GMP Site Quality Self-Assessment

based on

Rx-360 Supplier Assessment Questionnaire

Module 2, Site Specific Information

Relevant for

Merck KGaA
Frankfurter Str. 250
64293 Darmstadt
Germany

The site Self-assessment covers our quality management system for the following regulated applications:
- Manufacturing of Excipients, APIs, food additives and cell culture media

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
Corporation with General Partners
Frankfurter Str. 250
64293 Darmstadt, Germany

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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64293 Darmstadt, Germany

☒ Please check here if additional documents are attached.	

SECTION 1. General Site Information

1.1	Site or Facility-Specific Name: Merck KGaA, Darmstadt, Germany (Life Science, Site Darmstadt)
1.2	Address: Frankfurter Str. 250, 64293 Darmstadt Germany GPS Coordinates: 49.89510°N, 8.65384°E
1.3	Phone: +49 6151 72-0
1.4	Email: Please refer to your local Sales representative
1.5	Fax: Please refer to your local Sales representative
1.6	Website: www.sigmaaldrich.com

SECTION 2. General Site Operating Information

2.1	What year did the site start operating? 1904
2.2	What is the primary activity of the site? (e.g. manufacturing, distribution, etc.) Manufacturing of GMP products: API, pharmaceutical excipients, food ingredients, cell culture media; Manufacturing of IVDs, reference materials and ISO regulated products: see non-GMP Site Self-Assessment
2.3	To which, if any, subdivision of the parent company does the site belong? Life Science
2.4	Size of site (in sq. ft. or m.): 1.2 km²
2.5	Please list or attach the normal hours/schedule of the facilities, including shutdown dates (if applicable): 24 h hours of production, 7 days a week, 5 shifts, few shutdowns every year
2.6	Total number of employees on site: approx. 10000
2.7	Total number of employees in Quality: approx. 390 (Life Science)

2.8	Total number of employees in Manufacturing: approx. 1360 (Life Science)	
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: DIN EN ISO 17034, DIN EN ISO/IEC 17025, ISO 14001, ISO 45001, ISO 50001, EXCiPACT®, AMWHV, AMG, LMHV, IVDR 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. FDA FEI 3002806906 Hessisches Landesamt für Gesundheit und Pflege, Germany	
2.12	By whom is the site inspected (regulatory or third party) and list inspections within the last three years: Regierungspräsidium Darmstadt (API): 2021; 2022 Hessisches Landesamt für Gesundheit und Pflege (API): 2023 Blue Inspection (EXCiPACT®): 2021 SGS (EXCiPACT®): 2022, 2023 DQS (ISO 9001): annually TÜV SÜD (ISO 13485, IVDR): annually DAkkS (DIN EN ISO 17034, DIN EN ISO/IEC 17025): annually	
2.13	How often, as an annual average, is the site audited by customers or third parties? 45	
2.14	Has an Rx-360 audit been performed at this site? ☒ Yes ☐ No Please also state the date of the audit if applicable. 21.02.2023 - 22.02.2023 Learn more about the Rx-360 Joint Audit Program® here.	
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: partially manufacturing, partially warehousing, partially laboratory testing, partially services like pest control			
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:

SECTION 3. Objectionable Materials On Site

	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): Highly sensitizing materials, such as penicillins, are not produced on site Darmstadt. Cephalosporines and Penicillins are only handled in separated non-GMP production areas in separated buildings. Other beta-lactam drugs, compounds, intermediates or products are neither produced nor handled in production, distribution, warehousing or sampling facilities. Live viruses, allergens and agrochemicals (pesticides, herbicides, fungicides, etc.) are not handled on the site resp. in the facilities. Microorganisms are only handled in one specialized production area as well as in microbiological laboratories with relevant safety zones. Materials with high pharmacological activity or toxicity (e.g. certain steroids or cytotoxic anti-cancer agents) are not produced in shared equipment unless validated and/or cleaning procedures as well as other risk-minimizing actions are established and maintained. Handling of materials of animal origin, biologics and genetically modified organisms is under control by a validated ERP system and separated equipment and production / processing lines or buildings while risk-minimizing actions are established and maintained.

SECTION 4. Cross-Contamination Control

		Yes	No	Not Applicable
4.1	Are any of the following cross-contamination controls in place?			
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): Shared facilities for sampling. Risk assessment is in place			

Additional Comments:

Dedicated facilities in production for product families, but not on product level. Procedural controls comprise cleaning verification/validation and campaign manufacturing.

SECTION 5. Site Operating Policies

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

5.1y	Sampling Procedure/Sampling Plan	☒	☐	☐
5.1z	Raw Material Retention Program	☒	☐	☐
5.1aa	CAPA Procedure	☒	☐	☐
5.1bb	Label Control and Accountability	☒	☐	☐
5.1cc	Product Release Procedure	☒	☐	☐
5.1dd	Employee Training Program	☒	☐	☐
5.1ee	Stability, Expiration, and Shelf-Life Program	☒	☐	☐
5.1ff	Product Retention Program	☒	☐	☐
5.1gg	Recall Procedure	☒	☐	☐
5.1hh	Customer Complaint Handling	☒	☐	☐
5.1ii	Equipment validation/qualification procedure	☒	☐	☐
5.1jj	Internal audit/self-inspection program procedure	☒	☐	☐
5.1kk	Site Security/Site Access Control Policies	☒	☐	☐
5.1ll	New Hire Program/Induction Program	☒	☐	☐
Business Continuity/Contingency Plan:				
5.1mm	Disaster Recovery Plan	☒	☐	☐
5.1nn	Pandemic Preparedness Plan	☒	☐	☐
5.1oo	Supply Chain Emergency Preparedness Plan	☒	☐	☐
5.1pp	Business Continuity/Contingency Plan	☒	☐	☐
5.1qq	Can the company provide a plan upon request? OR provide a short description below: can be provided in an audit			

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?	☒	☐	☐
6.4	Does QA/QM investigate and resolve internal deviations?	☒	☐	☐
6.5	Does QA/QM have the authority to assign a disposition to materials?	☒	☐	☐
6.6	Does QA/QM review manufacturing and testing records prior to release?	☒	☐	☐
6.7	Does the facility utilize computerized systems for managing GxP activities and 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 solvents used in the manufacturing process of supplied materials?	☒	☐	☐
6.15a	If Yes, what class of solvent is used? product-specific			
6.16	Are stability studies carried our 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: WFI applied where applicable; purified water according to Ph Eur			
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?	☒	☐	☐
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: *6.16: where required by regulations; *6.19c/d depends on product / production process, a batch definition is always applied; *6.30: for API not allowed			

Additional Comments:

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 retesting samples?	☒	☐	☐
7.2	Does the site have written and approved specifications and test methods?	☒	☐	☐
7.3	Are laboratory instruments calibrated regularly?	☒	☐	☐
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 products 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	Is 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: 7.14: Our life science products produced at Darmstadt are not repacked externally			

Additional Comments:

*7.15: for food indredients not applicable

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?	☒	☐	☐
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:

*8.6 products are always labeled in production / filling line

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

Title: QMS & Compliance Life Science Darmstadt

Date: August 2024

Additional Site-Specific Information

(not based on Rx 360 Supplier Assessment Questionnaire)

9. Data Management and Controls		Yes	No
9.1	List the GMP/GXP computerized systems register that are used for GMP operations. Note: Far too many validated IT-systems to list them in this document, an Inventory is available.		
9.2	Are the electronic systems in use validated?	☒	☐
9.3	Are validation documents for the computerized systems available and approved?	☒	☐
9.4	Are changes to the systems managed under the change control procedure? i.e., hardware, software, system documents and records and data contained within the system?	☒	☐
9.5	Is there a procedure for dealing with incidents/issues/ deviations with electronic systems?	☒	☐
9.6	Is there a procedure to document periodic evaluations of electronic systems against the relevant regulation requirements? i.e., 21 CFR Part 11, EMA Annex 11 Computerized systems Frequency:	☒ 1 year	☐
9.7	Is there a procedure for audit trail review, including both system owner and IT administrator?	☒	☐
9.8	Are there plans to upgrade software systems that do not have full audit trail capabilities?	☒	☐
9.9	Is all data available in human readable format for inspections?	☒	☐
9.10	Is there a procedure which defines the retention periods for electronic for electronic records?	☒	☐
9.11	Is there a procedure for the backup, recovery and archival of electronic data?	☒	☐
9.12	Is the backup completed automatically by the system or manually with a defined frequency?	Automatic	

		Yes	No
9.13	Does back up data include relevant raw data, metadata and audit trail data?	☒	☐
9.14	Where is the backup data stored?	Data Center / TSM	
9.15	Is there a disaster recovery procedure?	☒	☐
9.16	Are individual user ID's assigned to users of an electronic system?	☒	☐
9.17	Is the individual's identity verified prior to assignment of their electronic signature?	☒	☐
9.18	Is there a procedure which defines how access to the electronic system is limited to authorized individuals?	☒	☐
9.19	Is there a procedure that defines how access is granted and removed for users of validated systems?	☒	☐
9.20	Is a review performed to ensure that the ability to apply electronic signatures is withdrawn for individuals whose responsibilities change or no longer need access or who have left the company?	☒	☐
9.21	Is the responsibility of the administrator role assessed?	☒	☐
9.22	Is there a procedure which defines the following?		
9.22.a	How re-setting of an electronic password is managed (i.e., token or temporary password)	☒	☐
9.22.b	Periodic changing of passwords?	☒	☐
9.22.c	Delegation of an electronic signature responsibilities (e.g., holidays, period of absence, employee leaves the company)	☐	☒
9.22.d	The controls in place to prevent deleting, copying, or transferring to falsify an electronic record within the system	☒	☐
9.23	Does the Self-inspection program include data integrity elements?	☒	☐
9.24	Can it be demonstrated that the electronic signature used in computerized systems show the following:		
9.24.a	Name of the signatory	☒	☐
9.24.b	System date that the signature was applied	☒	☐
9.24.c	System time (if time of actions is required/critical)	☒	☐
9.24.d	Meaning of signature	☒	☐
9.25	Do Computer from Automated systems have physical and/or logical security controls including:		
9.25.a	Authority checks to ensure that only authorized individuals can use the system, electronically sign a record, alter a record, or perform the operation at hand	☒	☐

Additional Site-Specific Information

(not based on Rx 360 Supplier Assessment Questionnaire)

10. Lot numbering information

E.g.: A12345678
letters = plant code
digits = running identification number, the last two digits = last two digits of item number

A lot is defined as a product volume produced in a continuous process in a set period of time without interruption and regarded as homogenous due to product specific criteria. The homogeneity is ensured by fulfilling the requirements defined in the SOP "Assessment of Batch Homogeinity"