GMP Site Quality Self-Assessment

based on

Rx-360 Supplier Assessment Questionnaire

Module 2, Site Specific Information

Relevant for

Sigma Aldrich Production GmbH
Sigma Aldrich Chemie GmbH
Industriestraße 25, 9470 Buchs SG
Switzerland
An affiliate of Merck KGaA, Darmstadt, Germany

The site Self-assessement covers our quality management system for the following regulated applications:
- Manufacturing of Excipients and APIs
- Development, Manufacturing and Distribution of Components for Medical Devices

The site also processes products which do not fall under any of the above mentioned regulated areas. For these products, other quality standards apply. For details, please refer to our 'non-GMP' Quality Site Self-Assessment.

Rx 360 An International Pharmaceutical Supply Chain Consortium

Merck KGaA, Darmstadt, Germany is an active member of the Rx 360 Consortium.

As a trusted partner of our customers, we deliver quality - always.

Merck KGaA, Darmstadt, Germany
Corporation with General Partners
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Sigma-Aldrich Corporation
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3050 Spruce Street
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Phone +1 (800) 521-8956 / +1 (314) 771-5765

EMD Millipore Corporation
A subsidiary of Merck KGaA, Darmstadt, Germany
400 Summit Drive Burlington,
MA 01803, USA
Phone +1 (781) 533-6000

Information

This document is based on the Rx-360 Consortium's Supplier Assessment Questionnaire template, Module 2. The contents of this questionnaire are built on the Rx-360 questionnaire version 2.0 intact with no question added or deleted.
Rx-360's CEO/COO gave permission to Life Science to use the Rx-360 logo.

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Rx-360 Supplier Assessment Questionnaire : Site-Specific Information

☐ Please check here if additional documents are attached.

SECTION 1. General Site Information	
1.1	Site or Facility-Specific Name: This questionnaire reflects GMP materials coming from this site. Two legal entities: Sigma-Aldrich Production GmbH Sigma-Aldrich Chemie GmbH
1.2	Address: Industriestrasse 25, 9470 Buchs SG, Switzerland GPS Coordinates: 47°10' N, 9°29' E
1.3	Phone: +41 (0)81 755 2511
1.4	Email: Please refer to your local Sales Representative
1.5	Fax: Please refer to your local Sales Representative
1.6	Website: http://www.sigmaaldrich.com/

SECTION 2. General Site Operating Information	
2.1	What year did the site start operating? 1953
2.2	What is the primary activity of the site? (e.g. manufacturing, distribution, etc.) Purchasing, manufacturing, testing and filling, analytical standards and reagents, biochemicals, research chemicals, fine chemicals and intermediates, excipients and active pharmaceutical ingredients (API)
2.3	To which, if any, subdivision of the parent company does the site belong? Merck KGaA, Darmstadt, Germany
2.4	Size of site (in sq. ft. or m.): approx. 37500 square meters building surface. 102000 square meters site surface
2.5	Please list or attach the normal hours/schedule of the facilities, including shutdown dates (if applicable): reception desk: Monday to Friday 07:30 to 12:00 and 13:00 to 17:00; production and filling: 2 shifts; shutdown for maintenance between Christmas and New Year
2.6	Total number of employees on site: approx. 475
2.7	Total number of employees in Quality: Quality Assurance 32, Quality Control: 38
2.8	Total number of employees in Manufacturing: 110
2.9	What quality management system is utilized on site? ☒ ISO 9001 ☒ ISO 13485 ☒ 21 CFR Part 210/211 ☒ 21 CFR Part 820 ☒ European GMP, Eudralex Volume 4 Part I ☒ European GMP, Eudralex Volume 4 Part II ☒ ICH Q7 ☐ HACCP ☐ ISO 22000 ☒ Other Please describe: IPEC GMP, ISO 17025, ISO 17034, ISO 14001, ISO 45001

SECTION 2. General Site Operating Information		
	Which Regulatory Initiatives does the site follow/comply with? ☒ REACH ☐ RoHs ☐ Ca Prop. 65 ☐ WEEE	
2.10	Does the company/site have an export license?	☒ Yes ☐ No ☐ N/A
2.11	Is the site registered with any government regulatory agency (FDA registration, GMP certification, etc.)? ☒ Yes ☐ No ☐ N/A If yes, please specify. GMP and GDP certification from Swissmedic, FDA registered MFDS Korea and PMDA Japan registered	
2.12	By whom is the site inspected (regulatory or third party) and list inspections within the last three years: For GMP related products: Swissmedic: March 2021 SQS: November 2021 for ISO 13485 SAS: March 2022 for ISO 17025, 17034	
2.13	How often, as an annual average, is the site audited by customers or third parties? 20 Audits per year	
2.14	Has an Rx-360 audit been performed at this site? ☒ Yes ☐ No Please also state the date of the audit if applicable. August 2018 http://rx-360.org/audit-programs/	
2.15	Are you willing to have Rx-360 conduct an audit on behalf of your customers according to the Rx-360 audit programs on your site? ☒ Yes ☐ No	
2.16	Are you willing to have your customers conduct audits on your site? ☒ Yes ☐ No	
2.17	Please list regulatory sanctions impacting the site within the last five years (i.e. warning letters, CEP suspension, import alerts, etc.): none	
2.18	Does the site outsource any quality-related activity? ☒ Yes ☐ No ☐ N/A If answering yes, please specify the activities:	

SECTION 2. General Site Operating Information				
	Micronization, some analytical tests			
2.19	Please check the supplier controls in place for this facility:			
2.19a	Quality Agreements with Suppliers	☒ Yes	☐ No	☐ N/A
2.19b	Subcontractor Qualification/Audit Program	☒ Yes	☐ No	☐ N/A
2.19c	Periodic Review of Supplier Performance	☒ Yes	☐ No	☐ N/A
2.19d	Supplier Feedback Program	☒ Yes	☐ No	☐ N/A
2.19e	Approved Material Supplier List	☒ Yes	☐ No	☐ N/A
2.19f	Approved Service Supplier List	☒ Yes	☐ No	☐ N/A
Additional comments: 2.9: 21 CFR 210 is YES, 21 CFR 211 is NO 2.19a: for critical suppliers				

SECTION 3. Objectionable Materials on Site				
3.1	Does the site or production plant produce, process or store any of the following:	**Yes**	**No**	**Not Applicable**
3.1a	Beta-Lactam Antibiotics	☐	☒	☐
3.1b	Steroids and/or hormones	☐	☒	☐
3.1c	High potency compounds	☐	☒	☐
3.1d	Materials of animal origin/Biologics	☒	☐	☐
3.1e	Live virus or micro-organism	☐	☒	☐
3.1f	Allergens	☐	☒	☐
3.1g	Genetically Modified Organisms (GMO)	☐	☒	☐
3.1h	Agrochemicals (Pesticides, Herbicides, Fungicides, etc.)	☐	☒	☐
3.1i	Other (Please specify): 3.1d: No raw materials directly from slaughter or similar are used. All materials from animal origin are highly purified from the animal raw material and can be seen as purified chemicals.			

	Documented cleaning processes are in place to avoid cross contamination. A risk based approach is conducted, when a material of animal origin is handled in the GMP area.

SECTION 4. Cross Contamination Control				
4.1	Are any of the following cross-contamination controls in place?	**Yes**	**No**	**Not Applicable**
4.1a	Dedicated Facilities	☒	☐	☐
4.1b	Access Controls	☒	☐	☐
4.1c	Dedicated Personnel	☒	☐	☐
4.1d	Dedicated Gowning	☒	☐	☐
4.1e	Procedural Controls	☒	☐	☐
4.1f	Other (please specify):			
Additional Comments:				

	SECTION 5. Site Operating Policies			
		Yes	**No**	**Not Applicable**
5.1	Does the site utilize the following written policies, programs, or procedures?	☒	☐	☐
Site Specific:				
5.1a	Environmental, Health, and Safety	☒	☐	☐
5.1b	Facility Environmental Control Policy	☒	☐	☐
5.1c	General Facility Cleaning Procedures	☒	☐	☐
5.1c	Hygiene and Sterilization Procedures	☒	☒	☐
5.1d	Validated Equipment Cleaning Procedures	☒	☐	☐
5.1e	Preventative Maintenance Program/Procedures	☒	☐	☐
5.1f	Pest Control Program	☒	☐	☐
5.1g	Master Production Procedure	☒	☐	☐
Quality:				
5.1h	Quality Control/Quality Management Policy	☒	☐	☐
5.1i	Quality Manual	☒	☐	☐
5.1j	Periodic Product Quality Review	☒	☐	☐
5.1k	Master Validation Plan	☒	☐	☐
5.1l	Risk Assessment Program	☒	☐	☐
5.1m	Supplier Approval Procedure	☒	☐	☐
5.1n	Monitoring and Review of Approved Suppliers	☒	☐	☐
5.1o	Mechanism to Reduce Testing	☒	☐	☐
5.1p	Receiving Incoming Inspection	☒	☐	☐
5.1q	Change Control Procedures	☒	☐	☐
5.1r	Document Management Policy	☒	☐	☐

5.1s	Document Retention Policy	☒	☐	☐
5.1t	Change Notification Procedures for Clients	☒	☐	☐
5.1u	Control of Nonconforming Material	☒	☐	☐
5.1v	Deviation/Investigation Procedure	☒	☐	☐
5.1w	Out of Specification Policy and Procedure	☒	☐	☐
5.1x	Sampling Procedure/Sampling Plan	☒	☐	☐
5.1y	Raw Material Retention Program	☒	☐	☐
5.1z	CAPA Procedure	☒	☐	☐
5.1aa	Label Control and Accountability	☒	☐	☐
5.1bb	Product Release Procedure	☒	☐	☐
5.1cc	Employee Training Program	☒	☐	☐
5.1dd	Stability, Expiration, and Shelf-Life Program	☒	☐	☐
5.1ee	Product Retention Program	☒	☐	☐
5.1ff	Recall Procedure	☒	☐	☐
5.1gg	Customer Complaint Handling	☒	☐	☐
5.1hh	Equipment validation/qualification procedure	☒	☐	☐
5.1ii	Internal audit/self-inspection program procedure	☒	☐	☐
5.1jj	Site Security/Site Access Control Policies	☒	☐	☐
5.1kk	New Hire Program/Induction Program	☒	☐	☐
Business Continuity/Contingency Plan:				
5.1ll	Disaster Recovery Plan	☒	☐	☐
5.1mm	Pandemic Preparedness Plan	☒	☐	☐
5.1nn	Supply Chain Emergency Preparedness Plan	☒	☐	☐
5.1oo	Business Continuity/Contingency Plan	☒	☐	☐
5.1pp	Can the company provide a plan upon request? OR provide a short description below: A Business Continuity Plan can be shown during an audit on site. Additional Comment: 5.1c: "Yes" for hygiene procedures, "No" for sterilization procedures			

SECTION 6. Quality Assurance and Production				
		Yes	**No**	**Not Applicable**
6.1	Does the site have an independent and defined Quality Assurance/Quality Management Division?	☒	☐	☐
6.2	Does QA/QM have authority over the following:	☒	☐	☐
6.2a	Policies and procedures?	☒	☐	☐
6.2b	Review of documentation for release?	☒	☐	☐
6.2c	Release or rejection of incoming materials?	☒	☐	☐
6.3	Does QA/QM investigate and resolve quality complaints?	☒	☐	☐

SECTION 6. Quality Assurance and Production				
		Yes	**No**	**Not Applicable**
6.4	Does QA/QM investigate and resolve internal deviations?	☒	☐	☐
6.5	Does the QA/QM have the authority to assign a disposition to materials?	☒	☐	☐
6.6	Does the QA/QM review manufacturing and testing records prior to release?	☒	☐	☐
6.7	Does the facility utilize computerized systems for managing GxP activities or data?	☒	☐	☐
6.8	Are relevant computerized systems 21 CFR part 11 and EU GMP annex 11 compliant?	☒	☐	☐
6.9	Does the site use statistical methods for consistency and uniformity?	☒	☐	☐
6.10	Does the site use controlled documents for following and recording manufacturing instructions?	☒	☐	☐
6.11	Does the company qualify and/or validate manufacturing procedures?	☒	☐	☐
6.12	Is any environmental monitoring conducted in production/finishing areas?	☒	☐	☐
6.13	Does the site supply BSE/TSE declarations?	☒	☐	☐
6.14	Does the site supply a declaration of Elemental Impurities?	☒	☐	☐
6.15	Are ICH Q3C(R4) solvents used in the manufacturing process of supplied materials?	☒	☐	☐
6.16	Are stability studies carried out according to ICH guidance?	☒	☐	☐
6.17	Are solvents and mother liquor reused/recycled?	☐	☒	☐
6.18	Does the site have a process water treatment system?	☒	☐	☐
6.18a	Please check all that apply to the system: ☐ City/potable water ☐ Distilled water ☐ Dionized water ☒ Water for injection (WFI) ☒ Reverse Osmosis ☐ Clean steam ☒ Ultra-filtrated water (purified water) ☐ Other:			
6.19	Does the plant have a batch/lot system?	☒	☐	☐
6.19a	Is the system traceable?	☒	☐	☐
6.19b	Is it unique?	☒	☐	☐
6.19c	Is batch/lot manufacturing continuous?	☒	☐	☐
6.19d	Is manufacturing batch by batch?	☒	☐	☐

SECTION 6. Quality Assurance and Production				
		Yes	No	Not Applicable
6.20	Does the site perform on-plant audits prior to approving critical GxP suppliers?	☒	☐	☐
6.21	Does the site audit critical GxP suppliers after initial approval?	☒	☐	☐
6.22	Does the site inspect incoming materials?	☒	☐	☐
6.23	Does the site test incoming materials to defined specifications?	☒	☐	☐
6.24	Does the site establish purchase specifications for raw materials?	☒	☐	☐
6.25	Is the equipment multi-use?	☒	☐	☐
6.26	Does the site qualify equipment installation?	☒	☐	☐
6.27	Does the site qualify equipment operation?	☒	☐	☐
6.28	Does the site qualify equipment performance?	☒	☐	☐
6.29	Are production critical use instruments calibrated regularly?	☒	☐	☐
6.30	Is rework allowed?	☒	☐	☐
6.31	Is reprocessing allowed?	☒	☐	☐
6.32	Are manufacturing and packaging activities traceable to the equipment, areas, and materials used?	☒	☐	☐
6.33	Are production materials handled and stored in a manner to prevent degradation, contamination and cross-contamination?	☒	☐	☐
6.34	If answering 'not applicable' for any of the above, please elaborate:			
Additional Comments: 6.18a Water for injection (WFI) is delivered from other site within the company. 6.19c and 6.19d both YES, because both types of manufacturing are available on site. 6.25 We have both, dedicated and multi-use equipment. 6.30 and 6.31 Yes, according to ICH Q7				

SECTION 7. Laboratory Procedures		☐ N/A for this Site		
		Yes	No	Not Applicable
7.1	Does the site have standard procedures for sample handling/tracking?	☒	☐	☐
7.1a	Does the site have standard procedures for retaining samples?	☒	☐	☐
7.1b	Does the site have standard procedures for re-testing samples?	☒	☐	☐
7.2	Does the site have written and approved specifications and test methods?	☒	☐	☐
7.3	Are laboratory instruments calibrated regularly?	☒	☐	☐

SECTION 7. Laboratory Procedures		☐ N/A for this Site		
		Yes	**No**	**Not Applicable**
7.4	Is there a standard procedure in place for analytical method development?	☒	☐	☐
7.5	Does the site qualify and/or validate analytical test procedures?	☒	☐	☐
7.6	Does the site perform stability testing on materials and/or products?	☒	☐	☐
7.7	Are retention samples of key raw materials maintained?	☒	☐	☐
7.8	Are standards traceable to their preparation and reagents used?	☒	☐	☐
7.9	Are retention samples of finished product maintained?	☒	☐	☐
7.10	Are shelf life/retest/expiration dates available and standardized?	☒	☐	☐
7.11	Does the company provide a certificate of analysis (CoA) and/or a Certificate of Conformation/Compliance (CoC) for each lot or batch?	☒	☐	☐
7.12	Does the CoA/CoC contain the manufacture name and location?	☒	☐	☐
7.13	Does the CoA/CoC signed/e-signed by a Quality representative?	☒	☐	☐
7.14	If a repacker performs analyses, will the CoA reflect both the original manufacturing site data as well as the repacking site data?	☒	☐	☐
7.15	If answering ‘not applicable’ for any of the above, please elaborate:			
7.16	Additional Comments: 7.11 A Certificate of Compliance (CoC) can be provided if applicable 7.12 and 7.14 Depends on grade of product, but source may be disclosed upon request, after signing of a Disclosure Agreement.			

SECTION 8. Packaging, Storage, and Transport		☐ N/A for this Site		
		Yes	**No**	**Not Applicable**
8.1	Does the site have a validated or qualified labeling system?	☒	☐	☐
8.2	Are batch production records retained and available?	☒	☐	☐

SECTION 8. Packaging, Storage, and Transport		☐ N/A for this Site		
		Yes	**No**	**Not Applicable**
8.3	Are packaging and labeling areas separate from production?	☐	☐	☐
8.4	Are barcode readers in use and challenged regularly?	☒	☐	☐
8.5	Are vision systems in use?	☐	☒	☐
8.6	Is product ever packaged without a label being initially applied (i.e. bright stocking)?	☐	☒	☐
8.7	Do labels include shelf life/expiration dates?	☒	☐	☐
8.8	Do labels include lot/batch number?	☒	☐	☐
8.9	Do labels include requirements for storage conditions?	☒	☐	☐
8.10	Is tamper evident seal used for each container of supplied materials?	☒	☐	☐
8.11	Does the company use a First-In-First-Out or First-Expiration-First-Out system?	☒	☐	☐
8.12	Does the company maintain appropriate storage conditions?	☒	☐	☐
8.12a	Are those storage conditions monitored and documented?	☒	☐	☐
8.13	Does the site make available a description of storage and/or warehouse conditions?	☐	☐	☒
8.14	Does the site distribute products via a third party?	☐	☒	☐
8.15	Are good distribution policies implemented?	☒	☐	☐
8.16	Are transport mechanisms dedicated?	☒	☐	☐
8.17	Does the company validate shipping method?	☒	☐	☐
8.18	Does the company validate packaging methods?	☒	☐	☐

Additional Comments:
8.3 All steps, also packaging and labeling are done in GMP production building
8.7 Yes, but only if batch is classified with expiry period
8.9 Yes, if storage conditions other than storage at ambient temperature apply
8.13 No long-term storage of GMP/Emprove products in Buchs.
8.15 - 8.18 if applicable and upon customer agreement.

I (Supplier) confirm that the information provided in this questionnaire is correct and can be verified.

Date:25. July 2022

Title:Manager Quality