Product Quality Designations at Cambridge Isotope Laboratories, Inc.

Cambridge Isotope Laboratories, Inc. produces stable isotope labeled products at several levels of control beyond the standard research product grade (xLM-nnn-0). These grades are designated as xLM-nnn-**MPT** and xLM-nnn-**CTM**, where "x" refers to the type of labeling (C, N, D, CN, etc.) and "nnn" is the catalog number. The table below shows the levels of control applied to manufacturing, quality control, quality assurance, and the level of testing applied to each grade of product. The two grades of products are:

- **-MPT** – Microbiological and Pyrogen Tested. Products prepared under the –MPT classification are research grade products that are tested in the bulk form for *S. aureus, P. aeruginosa, E. coli, Salmonella sp.,* aerobic bacteria, yeast and mold and for bacterial endotoxins.
- **-CTM** – Clinical Trial Material. Products prepared under the –CTM classification may conform to materials suitable for Phase 1 Clinical Trials as described in Section 19 of the ICH Guidance Q7A, "GMP Guidance for Active Pharmaceutical Ingredients (APIs)". Additional data may be needed for APIs to be used in Phase 2 and Phase 3 Clinical Trials. CIL can also supply materials suitable for Phase 2 and 3 Clinical Trials.

CIL offers an Enhanced Data Package (EDP) for most –MPT products. It includes all data that normally accompanies the –MPT product, plus additional information pertaining to the synthesis, purity, and stability of the product. This is available for an additional charge. Please inquire for further details.
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		-MPT Products	-CTM Products, Q7A Compliant
Manufacturing	Synthetic Methods	Catalog products may be prepared under SOP or following laboratory notebook procedures	Products prepared according to an approved, documented batch record
	Packaging	Performed in dedicated Packaging Dept with environmental controls. Labels are produced and reviewed by the Packaging Department. Records are maintained by the Operations and Logistics Department.	Performed in dedicated GMP Facility with QA release. Validated and monitored environmental controls. Labels are reviewed and approved by QA with label reconciliation.
	SOPs	SOPs controlled by departmental management	Batch record and SOPs review and approved by Quality Assurance (QA)
	Change Control	Departmental management approval	Documented QA Controlled Procedure
	Raw Material Traceability	May be available upon request	Draft material specifications for all raw materials, including vendor COAs for raw materials.
	Contact Glassware	Standard laboratory cleaning, glassware - multiple use	New glassware and/or glassware cleaned per cleaning verification protocol
	Facility Management	Environmentally Controlled. Certified Hoods.	Environmentally controlled GMP Facility with room clearance procedure and/or Product Changeover Procedure
	In-Process Testing	Performed by Production or Quality Control personnel	Performed by Quality Control using scientifically sound, documented methods
	Deviations	Departmental management approval	Documented QA Controlled procedure

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		-MPT Products	-CTM Products, Q7A Compliant
Quality Control	Test methods	Standard practice or written test methods	Documented, scientifically sound test methods
	SOPs	SOPs controlled by departmental management	QA Reviewed and approved
	Change Control	Departmental management approval	Documented QA Controlled procedure
	Out of Specification	Departmental management approval	Documented QA/QC Controlled procedure. Reprocessing may occur per ICH/FDA guidance and QA approval.
	Deviation	Departmental management approval	Documented QA Controlled procedure
Product Quality and Release	Final Data Review	Reviewed by QC	Reviewed by QC and QA
	Certificate of Analysis	Provided by Operations and Logistics / Quality Control	Prepared/approved by QA
	Material Specifications	Determined by CIL	Material Specifications agreed with Customer. Approved by QA.
	USP or EP Specifications	Does not apply	Specifications and methods follow USP/EP and/or by agreement with Customer
	Microbiological Testing	Bulk material tested at release for *S. aureus, P. aeruginosa, E. coli, Salmonella sp.,* aerobic bacteria, yeast and mold and for bacterial endotoxins.	Bulk material tested at release for bacterial endotoxin and USP <61> Microbial Enumeration
	BSE/TSE	Certificate may be available upon request	Certificate Provided
	Retain Samples	Not required	Reserve samples of each API batch are retained for a minimum of 3 years after distribution of the batch
	Record Retention	Records are retained for a minimum of 5 years	Records are retained for a minimum of 5 years, or as defined in the customer specific agreements
	Product Stability	Not routinely tested	Not routinely tested, available by contract
	Drug Master Files	Not applicable	May be available if contracted

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NOTES:

1. CIL –MPT products are labeled “For Research Use Only. Not for use in diagnostic procedures”. CIL –CTM products are labeled “For Investigational Use Only. The performance characteristics of this product have not been established”.

2. Please note that –MPT and –CTM products are not guaranteed to be sterile and pyrogen-free when received by the customer and microbiological and pyrogen testing does not imply suitability for any desired use. If the product must be sterile and pyrogen-free for a desired application, CIL recommends that the product be packaged or formulated into its ultimate dose form by the customer or appropriate local facility. The product should always be tested by a qualified pharmacy/facility prior to actual use.

3. Systems or procedures controlled by departmental management or subject to departmental management approval are the responsibility of the operating department.

4. BSE/TSE statements are developed on a risk estimate basis that meets or exceeds the guidelines laid out in section 5.2.8 European Pharmacopeia Fifth Edition. CIL does not use mammalian sourced materials whenever possible and rarely uses materials of bovine origin.

5. Technical data packages may be available upon receipt of an executed CDA.