# Research Use of CIL Products

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Cambridge Isotope Laboratories, Inc., manufactures highly pure research biochemicals that are produced for research applications. As a service to our customers, some of these materials have been tested for the presence of *S. aureus, P. aeruginosa, E. coli, Salmonella sp.,* aerobic bacteria, yeast and mold, as well as the presence of endotoxin in the bulk material by taking a random sample of the bulk product. Subsequent aliquots are not retested. Presence of endotoxin is assessed by determining endotoxin content following established protocols and standardized Limulus Amebocyte Lysate (LAL) reagents. These tests are provided at no charge for any materials listed in our catalog or website that is designated as "MPT" in the item product number (e.g., DLM-349-MPT).

CIL is able to provide microbiological testing for other products. Depending on the compound and the quantity ordered, an additional charge may apply. Please note that microbiological-tested products are not guaranteed to be sterile and pyrogen-free when received by the customer, and microbiological 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.

CIL research products are labeled "For Research Use Only. Not for use in diagnostic procedures." Persons intending to use CIL products in applications involving humans are responsible for complying with all applicable laws and regulations including but not limited to the US FDA, other local regulatory authorities and institutional review boards concerning their specific application or desired use.

It may be necessary to obtain approval for using these research products in humans from the US FDA or the comparable governmental agency in the country of use. CIL will provide supporting information, such as lot-specific analytical data and test-method protocols, to assist medical research groups in obtaining approval for the desired use.

CIL will allocate a specific lot of a product to customers who are starting long-term projects requiring large amounts of material. Benefits from this type of arrangement include experimental consistency arising from use of only one lot, no delay in shipments, and guaranteed stock. Please note that some CIL products have a specific shelf life and cannot be held indefinitely. If interested, please contact your sales representative for further details.

## Product Quality Designations

CIL 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, D, N, CN, *etc.*) and "nnn" is the catalog number. The chart on the next page 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 on this chart 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, "cGMP 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 Technical 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.

# Product Quality Designation Chart

| | | -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 Department with environmental controls. Labels are produced and reviewed by the Packaging Department. Records are maintained by the Operations and Logistics Department. | Performed in dedicated cGMP 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 cGMP 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 |
| 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 |

**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.