5. Installation And Servicing 4.5.1. Installation
7.5.1.2.3 Servicing activities	4.5.2. Servicing
7.5.1.3 Particular requirements for sterile medical devices 7.5.2 Validation of processes for production and service provision 7.5.2.1 General requirements 7.5.2.2 Particular requirements for sterile medical devices 7.5.3 Identification and traceability 7.5.3.1 Identification	None
7.5.3.2 Traceability 7.5.3.2.1 General	5. TRACEABILITY
7.5.3.2.2 Particular requirements for active implantable medical devices and implantable medical devices 7.5.3.3 Status identification 7.5.4 Customer property	None
7.5.5 Preservation of product	4. STORAGE AND STOCK HANDLING 4.1. Receipt Of Stock 4.2. Calibration 4.3. Storage 4.3.1. Storage Condition 4.3.2. Stock Rotation 4.4. Delivery To Customers
7.6 Control of monitoring and measuring devices 8 Measurement, analysis and improvement 8.1 General 8.2 Monitoring and measurement 8.2.1 Feedback	None
8.2.2 Internal audit	11. INTERNAL AUDITS
8.2.3 Monitoring and measurement of processes 8.2.4 Monitoring and measurement of product 8.2.4.1 General requirements 8.2.4.2 Particular requirement for active implantable medical devices and implantable medical devices 8.3 Control of nonconforming product 8.4 Analysis of data	None
8.5 Improvement 8.5.1 General	None
8.5.2 Corrective action	6. MEDICAL DEVICE COMPLAINTS 7. FIELD SAFETY CORRECTIVE ACTION (FSCA)
8.5.3 Preventive action	None
None	8. RETURN OF MEDICAL DEVICES
None	9. DISPOSAL OF MEDICAL DEVICES
None	10. COUNTERFEIT, ADULTERATED, UNWHOLESOME OR TAMPERED MEDICAL DEVICES
None	13. OUTSOURCED ACTIVITIES
None	14. SECONDARY ASSEMBLY 14.1. General requirements 14.2. Assembly documents 14.3. Materials control 14.3.1. Medical devices to be repacked 14.3.2. Packaging materials 14.3.3. Medical device labeling 14.4. Good assembly practices 14.4.1. Special considerations 14.4.2. Assembly equipment 14.5. Quality control
None	Annex 1
None	Annex 3

Product Realization

Almost the entire title section of product realization is omitted in GDPMDS, including planning of product realization, customer-related processes, design and development and purchasing. The following sections are retained and reworded:

- The traceability section has been set apart in its own title section called "traceability" in GDPMDS. Unlike ISO 13485, GDPMDS does not explicitly require the

organization to state how to ensure traceability, but it only states requirements for retaining records of traceability.
- The preservation of product section has been set apart in its own title section called "storage and stock handling" in GDPMDS. Detailed requirements are included for receipt of stock, calibration, storage (storage condition, stock rotation), delivery, installation and servicing.

As GDPMDS stakeholders are not involved in design and development of products, much of this section from ISO 13485 is not applicable. Traceability has been given its own title section to highlight its importance. Storage and stock handling are critical components of GDPMDS, therefore elaborated requirements are added that are absent in ISO 13485.

Measurement, Analysis and Improvement

This section of ISO 13485 addresses aspects of postmarket activities and is completely reorganized and rewritten in GDPMDS:
- Aspects related to manufacturing processes, such as process monitoring, control, analysis and improvement, are completely removed in GDPMDS.
- The internal audit section is given its own title section in GDPMDS. Texts are simplified, requiring the organization to conduct periodic internal audits, document the responsibilities and requirements and respond with corrective actions.
- A new title section called "medical device complaints" is created in GDPMDS, requiring the organization to establish procedures for handling complaints, maintain records of investigation and follow-up actions and report to regulatory authorities.
- A new title section called "field safety corrective action (FSCA)" is created in GDPMDS, requiring the organization to establish procedures for handling FSCA, informing regulatory authorities prior to execution of FSCA and maintaining FSCA records.
- There is no specific section in GDPMDS that corresponds to "preventive action" in ISO 13485.

Internal audits, complaints handling and FSCA have been given their own title sections to highlight their importance, as importers and distributors are largely involved in postmarket activities only (as opposed to premarket activities). On the contrary, there is no specific section in GDPMDS corresponding to preventive actions, reflecting the fact that preventive actions relating to potential product nonconformities must be addressed at the manufacturer level.

Additional Sections in GDPMDS

GDPMDS also contains additional sections that are completely absent in ISO 13485:
- The "return of medical devices" section requires the organization to establish procedures for handling returns and for re-evaluation of such devices.
- The "disposal of medical devices" section requires the organization to establish procedures for the disposal of devices.
- The "counterfeit, adulterated, unwholesome or tampered medical devices" section requires the organization to segregate such devices and report to the appropriate regulatory authority, registrant and product owner.
- The "outsourced activities" section is implied in ISO 13485 but explicitly set out in GDPMDS. It requires the organization to ensure that the outsourced processes are controlled. It also states that outsourced organizations may still be required to be certified to GDPMDS.
- The "secondary assembly" section is applicable to organizations that carry out secondary assembly and consists of detailed requirements in batch assembly records, materials control, good assembly practices and quality control. Under GDPMDS, secondary assembly is defined as "the process of repackaging a medical device from its original packaging into another packaging, without breach of the primary package, before the medical device is supplied."

While return of medical devices, disposal of medical devices and outsourced activities are all implied in ISO 13485, their importance for regulating importers and distributors is highlighted. The problem of counterfeit products tends to be more common in developing Asia than in developed countries, therefore the issue is emphasized. Secondary assembly is unique to importers and is never addressed in ISO 13485.

Summary and Conclusion

Table 4 summarizes the corresponding sections between ISO 13485 and GDPMDS that were discussed above.

For seasoned quality system professionals, the GDPMDS requirements contain no ground-breaking concepts. However, for regulators, businesses and consumers in today's increasingly complex supply chain, GDPMDS represented a success story in implementing a reasonable level of regulation in a business area that was previously uncategorized and nearly uncontrolled.

At the time this article was written, further enhancements in GDPMDS requirements were expected from the Health Sciences Authority (HSA) of Singapore, such as simplified requirements for importers and wholesalers that solely deal with Class A devices, expected to be effective in 2013. Neighboring economies, including Malaysia and Hong Kong, have publicly indicated their intentions to adopt similar regulations in light of their success in Singapore. We look forward to improving the quality of the medical device industry as well as the welfare of consumers in these markets.

References
1. Regulators in many developing countries use the term "reference country" to refer to a country with mature regulatory systems and capabilities. While each regulator may have a different list of reference countries, these commonly include the US, Canada, Australia, EU countries, Switzerland, the UK, etc.
2. TS-01, Revision 2.1, Good Distribution Practice for Medical Devices in Singapore – Requirements, 1 September 2012, Health Sciences Authority of Singapore.

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