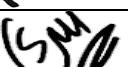


File	QUALITY MANAGEMENT SYSTEM RMT	
Scope of QMS	DESIGN, DEVELOPMENT & MANUFACTURING OF INTRAVASCULAR DEVICES (MICROSPHERES)	
Domain	QUALITY ASSURANCE	
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This document is a part of the QUALITY MANAGEMENT SYSTEM folder of REVIVE MEDITECH PVT LTD. compiled for compliance of ISO 13485:2016 requirements.		

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REVISION HISTORY

Revision	Status	Date	Description of Change
1.0	Obsolete	18-10-2024	Initial version

NOTE:

Document Status	Description	Marking Type	Document Type
DRAFT	Documents under creation, revision or review	In document background	Electronic
APPROVED	Approved documents in electronic Document Management System	In revision history table	Electronic
MASTER COPY	Approved documents in QA office	Stamped	Physical
CONTROLLED	Approved documents sent to concerned department for reference	Stamped	Physical
OBSOLETE	Documents replaced by new revisions	Stamped/Moved to archive	Physical/Electronic

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1. PURPOSE

This Standard Operating Procedure establishes controls for all chemicals used for **Intravascular Devices (Microspheres)** at **Revive Meditech Pvt Ltd.**, to:

- Ensure safe procurement, storage, handling, Safety hazards and disposal
- Maintain clear labelling and traceability
- Protect personnel, products and the environment
- In compliance with applicable Quality Management System requirements

Detailed chemical-specific data, including CAS numbers, hazards, storage, handling controls and disposal methods, are consolidated in **Section 6 and 7 tables** for operational clarity and compliance.

2. SCOPE

This SOP applies to all chemicals used, handled or stored at **Revive Meditech Pvt Ltd.**'s:

- R&D/Formulation Area
- Production, QC and Microbiology Areas
- Raw materials and Chemical Store

3. NORMATIVE REFERENCES

Revive Meditech Pvt Ltd. maintains compliance with the following standards and internal procedures related to chemical safety and management:

- ISO 13485:2016 – *Medical devices – Quality management systems – Requirements for regulatory purposes*
- ISO 14971:2019 – *Medical devices – Application of risk management to medical devices*

4. DEFINITIONS AND ABBREVIATIONS

Chemical Management: A set of processes (procurement, storage, handling, use, transfer, and disposal) to ensure safe and compliant management of all chemicals used in **Intravascular Devices (Microspheres)** production

Hazardous Chemical: Any chemical that poses physical, health, or environmental hazards such as being flammable (Ethanol, IPA), corrosive (NaOH), toxic (Lidocaine), reactive, or carcinogenic (DCM) etc.

Materials Material Safety Data Sheet (MSDS): A supplier-provided document detailing the hazards, safe handling, storage, PPE and disposal of chemicals. MSDSs are controlled within the QMS.

Corrective and Preventive Action (CAPA): A formal QMS process for investigating, correcting and preventing recurrence of chemical-related nonconformance

Personal Protective Equipment (PPE): Safety gear (e.g., nitrile gloves, goggles, lab coats, face shields, respirators) required per Section 6.6 to mitigate chemical hazards.

Standard Operating Procedure (SOP): A controlled QMS document defining standard processes, roles, and responsibilities.

AM: Assistant Manager

QA: Quality Assurance

QC: Quality Control

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5. ROLES & RESPONSIBILITIES

Role	Key Responsibilities	Designation
Initiator	<p>Request and Dispense chemicals through proper store management system.</p> <p>Verify COA/ MSDS, expiry, and storage conditions before use</p> <p>Label secondary containers with name, concentration, date, expiry, and user initials.</p> <p>Handle chemicals using appropriate PPE (gloves, goggles, lab coat, mask).</p> <p>Handle and use in for volatile/flammable/toxic chemicals or only in aseptic conditions as per requirement.</p> <p>Avoid cross-contamination by using dedicated tools and separating incompatible substances.</p> <p>Return unused stock promptly to correct storage, and report spills, breakages, or exposure.</p>	AM Store Technician AM QC Jr. Scientist AM Microbiology
Supervisor	<p>Review chemical requisitions for necessity and approval.</p> <p>Ensure safe chemical transfer and store between storage and work areas (secondary containment, cold chain if needed).</p> <p>Verify segregation of incompatible chemicals (oxidizers vs solvents, acids vs bases, flammable vs oxidizing agents).</p> <p>Confirm personnel are trained and adhering to MSDS guidelines.</p> <p>Oversee thawing/conditioning steps for frozen/refrigerated chemicals.</p> <p>Manage spill response, emergency first aid, and escalate to QA/EHS where needed.</p>	Production Manager Chief Supply Chain Officer Senior Biomaterial Scientist Quality Manager
Quality Assurance	<p>Approve chemicals for use only after QC release.</p> <p>Conduct routine audits of chemical stores and handling areas (ambient, refrigerated, frozen).</p> <p>Verify chemicals are labelled with storage conditions and expiry.</p> <p>Maintain chemical usage traceability in production/lot records.</p> <p>Ensure risk assessments are performed for hazardous chemicals.</p> <p>Evaluate supplier quality for chemicals used in Manufacturing processes.</p>	AM QA
Quality Control	<p>Verify incoming chemicals via COA/COC/MSDS and physical inspection.</p> <p>Assign storage category and apply QC labels.</p> <p>Perform re-testing for chemicals approaching expiry if applicable.</p> <p>Monitor stability and report changes in appearance, odor, or performance.</p> <p>Support investigations for product complaints linked to chemical quality.</p>	AM QC
Production Management	<p>Ensure only released and approved chemicals are used in production.</p> <p>Oversee proper dispensing, mixing, or dilution according to SOP.</p> <p>Confirm production records reflect chemical batch/lot traceability.</p> <p>Monitor chemical consumption and prevent unauthorized access/use.</p> <p>Ensure safe disposal of leftover or excess chemicals after production.</p>	Production Manager
Production/Maintenance	<p>Maintain storage equipment (freezers, refrigerators, ambient-controlled rooms) to ensure -20 °C, 2–8 °C, or ambient limits are consistently met.</p> <p>Calibrate and service temperature monitoring systems, alarms, and sensors.</p> <p>Maintain exhaust ventilation, and eye-wash/safety showers for chemical handling.</p> <p>Provide backup power for cold storage to prevent chemical degradation.</p> <p>Record and address temperature excursions promptly.</p>	Production Manager AM Store AM Microbiology AM Admin
Store Keeper	<p>Receive chemicals against purchase order and verify labeling.</p> <p>Place chemicals in appropriate storage conditions immediately</p>	AM Store

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	Segregate hazardous, flammable, corrosive, and incompatible categories. Maintain inventory log with lot number, expiry, and storage location. Implement FIFO/FEFO for chemical issuance. Quarantine expired/ damaged/ returned chemicals with “Do Not Use” labels. Issue chemicals only against authorized requisition.		
Microbiologist	Monitor and handle sterile chemicals, microbiological media, and reagents. Ensure aseptic practices when aliquoting sterile chemicals. Inspect cold chain integrity for media and microbial reagents. Support QA in risk assessments of contamination events linked to chemical handling/storage.		AM Microbiology
Procurement	Procure chemicals only from approved, qualified vendors. Ensure transport complies with storage needs (cold chain, dry ice, insulated shipping). Verify vendor-supplied COA, COC and MSDS availability. Track vendor performance and escalate quality issues to Quality. Coordinate replacements for delayed or rejected shipments.		AM Supply Chain
EHS Officer	Define hazard classes for chemicals and ensure segregation in storage and handling. Provide spill kits, neutralizing agents, fire extinguishers, and PPE. Train staff on spill response, first aid, and emergency evacuation. Manage hazardous chemical waste disposal as per environmental regulations. Investigate accidents/exposures and implement corrective actions. Monitor ventilation and air quality in chemical handling areas.		AM Microbiology AM QA AM Admin
HR (Training)	Conduct training of staff on SOP for chemical handling, MSDS usage, PPE, and hazard communication. Conduct refresher trainings after spills/incidents. Maintain training records for personnel handling hazardous chemicals. Ensure competency checks before authorizing personnel to handle restricted chemicals.		Manager HR/Admin
Admin	Ensure restricted access to chemical stores and handling areas. Support disposal vendor coordination for expired/damaged chemicals. Maintain emergency contact lists and arrange drills with EHS/HR. Provide logistical support for facility preparedness (backup storage rooms, safe transport routes).		AM Admin
Approving Authority	Give final approval for procurement, handling procedures, and risk assessments. Approve any planned temporary changes in storage/handling (e.g., alternate freezer during maintenance).		CEO CPO Quality Manager

6. CHEMICAL MASTER DATA

The table below provides essential data for chemicals, including CAS numbers, storage conditions, hazards and disposal information.

Sr. No.	Material	Cas No.	Form/ Conc.	Storage Conditions	Key Hazards	Disposal Method
1.	PLGA	26780-5 0-7	Powder (75:25, 65 kDa)	-20 °C freezer	Dust inhalation; low toxicity	Solid non-hazardous; if dissolved in DCM →

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Sr. No.	Material	Cas No.	Form/ Conc.	Storage Conditions	Key Hazards	Disposal Method	
						collect in halogenated solvent waste (HDPE)	
2.	Lidocaine	137-58-6	Solid	4 °C refrigerator	Toxic if ingested	Pharmaceutical toxic waste container	
3.	Ethanol	64-17-5	≥ 95 % liquid	Ambient, flammable cabinet	Highly flammable	Flammable solvent waste container (HDPE)	
4.	Dichloromethane (DCM)	75-09-2	Liquid	Ambient, flammable cabinet	Carcinogenic; VOC	Halogenated solvent waste container (HDPE)	
5.	PVA	9002-89-5	Powder (130 kDa)	Ambient dry shelf	Low toxicity; viscous solution hazard	Drain it diluted with plenty of water, if it is contaminated. Otherwise dispose of as solid waste in labeled container.	
6.	NaOH (0.1 N)	1310-73-2	Aqueous solution	Ambient corrosives cabinet	Corrosive	Neutralize to pH 7 then drain	
7.	Isopropyl Alcohol	67-63-0	Liquid	Ambient flammable cabinet	Highly flammable; VOC	Flammable solvent waste container (HDPE)	
8.	DMSO	CAS No. 67-68-5		Keep away from ignition; store cool, dry, ventilated, sealed, away from incompatibles.			
9.	Hydrogen Peroxide	SDBB2 228	Liquid	Store hydrogen peroxide in a cool, dry, and well-ventilated area below 25°C , protected from light and keep tightly closed to prevent contamination. Keep away from flammable or	Hydrogen peroxide is a strong oxidizer and can cause burns on contact with skin or eyes.	Dispose by diluting with plenty of water or neutralizing with sodium bisulfite , following safety regulations.	

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Sr. No.	Material	Cas No.	Form/ Conc.	Storage Conditions	Key Hazards	Disposal Method
				incompatible materials like acids and metals.		
10.	Chemgene		Liquid	Store Chemgen at 5–30°C in a dry, well-ventilated area, away from direct sunlight and incompatible materials.	Chemgen may cause skin and eye irritation on contact and respiratory irritation if inhaled.	Dispose of Chemgen by diluting with plenty of water and discarding according to local hazardous waste regulations.

Users should consult this table before handling, storing or labeling chemicals.

7. CHEMICAL CONTROL PLAN

Note: This table consolidates chemical-specific controls: approval criteria, handling PPE, storage segregation, expiry monitoring and waste classification.

Sr. No.	Chemical	Handling Controls	Storage / Segregation	Expiry / Shelf-Life Monitoring	Waste Classification And Disposal
1.	PLGA	Weigh in ventilated area; wear nitrile gloves + dust mask + lab coat	-20 °C freezer; segregated from volatiles, keep in airtight container	Expiry alerts at 90/60/30 days Record manufacture and expiry on container.	Solid non-hazardous. If dissolved/in solvent, treat as organic halogenated waste
2.	Lidocaine	Handle in aseptic area with gloves, goggles	2–8 °C fridge; segregated from solvents, keep in airtight container	Expiry alerts at 90/60/30 days	Pharmaceutical toxic waste container
3.	Ethanol	No open flames; spark-proof tools; nitrile gloves + goggles + lab coat	Ambient flammable cabinet; segregate from oxidizers, keep in airtight container	Expiry alerts at 90/60/30 days	Flammable solvent waste container (HDPE)
4.	DCM	Use mask.	Protect from direct light exposure, keep in airtight container	Expiry alerts at 90/60/30 days	Halogenated solvent waste container (HDPE)
5.	PVA	Dissolve slowly to avoid clumps using	Ambient shelf, grouped with non-hazardous	No formal shelf-life; rotate/retest	Drain if clean; else use solid waste container

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		gloves and goggles under hood	solids, keep in airtight container	stock annually or use period defined by stability study; record in RMF if extended		
6.	NaOH (0.1 N)	Handle in Corrosive-safe fume hood or well-ventilated area; full PPE (nitrile gloves + face shield + lab coat)	Corrosive cabinet; separate storage, keep in airtight container	Label with prep date; discard solution >30 days old	Neutralize then dispose as per SOP-Waste Management Procedure	
7.	IPA	Handle in Ventilated bench; PPE per MSDS	Store tightly closed in a cool, dry, ventilated area; away from heat, ignition, oxidizers, and incompatibles.	Expiry alerts at 90/60/30 days	Flammable solvent waste container (HDPE)	
8.	DMSO	Use gloves and masks, open in ventilated area	Store tightly closed, cool, dry, ventilated; away from heat, sparks, flame, and incompatibles.	Expiry alerts at 90/60/30 days	Dispose of in compliance with all local and national regulations. Follow label instructions	
9.		Handle hydrogen peroxide with care using gloves, goggles, and lab coat , avoiding contact with skin, eyes, and combustible materials.	Store hydrogen peroxide at 2–8°C in a cool, ventilated area, away from flammable, organic, or metallic materials .	Expiry alerts at 90/60/30 days	Classify hydrogen peroxide as hazardous oxidizing waste and dispose by controlled dilution or neutralization as per local environmental regulations.	
10.	Chemgene	Handle Chemgen with gloves, goggles, and lab coat , avoiding skin contact, inhalation, and ingestion.	Store Chemgen at 5–30°C in a cool, dry, and ventilated area, away from acids, bases, and oxidizing agents .	Expiry alerts at 90/60/30 days	Classify Chemgen as chemical hazardous waste and dispose through authorized waste handlers according to local environmental regulations.	

8. CHEMICAL STORAGE

This section shall provide operational guidance that complements the chemical-specific data for individual chemical including their **storage conditions** and **hazard classification**. It outlines the procedure, environmental controls, segregation strategies and monitoring expectations required to ensure safe, compliant storage of chemicals.

8.1 STORAGE OF CLEANING CHEMICALS:

All kind of chemicals must be stored under absolute control at designated Chemical Store room.

All Chemicals used at RMT must be controlled and stored in such a manner as to preclude their accidental misuse in processing and packaging areas.

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Chemicals must be stored in an enclosed area.

The storage area must be solidly built, well ventilated, and the lock of such type that a person cannot be locked in a chemical storage room.

Medical devices are susceptible to absorption of vapors or dust contaminations emitted from chemicals; therefore, all chemicals must be kept in an area isolated from raw materials, processing and finished product.

The cleaning and sanitation chemicals must be stored in the designated area of the store.

All Chemical Containers must be clearly labeled and secured with a lid.

8.2 STORAGE OF PRODUCTION & LABORATORY CHEMICALS:

All chemicals must be stored under absolute control at designated Chemical Store room.

All chemicals found must be controlled and stored in such a manner as to preclude accidental misuse in surface treatment areas.

Chemicals must be stored in an enclosed area secured with a door.

All chemical storage cabinets must be labeled as to the contents in the chemical cabinet.

These labels shall be clean, intact, and easily readable.

All containers shall be stored in the upright position.

All containers shall be checked periodically for leaks.

No chemicals will be carried through the production or clean room unless they are secured with the lid.

All containers shall be labeled at all times.

The bulk chemical should be stored away from the production operation. The bulk chemical storage area shall be:

- well ventilated
- Temperature controlled like cool
- Dry and clean
- Insects and pest free
- Enclosed
- Under lock and key
- Having controlled inventory

Chemical store's ventilation system shall not be common or linked with any other ventilation system. Some of the chemicals have fumes and must be having a separate ventilation system.

In chemical store, no other items should be stores. Chemical store shall only be used for the storage of chemicals.

Acidic chemicals shall be stored away from basic – alkaline chemicals to avoid reaction and combustion / explosion.

Chlorine based chemicals shall always be stored away from the acidic chemicals.

Spillage control tools shall be made available like broom, plastic bags, wiper, gloves, mask, etc.

The empty canes shall be stored separately and away from the production operations.

Firefighting equipment and first aid kit shall be available near to the chemical store.

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All identified deficiencies must be reported immediately to Quality Manager or Production Manager.

8.3 LABELING REQUIREMENTS

Containers must display:

- Chemical name + concentration
- CAS Number
- Lot/batch number
- Storage temperature
- Expiry date

9. CHEMICAL HANDLING

Prior to initiating a new experiment or procedure, all RMT employees must evaluate/classify the potential physical and health hazards associated with its chemicals and processes, which may be covered in training sessions with relevant employees.

Container labels and material safety data sheets, as well as other references, will be used to conduct the classification.

The evaluation/classification and training shall include preparation for any potential emergencies including reporting any unsafe conditions or production area incidents to the relevant manager or supervisor. There must be prior intimation to the relevant manager before conducting any process involving chemical handling.

Chemical resistant Gloves and safety glasses must be worn at all times when handling chemicals to include receiving in chemicals.

When working with flammable chemicals, be certain that there are no sources of ignition near enough to cause a fire or explosion in the event of a vapor release or liquid spill.

The chemicals' hazards, as determined from the MSDS and other appropriate references, MSDS copies shall be available in relevant production areas.

Personal Protective Equipment (PPE) should be chosen on the basis of type of chemicals handled and the degree of protection required as well as the areas of the body that may become contaminated.

Gloves must be worn whenever there is a chance for hand contact with chemicals, such as during the transfer of chemicals from one container to another or during the transfer of chemical wastes. Gloves must be worn if the chemicals involved are easily absorbed through the skin and/or are acute or chronic toxins. When working with the corrosive liquids, also wear gloves made of material known to be resistant to permeation by the corrosive chemical. No glove totally resists degradation and permeation over time and must be replaced periodically, depending on frequency of use, chemical concentration, and duration of contact.

10. SPILL KIT AND SPILL RESPONSE

Spill response kit must be available at chemical store, as well as all Production Area Zones where operators are using chemicals with their processes.

10.1 SPILL KIT CONTENTS

Following material are the contents of spill response kit.

- Tissue paper / towels
- Absorbent cotton pads

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- Broom & Wiper
- Plastic bag for larger spills
- Rubber gloves
- Face mask & Goggles
- Waste Bag
- Dust pan

Only trained personnel equipped with proper PPE and spill kit should attempt cleanup of spills.

10.2 SPILL RESPONSE STEPS

- Isolate the area
- Report incident: immediately to Production Manager or Quality Manager
- Retrieve spill kit and don appropriate PPE if the spill is containable. Else, leave the area to be handled by trained personnel.
- Stop the leak, if it is safe (upright container, cap it, close valve).
- Contain spill perimeter using towels or tissue paper to prevent spread.
- Absorb leaked liquid using pads.
- Collect and bag all residues, absorbents, and contaminated materials into waste bag/container.
- Clean and decontaminate the surface
- Fill in the Incident Register as per SOP Emergency Response.

10.3 POST-SPILL PROCEDURES

- Ensure **waste bags** are sealed, labeled (chemical, volume, date) and stored for disposal.
- **Decontaminate spill kit items;** restock missing items

Note: *Waste Disposal's procedural guidance for classification, storage, treatment, record-keeping, and regulatory compliance of chemical waste, ensuring safe handling and traceability will be conducted in accordance with the SOP - Waste Management.*

ANNEXES

CHEMICAL SPILL RESPONSE FLOWCHART

