

# HEALTH SCIENCES AUTHORITY

## REGULATORY GUIDANCE

October 2011

# MEDICAL DEVICE GUIDANCE

GN-01: Guidance on the Application of Good Distribution  
Practice for Medical Devices

Revision 3



**PREFACE**

This document is intended to provide general guidance. Although we have tried to ensure that the information contained here is accurate, we do not, however, warrant its accuracy or completeness. The Health Sciences Authority (HSA) accepts no liability for any errors or omissions in this document, or for any action/decision taken or not taken as a result of using this document. If you need specific legal or professional advice, you should consult your own legal or other relevant professional advisers.

In the event of any contradiction between the contents of this document and any written law, the latter should take precedence.

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## **1. INTRODUCTION**

### **1.1. Purpose**

This document provides guidance to assist in the development, implementation and maintenance of the quality management system that aims to meet the requirements of the Good Distribution Practice for Medical Devices (GDPMDS).

### **1.2. Background**

This document recommends some approaches that an organisation can follow to implement and maintain a quality management system that conforms to the requirements of GDPMDS.

This document is useful in providing a better understanding of the requirements of GDPMDS and illustrates some of the approaches available to meet the requirements of GDPMDS.

This document also provides useful information to certification bodies and the Singapore Accreditation Council.

*NOTE Conformance to GDPMDS does not imply compliance to any written law; it is the responsibility of the organisation to ensure that they are in compliance with all applicable laws in force.*

*NOTE In the event of any contradiction between the requirements of this document and any written law, the latter shall take precedence.*

### **1.3. Scope**

This document provides guidance for the application of the requirements of GDPMDS. It does not add to or change the requirements of GDPMDS.

This document is not to be used as the basis of certification assessment activities or regulatory inspection.

#### **1.4. Definition**

Nil.

## **2. QUALITY MANAGEMENT SYSTEM**

### **2.1. General Requirements**

#### **Good Distribution Practice For Medical Devices**

## **2. QUALITY MANAGEMENT SYSTEM**

### **2.1 General Requirements**

The organisation shall establish, document, implement and maintain a quality management system and maintain its effectiveness in accordance to the requirements of GDPMDS.

Where an organisation chooses to outsource any activities that may affect the quality of medical devices, the organisation shall ensure control over such processes.

#### **Guidance:**

The quality management system established should be sufficiently robust to meet external and internal factors such as changes in regulatory requirements, customer feedback, changes to key personnel, facilities, etc.

For outsourced processes or processes, see clause 13.

### **2.2. Documentation Requirements**

#### **2.2.1. General**

#### **Good Distribution Practice For Medical Devices**

## **2.2 Documentation Requirements**

### **2.2.1 General**

The documentation shall include:

- a site master file,
- documented procedures required by the GDPMDS,

- documents needed by the organisation to ensure the effective planning, operation and control of its processes,
- records required by the GDPMDS, and
- any other documentation specified by the regulatory authorities.

All documented requirements, procedures and activities shall also be implemented and maintained.

**Guidance:**

It is important to recognise that the structure and level of detail required in the procedures should be tailored to the needs of the organisation. It is also dependent on the methodology or approach taken to implement the GDPMDS requirements, and the skills and qualifications of the personnel involved in the activities.

Procedures or instructions may be presented in any form (text, graphic or audio-visual) or medium.

**2.2.2. Site Master File****Good Distribution Practice For Medical Devices****2.2.2 Site Master File**

The organisation shall establish and maintain a site master file that includes

- the scope of the GDPMDS implemented, including the details of, and justification for any exclusion and/or non-application,
- the documented procedures established for the GDPMDS, or reference to them, and
- information regarding the premises where activities are conducted.

See Guidance on Preparation of a Site Master File for Establishment Licensing.

### 2.2.3. Control Of Documents

#### Good Distribution Practice For Medical Devices

##### 2.2.3 Control Of Documents

Documents required by GDPMDS shall be controlled.

A documented procedure shall be established for the control of documents.

All documents shall be prepared, approved, signed and dated by an appropriate authorised person(s) and any change in person(s) permitted to carry out this task requires authorisation.

Documents shall be reviewed regularly and kept up-to-date. When a document has been revised, a control system shall be established to prevent the unintended use of the superseded version.

There is no specific guidance for this subclause of GDPMDS.

### 2.2.4. Control Of Records

#### Good Distribution Practice For Medical Devices

##### 2.2.4 Control Of Records

Records shall be established and maintained to provide evidence of conformity to requirements of GDPMDS. Records shall be legible, readily identifiable and retrievable.

A documented procedure shall be established to define the controls needed for the identification, storage, protection, retrieval, retention time and disposition of records.

The organisation shall retain the records for a period of time:-

- specified by relevant regulatory requirements, or
  - at least equivalent to the lifetime of the medical device as defined by the product owner of the medical devices, or
  - no less than two years from the date that the medical device is shipped from the organisation,
- whichever is the longest.

**Guidance:**

Records should be kept of each purchase and sale, showing the date of purchase and supply, name of medical device, quantity received or supplied and name and address of supplier or consignee.

For transactions between product owners and wholesalers, records should ensure traceability of the origin and destination of products. For example, by the use of batch numbers, all suppliers of, or those supplied with, a medical device can be identified.

Where an electronic records system is used in place of a paper-based system, the system utilised should have built-in checks and balances to ensure the integrity of the records and to protect against unauthorised entries. The system should also incorporate audit trails for tracking changes.

**3. RESOURCE MANAGEMENT****3.1. Personnel****3.1.1. General****Good Distribution Practice For Medical Devices****3. RESOURCE MANAGEMENT****3.1 Personnel****3.1.1 General**

Key personnel in charge of warehousing operations shall possess the necessary competence in terms of education, training, skills and experience, prior to performing their work.

**Guidance:**

The organisation should consider the experience, qualifications, capabilities and abilities of personnel in charge of the warehousing operations.

Personnel working within the quality system require a certain level of competence or training (internal or external) before they can perform the tasks properly. Training may take the form of on-the-job training, on-the-job coaching by supervisors, instructional briefings, courses, workshops, etc.

Special training may be necessary for personnel dealing with certain categories of substances/materials such as chemicals, biological, radiation emitting or energy source components and products.

**3.1.2. Training****Good Distribution Practice For Medical Devices****3.1.2 Training**

The organisation shall

- determine the necessary competence for the key personnel,
- provide training to satisfy these needs,
- evaluate the effectiveness of the training, and
- maintain training records.

**Guidance:**

Training for personnel will be tailored to the person's assignment. Typical training and education should cover:

- nature of business,
- health, safety and environmental regulations,

- organisation's policies,
- function of the personnel,
- procedures and instructions of relevance to personnel.

Effectiveness of the training should be evaluated to ensure competency. Evaluation can consist of polling the trainee, evaluating the work performed after training, etc.

Records should be maintained to show the competencies that a person possesses. These include training received and results of that training.

### 3.1.3. Responsibility And Authority

#### **Good Distribution Practice For Medical Devices**

### **3.1.3 Responsibility And Authority**

The organisation shall ensure that responsibilities and authorities are defined, documented and communicated within the organisation. The organisation shall establish the interrelation between all personnel who manage, perform and verify work that affects quality, and shall ensure the independence and authority to perform these tasks.

#### **Guidance:**

The organisation may document job descriptions, including key responsibilities and authorities, in the Site Master File.

The personnel holding key responsibilities and authorities may also be documented as part of procedures.

### 3.1.4. Management Representative

#### **Good Distribution Practice For Medical Devices**

### **3.1.4 Management Representative**

The organisation shall appoint a member of the management who, irrespective of other responsibilities, shall have the ultimate responsibility of:

- ensuring that processes needed for the quality management system are established, implemented and maintained,
- reporting to top management on the performance of the quality management system and any need for improvement, and
- ensuring the promotion of awareness of regulatory and customer requirements throughout the organisation.

*NOTE The responsibility of a management representative can include liaising with external parties on matters relating to the quality management system.*

#### **Guidance:**

Only one member of management is to be designated as the organisation's management representative.

There should be no conflict of interest between the other responsibilities and functions that the management representative performs and those relating to the quality management system.

The management representative may delegate responsibilities to others within the organisation.

## **3.2. Premises And Facilities**

### **3.2.1. General**

#### **Good Distribution Practice For Medical Devices**

### **3.2 Premises And Facilities**

#### **3.2.1 General**

The organisation shall ensure that the premises and equipment used are

suitable and adequate to ensure proper conservation and distribution of medical devices.

There is no specific guidance for this subclause of GDPMDS.

### 3.2.2. Cleanliness

#### **Good Distribution Practice For Medical Devices**

##### **3.2.2 Cleanliness**

The organisation shall establish documented requirements for cleaning of premises, including frequency and methods.

Records of cleaning shall be maintained.

#### **Guidance:**

Storage areas should be cleaned and accumulated waste removed at regular intervals. The frequency and methods of cleaning the premises and areas should be recorded.

No smoking, eating and drinking should be permitted in areas used for storage and handling of medical devices.

### 3.2.3. Pest Control

#### **Good Distribution Practice For Medical Devices**

##### **3.2.3 Pest Control**

The organisation shall establish a pest control programme to identify and prevent pest infestation.

Records of pest control programme shall be maintained.

**Guidance:**

The storage area should be designed and equipped to prevent the entry of insects, rodents and other pests/animals.

There should be a pest control programme to identify and prevent pest infestation. Appropriate records should be kept for these purposes.

**4. STORAGE AND STOCK HANDLING****4.1. Receipt Of Stock****Good Distribution Practice For Medical Devices****4. STORAGE AND STOCK HANDLING**

The organisation shall provide suitable and adequate storage to ensure proper conservation of the medical devices.

**4.1 Receipt Of Stock**

The organisation shall establish and implement inspection or other activities necessary to ensure that medical devices received meet specified requirements.

Medical devices subject to specific storage measures shall be immediately identified and stored in accordance with the specified instruction(s).

Records of the verification shall be maintained.

**Guidance:**

The receiving bays should protect deliveries from bad weather during unloading. The reception area should be separate from the storage area.

Medical devices requiring special storage conditions (e.g. temperature and/or humidity or narcotics requiring additional security measures) should be placed

in separate areas constructed and equipped to provide the desired conditions.

A list of such medical devices should be maintained and the medical devices properly identified.

## **4.2. Calibration**

### **Good Distribution Practice For Medical Devices**

#### **4.2 Calibration**

Equipment used to ensure proper conservation and distribution of medical devices shall be calibrated or verified at specific intervals, or prior to use, against measurement standards traceable to international or national standards.

#### **Guidance:**

The instruments used for measuring and monitoring temperature and humidity should be calibrated or verified for accuracy and the results of such calibrations or verifications should be recorded and retained.

## **4.3. Storage**

### **4.3.1. Storage Condition**

### **Good Distribution Practice For Medical Devices**

#### **4.3 Storage**

##### **4.3.1 Storage Condition**

Medical devices shall be stored under conditions specified to prevent deterioration by light, moisture, temperature or other conditions.

Storage conditions shall be monitored and recorded periodically, where appropriate.

Records of the storage conditions shall be maintained.

**Guidance:**

The storage of medical devices should be carried out in buildings or parts of buildings that have been built for, or adapted to this purpose.

Buildings should protect medical devices from contamination and deterioration, including protection from excessive heat or undue exposure to direct sunlight.

Buildings should have sufficient security to prevent unauthorised access and misappropriation of the medical devices.

Premises should be constructed, serviced and maintained regularly to protect stored medical devices, from all potentially harmful influences such as undue variations of temperature and humidity.

There should be adequate storage areas, and where applicable, physically separated zones for the orderly segregation of medical devices.

The storage areas should have adequate lighting and ventilation.

Medical devices should be stored off the ground and suitably spaced to permit cleaning and inspection. Pallets should be well maintained and kept in a good state of cleanliness.

There should be designated areas for quarantined, saleable stock, expired, rejected/damaged, recalled and returned medical devices. Alternative means of segregation should be considered if proven, to prevent mix-up.

Appropriate and suitable storage conditions should be provided for hazardous, sensitive and dangerous materials such as combustible liquids

and solids, pressurised gases, highly toxic and radioactive substances.

Adequate precautions should be taken against spillage or breakage, attack by micro-organisms, contamination and cross-contamination.

Where controlled environmental storage conditions are required, these conditions should be continuously monitored and documented. Appropriate actions, on the premise, equipment and/or materials should be taken when the storage conditions are not met. As far as possible, the actual storage temperature should be expressed quantitatively. Where the storage temperature is not expressed quantitatively or stated (in terms of a range) on the labels of the registered medical device, a set of definitions, given in Table 1 (Storage Temperature Values) of Annex 1, should be used as guidance.

Where storage conditions are stated on the label, the set of definitions, given in Table 2 (Storage Condition Guidelines) of Annex 1, should be used as guidance.

Temperature of the storage areas must be measured at suitable predetermined intervals to show the maximum and minimum temperatures for the day and recorded. Where applicable, humidity measurements should also be performed.

It is recommended that temperature monitors be located in areas that are most likely to show fluctuations.

#### **4.3.2. Stock Rotation**

##### **Good Distribution Practice For Medical Devices**

#### **4.3.2 Stock Rotation**

The organisation shall establish a system to ensure stock rotation.

Medical devices beyond their expiry date or shelf life shall be segregated from usable stock. They shall be clearly labelled as “Not for Sale” or in other similar phrases/words.

The expired medical devices shall be disposed of in accordance to Clause 9.

**Guidance:**

Comprehensive records should be maintained showing all receipts and issues of medical devices according to batch number or equivalent.

Periodic stock reconciliation should be performed comparing the actual and recorded medical devices quantity. In any case, this should be performed when each batch is totally exhausted. All significant stock discrepancies should be subjected to investigation to check for inadvertent mix-ups and wrong issues.

A system should be in place to ensure that medical devices due for expiry earliest are sold and/or distributed first (Earliest-Expiry-First Out, EEFO). For cases where no expiry dates exist for the medical devices, FIFO (First-In-First-Out) should be applied. Deviations from this system may be permitted for exceptional cases however, such deviations should be temporary and appropriate.

Medical devices with broken seals, damaged packaging or suspected tampering/contamination must not be sold or supplied.

Medical devices bearing an expiry date must not be received or supplied close to or after the expiry date such that this date is likely to occur before the consumer uses the medical devices.

All labels and containers of medical devices should not be altered, tampered or changed.

#### 4.4. Delivery To Customers

##### Good Distribution Practice For Medical Devices

#### 4.4 Delivery To Customers

The organisation shall establish adequate methods of transportation to achieve safe and secure delivery of all medical devices from their point of collection to their point of delivery.

Medical devices shall be transported in such a way that:-

- their identification is not lost;
- they do not contaminate, and are not contaminated by, other medical devices or materials/substances;
- adequate precautions are taken against spillage, breakage or theft;
- they are secure and not subjected to unacceptable degrees of heat, cold, light, moisture or other adverse influence, or to attack by microorganisms and pests.

Medical devices requiring controlled temperature storage or other special control and conditions shall be transported by appropriate or specialised means.

#### Guidance:

Procedures should be in place to achieve safe and secure delivery of all medical devices from their point of collection to their point of delivery.

There should be adequate provision for the security, storage condition and protection of the quality of medical devices during all transportation. The transport process should not affect the integrity and quality of the medical devices.

*NOTE Medical devices should be supplied to an authorised person only. When the medical device is intended solely for professional use, such medical device should be supplied to the targeted type of user.*

Medical devices requiring controlled temperature storage should be transported by appropriate or specialised means. Special care should be exercised when using dry ice during transportation. Medical devices should not come into contact with dry ice as this may cause freezing of the medical devices.

The use of medical devices to monitor temperature during delivery is recommended. Such records should be reviewed.

Vehicles used should be adapted and maintained to suit the operations to be carried out. Vehicles should not be used as a store for medical devices.

Deliveries should be made only to authorised wholesalers, distributors or persons authorised to supply medical device products.

#### **4.5. Installations And Servicing**

##### **Good Distribution Practice For Medical Devices**

#### **4.5 Installation And Servicing**

##### **4.5.1 Installation**

Where installation of medical device is a specified requirement, the organisation shall establish and maintain adequate installation and inspection instructions, and where appropriate test procedures.

Instructions and procedures shall include directions for ensuring proper installation so that the medical device will perform as intended after installation. Installation, inspection and any required testing are to be performed in accordance with the instructions and procedures.

The records of inspection and any test results to demonstrate proper installation shall be maintained.

#### **4.5.2 Servicing**

Where servicing is a specified requirement, the organisation shall establish and maintain instructions and procedures for performing and verifying that the servicing meets the specified requirements.

Records of servicing shall be maintained.

#### **Guidance:**

When an organisation specifies that they perform installation and/or servicing of medical devices, instructions and procedures for performing and verifying that the installation and servicing meets the specified requirements should be established.

Appropriately trained personnel should conduct installation and servicing of medical devices.

## **5. TRACEABILITY**

### **Good Distribution Practice For Medical Devices**

#### **5. TRACEABILITY**

Records providing traceability of medical devices from supplier and to the customers shall be maintained.

The organisation shall retain the records for a period of time:-

- specified by relevant regulatory requirements, or
  - at least equivalent to the lifetime of the medical device as defined by the product owner of the medical devices, or
  - no less than two years from the date that the medical device is shipped from the organisation,
- whichever is the longest.

**Guidance:**

Identification of product by batch/lot/serial number permits traceability in two directions: forward to the customers and backward to the manufacturer.

Traceability to the customers is important as it is necessary to track medical devices right down to the user (e.g. Patients or hospitals) in the event of a field safety corrective action (FSCA). The traceability to the manufacturers allows for investigation of quality-related problems and feedback to prevent recurrence of nonconforming products.

Records providing traceability may include delivery order from the supplier, distribution or sales records etc. The records should allow for the date, name of medical device, quantity supplied, lot/batch number or serial number, name and address of the supplier and addressee to be ascertained.

Proof of delivery transactions should be also be kept.

**6. MEDICAL DEVICE COMPLAINTS****Good Distribution Practice For Medical Devices****6. MEDICAL DEVICE COMPLAINTS**

The organisation shall establish a documented procedure for handling of complaints regarding medical devices.

Any reports of adverse event that meets the regulatory reporting criteria received by the organisation shall be reported to the regulatory authority.

*NOTE Reporting criteria and specific timelines for reporting of adverse events are stipulated in the Health Products (Medical Devices) Regulations*

Records of the complaint, investigation and any subsequent actions taken shall be maintained.

**Guidance:**

A procedure describing the actions to be taken in the handling of all written and oral complaints regarding a medical device should be available. There should be a record for each individual complaint.

The procedure for handling complaints shall ensure that the complaints received are investigated and followed through, and that corrective actions are taken to prevent repeated complaints, and, where a decision is made to recall the medical device, the details of the recall.

Within the company, a person shall be designated to handle complaints. This person must have the authority to initiate investigations. All investigations should be documented in writing.

If a medical device defect is discovered or suspected in a batch, consideration should be given to determine whether other batches are also affected.

The investigation should take into consideration the condition and circumstances under which the medical device was distributed, stored and used.

*NOTE Complaints regarding a medical device or its packaging distinct from those relating solely to matters within the control of the distribution chain, must be notified promptly to the product owner. When the complaint is an adverse event related to a medical device, the regulatory authority must be notified promptly.*

An investigation report must be prepared with all corrective/preventative actions clearly stated.

Complaints records should be reviewed regularly for any indication of specific or recurring problems requiring attention.

## 7. FIELD SAFETY CORRECTIVE ACTION (FSCA)

### Good Distribution Practice For Medical Devices

#### 7. FIELD SAFETY CORRECTIVE ACTION (FSCA)

The organisation shall establish documented procedures for handling of FSCA. The responsibilities for planning, conducting, reporting of the corrective action shall be defined in the documented procedure.

The regulatory authority shall be informed prior to execution of the FSCA. If the medical devices are exported, the overseas counterparts shall be informed of the FSCA.

Records of all actions taken in connection with the FSCA and their approval by the company and regulatory authority shall be maintained.

#### **Guidance:**

All customers to whom any medical devices affected by an FSCA have been distributed, shall be informed with the appropriate degree of urgency.

The field safety notice should indicate whether the action needs to be carried out at the retail level, and whether there is a need to remove all medical devices immediately from the shelves, preventing their mixing with other saleable stocks, etc.

Where the FSCA affects a particular batch, consideration should also be given to determine whether other batches/materials are also affected.

The regulatory authority must be informed prior to execution of any field safety corrective action. If the medical device is exported, the overseas counterparts and/or regulatory authorities must be informed of the recall.

All actions taken in connection with the FSCA must be approved by the

company and/or regulatory authorities, and recorded.

Upon completion of each FSCA, a final report must be provided to the regulatory authority. Reconciliation should be made between delivered and recovered quantities of medical devices.

## **8. RETURN OF MEDICAL DEVICES**

### **Good Distribution Practice For Medical Devices**

#### **8. RETURN OF MEDICAL DEVICES**

The organisation shall establish documented procedures for handling of returned medical devices.

All returned medical devices shall be segregated apart from saleable stock to prevent redistribution until a decision has been reached regarding their disposal.

The criteria for re-evaluation of the returned medical devices shall be documented. Records of the re-evaluation and any subsequent actions taken shall be maintained.

#### **Guidance:**

Any product returned to the organisation should be treated as a nonconforming product.

Written procedures describing the handling of returned medical devices and the corresponding records of all returns should be kept.

All returned medical devices should be kept separate from saleable stock to prevent redistribution until a decision has been reached regarding their disposal.

Some criteria for medical devices to be returned to saleable stock are:-

- the medical devices are in their original unopened containers and in good condition;
- it is known that the medical devices have been stored and handled under proper conditions;
- the remaining shelf life period is acceptable; and
- the medical devices have been examined and assessed by appropriate personnel. This assessment should take into account the nature of the medical device, any special storage conditions required, and the time that has elapsed since it was distributed. Special attention should be given to thermo-labile medical devices. Advice should be sought from the product owner as necessary.

The returned medical devices should only be formally released to saleable stock, following a satisfactory quality re-evaluation by a nominated, responsible person.

Medical devices returned to saleable stock should be placed in accordance with the stock rotation system established.

## **9. DISPOSAL OF MEDICAL DEVICES**

### **Good Distribution Practice For Medical Devices**

#### **9. DISPOSAL OF MEDICAL DEVICES**

The organisation shall establish a documented procedure for the disposal of medical devices.

If the medical devices have not been immediately sent for disposal, they shall be kept in a clearly segregated area and identified so that they will not be sold inadvertently or contaminate other medical devices.

Records of the disposal shall be maintained.

**Guidance:**

Medical devices that no longer meet specification (for example, expired, contaminated, damaged, defective, etc) should be disposed of properly.

Control should be established to ensure that:-

- the status is clearly identified;
- the products cannot re-enter the distribution system, and;
- it is disposed of safely.

Records of the disposal shall be maintained.

## **10. COUNTERFEIT, ADULTERATE, UNWHOLESOME OR TAMPERED MEDICAL DEVICES**

### **Good Distribution Practice For Medical Devices**

#### **10. COUNTERFEIT, ADULTERATE, UNWHOLESOME OR TAMPERED MEDICAL DEVICES**

Any counterfeit, adulterate, unwholesome or tampered medical devices found in the distribution network shall be physically segregated from other medical devices to avoid any confusion. They shall be clearly labelled as “Not for Sale” or in other similar phrases/words.

The organisation shall inform the regulatory authority, registrant and product owner immediately.

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**Guidance:**

Counterfeit medical devices are defective products that require reporting by the organisation to the regulatory authority. Any possession of counterfeit medical devices by the organisation must be reported to the regulatory authority.

Reporting shall be performed using the Adverse Event Report Form. Once the organisation becomes aware of possession of possibly counterfeit medical devices, a **48 hour reporting timeline shall apply**. Key information (i.e. brand, place and period of purchase) should be provided in the Adverse Event Report to assist in the detection of counterfeit medical devices supplied in Singapore.

Appropriate corrective measures should be undertaken for identified counterfeit medical device, which includes but are not limited to the following:-

- Reporting of possession of counterfeit medical devices to the regulatory authority,
- Segregation/quarantine of counterfeit medical devices,
- Investigation of supply chain breach,
- Communication to all affected wholesalers / distributors / retailers / consignees possibly supplied with counterfeit medical devices (prior notification to the regulatory authority is required for such communication)

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## 11. INTERNAL AUDITS

### Good Distribution Practice For Medical Devices

#### 11. INTERNAL AUDITS

The organisation shall conduct internal audits at planned intervals to monitor the implementation of and compliance with the requirements of GDPMDS.

The organisation shall define in a documented procedure, the responsibilities and requirements for planning and conducting audits and reporting of the results and maintenance of the audit records.

Actions to eliminate detected nonconformities and their causes shall be taken without undue delay. Verification of the actions taken and the reporting of verification results shall be recorded.

**Guidance:**

Internal audits should normally be conducted once a year.

Internal audits are conducted and recorded in order to monitor the implementation and conformance with requirements of GDPMDS.

The results of the audits are usually stated in a written report indicating the nonconformities found. Timely action should be taken to eliminate the nonconformities and their causes. The audit results should be communicated to management for review.

The organisation should identify and implement any changes necessary to ensure and maintain the continued suitability and effectiveness of the quality system through the use of the quality policy, quality objectives, audit results, analysis of data, corrective and preventive actions and management review.

**12. MANAGEMENT REVIEW****Good Distribution Practice For Medical Devices****12. MANAGEMENT REVIEW**

The top management shall review its quality management system at planned intervals, to ensure its continuing suitability, adequacy and effectiveness. This review shall include assessing opportunities for improvement and the need for changes to the quality management system.

Records from management reviews shall be maintained.

**12.1 Review input**

The input to management review shall include information on

- results of audits,
- customer feedback,

- process performance and product conformity,
- status of preventive and corrective actions,
- follow-up actions from previous management reviews,
- changes that could affect the quality management system,
- recommendations for improvement, and
- new or revised regulatory requirements

## **12.2 Review output**

The output from the management review shall include any decisions and actions related to

- improvement of the effectiveness of the quality management system and its processes,
- improvement of product related to customer requirements, and
- resource needs.

### **Guidance:**

The top management should review the quality management system on a regular basis. An annual review is generally acceptable for an established and effective quality management system.

Management records can be in any form that suits the organisation. These include notes of meeting and formal meeting minutes or notes, which can be produced, distributed and stored on paper or electronically.

Records of the management review should include the identity of those taking part in the review and all points of the review including description of any corrective or preventive action to be taken. For any action determined, the responsibility for such actions, the resources, target dates for completion, etc should be identified.

### 13. OUTSOURCE ACTIVITIES

#### Good Distribution Practice For Medical Devices

### 13. OUTSOURCE ACTIVITIES

Where the organisation outsources any process within the scope of the GDPMDS, the organisation shall ensure control over such processes.

The organisation shall establish requirements to ensure that the outsourced activities conform to specified requirements.

The type and extent of control applied to the supplier shall be dependent on the impact on meeting the requirements of GDPMDS.

The supplier shall be audited as part of the internal audit if the supplier has not been certified to GDPMDS.

For outsourced activities under Clause 4 of GDPMDS, the supplier of outsourced storage, warehousing, secondary assembly and distribution services shall be audited by the certification body as part of the organisation's system, unless the supplier is already certified to GDPMDS. The scope of the supplier's certification shall cover the scope of the organisation.

#### **Guidance:**

Certain processes such as cleaning, pest control, transportation, etc may be outsourced to third party service providers.

The organisation is required to demonstrate that it has control over the outsourced process by maintaining evidence that the selection of the supplier was based on appraisals appropriate to the service being purchased and the ability of the supplier to enable the organisation to meet requirements of GDPMDS and any other regulatory requirements. For example, if a supplier

carries out the cleaning operations, a written contract specifying the limits of responsibility of the organisation and the supplier should be considered. The contract should include areas to be cleaned, cleaning procedure and any training required for the cleaning staff, etc.

Specification may include any special conditions required for storage or transport of medical devices.

When monitoring the performance of the suppliers, the organisation should consider compliance trends and conformance history. The performance of the supplier should be monitored on a regular basis. Depending on the nature of the activities performed, the service provider may be subjected to inspection by the regulatory authority.

## **14. SECONDARY ASSEMBLY**

### **14.1. General Requirements**

#### **Good Distribution Practice For Medical Devices**

## **14. SECONDARY ASSEMBLY**

### **14.1 General Requirements**

The organisation shall plan and carry out secondary assembly of medical devices under controlled conditions.

Controlled conditions shall include, as applicable

- the availability of information that describes the characteristics of the medical device,
- the availability of documented procedures, documented requirements, work instructions, and reference materials and reference measurement procedures as necessary,
- the use of suitable equipment,
- the availability and use of monitoring and measuring devices,

- the implementation of monitoring and measurement activities,
- the implementation of release of medical devices, their delivery and post-delivery activities, and
- the implementation of defined operations for labelling and packaging of medical devices.

The organisation shall establish and maintain a record for each batch of medical devices that provides traceability (see clause 5) and identifies the amount assembled and the amount approved for distribution. The batch record shall be verified and approved by qualified personnel..

**Guidance:**

The size of assembly area must reflect the volume of assembly. The adequacy of the working space should permit the orderly and logical positioning of equipment and materials so as to avoid confusion and to minimize the risk of mix-up between different medical devices or their components.

Assembly areas should be well-lit and effectively ventilated, with air handling system (including temperature, humidity and filtration controls) where appropriate.

No smoking, eating and drinking should be permitted in areas used for storage and handling of medical devices.

Segregated areas should be provided for the storage of approved, quarantined, rejected, recalled and returned materials or products.

In considering which controlled conditions are applicable for a given process, a due consideration an organization should make is if in the absence of the control, whether there could be an adverse or potentially adverse affect on quality of the medical device. If yes, then control is necessary. The amount of control and level of detail may be commensurate with the degree of criticality

(e.g. based on the output of risk management activities) of the process in achieving the requirements for quality and the degree of training of personnel involved in the secondary assembly line.

Reference materials may be physical or visual, such as product examples indicating permissible colour variation, or visual such as photos of known non-conformities. Reference materials should be available at the point of use. An individual procedure could be in the form of a simple flowchart, or a processing sequence, combined with a checklist.

Suitable equipment should be designed and selected so that process and product specifications are met. It should be verified that new and/or significantly modified equipment meets purchasing/design specifications and is capable of operating within its defined limits and the process operating limits.

The risk of labelling and packaging errors can be minimised by the introduction of appropriate controls such as:-

- segregation of secondary assembly (e.g. packaging and labelling) operations from other operations,
- avoidance of packaging and labelling product of similar appearance in close proximity,
- secondary assembly line identification,
- application of line clearance procedures,
- destruction of unused batch-coded materials on completion of packaging and labelling,
- use of roll-feed labels,
- use of a known number of labels and reconciliation of usage,
- on-line printing, including batch coding,
- use of electronic code encoders/readers and label counters,
- use of labels designed to provide clear product differentiation,
- inspection of label content before use, and
- proper storage of labels in areas of restricted access.

Any secondary assembly work instructions should include:

- Name of product;
- Description of the applicable medical devices for assembly and pack size;
- A complete list of all the packaging materials required for a standard batch size, including quantities, sizes and types, with the code or reference number relating to the specifications of each packaging material;
- Where appropriate, an example or reproduction of the relevant printed packaging materials, and specimens indicating where to apply batch number references, and shelf-life of the product;
- Special precautions to be observed, e.g. a careful examination of the area and equipment in order to ascertain the line clearance before operations begin;
- A description of the packaging operation, including any significant subsidiary operations, and equipment to be used;
- Details of any in-process controls with instructions for sampling and acceptance limits, if applicable.

#### **14.2. Assembly documents**

##### **Good Distribution Practice For Medical Devices**

#### **14.2 Assembly documents**

A batch assembly record shall be kept for each batch or part batch assembled. The record shall carry the batch number and the quantity of bulk medical devices to be packed.

The assembly shall be made or completed at the time each action is taken and in such a way that all significant activities concerning the assembly of medical device are traceable.

These records shall be retained for a period of time:-

- specified by relevant regulatory requirements, or
- at least equivalent to the lifetime of the medical device as defined by the

- product owner of the medical devices, or
- no less than two years from the date that the medical device is shipped from the organisation,
- whichever is the longest.

**Guidance:**

Records that facilitate traceability and review of the secondary assembly of a batch of product, derived during the secondary assembly of that batch, should be contained in a batch record, and are frequently collated in a single file. Such files can be referred to as a “Device History Record”, “Batch Assembly Record”, “Lot History Record” or “Lot Record”

If it is not practical to include all the relevant documents in the batch record, then the record should list the titles of those documents and their location(s).

During secondary assembly, relevant information should be entered onto the batch record. Such information can include:

- the quantity of raw materials, components and intermediate products, and their batch number, if appropriate,
- the date of start and completion of different stages of secondary assembly, including sterilization records if appropriate,
- the quantity of product assembled,
- the signed results of all inspections and tests,
- the designation of the product line used, and
- any deviation from the secondary assembly specifications.

Data may be recorded by electronic data processing systems, photographic or other reliable means, but detailed procedures relating to the system in use should be available and the accuracy of the records should be checked.

If documentation is handled by electronic data processing methods, only authorized persons should be able to enter or modify data in the computer and there should be a record of changes and deletion; access should be

restricted by passwords or other means and the result of entry of critical data should be independently checked.

Batch records electronically stored should be protected by back-up transfer on magnetic tape, microfilm, paper or other means. It is particularly important that the data are readily available throughout the period of retention.

Records should be maintained of the distribution of each batch of the product in order to facilitate the recall of the batch if necessary.

### **14.3. Materials control**

#### **14.3.1. Medical devices to be re-packed**

#### **14.3.2. Packaging materials**

#### **14.3.3. Medical device labelling**

### **Good Distribution Practice For Medical Devices**

#### **14.3 Materials control**

##### **14.3.1 Medical devices to be re-packed**

For each delivery, the incoming medical devices shall be checked for integrity of package and seal, for correspondence between the delivery note and the supplier's labels, and for compliance with medical device quality specification.

Medical devices with breached primary package shall not be used for secondary assembly.

Medical devices in the storage area shall be appropriately labelled. There shall be appropriate procedures or measures to assure the identity of the contents of each packaging of the medical devices. Bulk containers from which quantities of the medical devices have been drawn shall be clearly identified.

Medical devices requiring special storage conditions shall be placed in separate areas constructed and equipped to provide the desired conditions. The storage conditions shall be continuously monitored and recorded.

As far as possible, the actual storage temperature shall be expressed quantitatively. Where the storage temperature is not expressed quantitatively or stated (in terms of a range) on the labels of the registered medical device, the definitions in Annex 1 of *GN-01 Guidance on the Application of Good Distribution Practice for Medical Devices (GDPMDS)* shall apply.

#### **14.3.2 Packaging materials**

The purchase, handling and control of all packaging materials shall be accorded attention similar to that given to starting materials.

When setting up a programme for the packaging operations, particular attention shall be given to minimising the risk of mix-ups or substitutions. Different medical devices shall not be packaged in close proximity unless there is physical segregation.

#### **14.3.3 Medical device labelling**

All original labelling (including instructions for use, label and any other informational sheet or leaflet, etc) and all original labelling information shall accompany the repackaged medical device when it is supplied. Additional secondary package labelling is permitted in accordance to Annex 3.

#### **Guidance:**

Medical devices should only be purchased from approved suppliers named in the relevant specifications and, where possible, directly from the producer. A batch certificate of analysis should be obtained from the supplier for each batch of product to be re-packed.

Inspection of breached primary packages has to be performed. Any breached packages should be disposed off and should not be re-processed and returned to the secondary assembly line.

Manufacturing activities such as sterilisation do not fall within the definition of secondary assembly. Please refer to Annex 3 of TS-01 Good Distribution Practice for Medical Devices (GDPMDS) for information on manufacturing activities that fall within the purview of secondary assembly.

The Quality Management System (QMS) Requirements for all other manufacturing activities other than secondary assembly is *ISO 13485:2003 Medical devices – Quality management systems – Requirements for regulatory purposes*.

Particular attention should be paid to printed materials. They should be stored in adequately secure conditions such as to exclude unauthorized access. Cut labels and other loose printed materials should be stored and transported in separate closed containers so as to avoid mix-ups. Packaging materials should be issued for use only by authorized personnel following an approved and documented procedure.

Each delivery or batch of printed or primary packaging materials should be given a specific reference number or identification mark.

Outdated or obsolete primary packaging material or printed packaging material should be destroyed and the disposal recorded.

#### **14.4. Good assembly practices**

##### **14.4.1. Special considerations**

##### **14.4.2. Assembly equipment**

<b>Good Distribution Practice For Medical Devices</b>
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## **14.4 Good assembly practices**

### **14.4.1 Special considerations**

All medical devices and materials used for assembly shall be checked before use by a designated person for quantity, identity and conformity with the packaging instructions. Line clearance shall be performed prior to commencement of the assembly operation.

The correct performance of any printing operation which is carried out separately or in the course of the packaging shall be checked and recorded.

### **14.4.2 Assembly equipment**

The organisation shall ensure that the assembly equipment used are suitable and adequate to ensure proper secondary assembly of medical devices.

The parts that come into contact with the medical devices must not affect the quality of the medical devices and present any hazard.

Control equipment shall be calibrated and checked at defined intervals by appropriate methods. Adequate records of such tests shall be maintained.

### **Guidance:**

Before any assembly begins, there should be recorded checks that the equipment and work station are clear of previous products, documents or materials not required for the planned process, and that equipment is clean and suitable for use.

Each batch of products produced must be assigned a unique batch number. Normally, filling and sealing should be followed as quickly as possible by labeling. If it is not the case, appropriate procedures should be applied to ensure that no mix-ups or mislabeling can occur.

The performance of the printing operation should be checked and recorded. Attention should be paid to printing by hand which should be re-checked at regular intervals.

Printed and embossed information on packaging materials should be distinct and resistant to fading or erasing.

On-line control of the product during packaging should include at least checking the following:

- General appearance of packages;
- Completeness of packages;
- Correctness of products and packaging materials used;
- Correctness of over-printing, e.g. batch number, expiry date.

Any significant or unusual discrepancy observed during reconciliation of the amount of bulk product and printed packaging materials and the number of units produced should be investigated and satisfactorily accounted for before release.

Upon completion of a packaging operation, any unused batch-coded packaging materials should be destroyed and the destruction recorded. A documented procedure should be followed if uncoded printed materials are returned to stock.

Where any packaging process validation applies, the study should be carried out in accordance with pre-defined and authorised protocols.

The appropriate marketing authorization of the product(s) to be assembled shall be complied with, and where necessary, the approval of the holder of the market authorisation and licensing authority shall be sought.

## 14.5. Quality control

### Good Distribution Practice For Medical Devices

#### 14.5 Quality control

Finished medical device assessment shall embrace all relevant factors, including assembly conditions, a review of packaging documentation, compliance with finished medical device specification and visual examination of the final finished pack.

The process of secondary assembly shall not compromise the medical device's conformance to the Essential Principles of Safety and Performance. Details of the essential principles of safety and performance can be found at *GN-16: Guidance on Essential Principles for Safety and Performance of Medical Devices*.

#### **Guidance:**

There should be designated and independent personnel in charge of Quality Control (QC).

If sampling is performed, the samples taken should be done in accordance with approved written procedures that describe:

- The method of sampling;
- The equipment to be used;
- The amount of the samples to be taken
- The storage conditions for the samples taken

Any in-process controls, including those carried out in the assembly area, should be approved by QC and the results recorded.

**ANNEX 1****T1: Storage Temperature Values**

<b>ON THE LABEL</b>	<b>GUIDANCE VALUES</b>
Freezer	The temperature is thermostatically controlled between – 20 °C and –10 °C.
Refrigerator	The temperature is thermostatically controlled between 2 °C and 8 °C.
Cold place	The temperature does not exceed 8 °C.
Cool place	The temperature is between 8 °C and 15 °C.
Room temperature	The temperature is between 15 °C and 30 °C.
Warm	The temperature is between 30 °C and 40 °C.
Excessive heat	The temperature is above 40 °C.
Do not store over 30 °C	The temperature is between 2 °C and 30 °C.
Do not store over 25 °C	The temperature is between 2 °C and 25 °C.
Do not store over 15 °C	The temperature is between 2 °C and 15 °C.
Do not store over 8 °C	The temperature is between 2 °C and 8 °C.
Do not store below 8 °C	The temperature is between 8 °C and 25 °C.

**T2: Storage Condition Guidelines**

<b>ON THE LABEL</b>	<b>GUIDANCE VALUES</b>
Protect from moisture	No more than 60% relative humidity in normal storage conditions; to be provided to the user in a moisture-resistant container.
Protect from light	To be provided to the user in a light resistant container.

# HEALTH SCIENCES AUTHORITY

Health Products Regulation Group  
Blood Services Group  
Applied Sciences Group

[www.hsa.gov.sg](http://www.hsa.gov.sg)

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