# Outline of Knowledge Base—CMC

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| Directory | Subdirectories |
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| Regulatory | • IND<br>• IMPD<br>• Annual Reports<br>• Correspondence<br>• Complaints and Recalls<br>Note: there should be a separate, controlled system for regulatory documents. In this directory are the uncontrolled versions that allow the CMC team to do large edits before the documents go under control |
| Quality Assurance | • Policies<br>• SOPs<br>• Forms<br>• Manuals<br>• CAPAs<br>• Drug Substance Release (includes: pharmaceutical company release document; CMO release documents are maintained with the individual lot documents in CMC directories)<br>• Drug Product Release (includes: pharmaceutical company release document; CMO release documents are maintained with the individual lot documents in CMC directories)<br>• Vendor Qualification Program (includes: paper and site audits)<br>• Correspondence<br>Note: assume that the bulk of controlled documents reside with CMOs and CROs; uncontrolled copies of those documents are maintained in CMC and Clinical directories. The documents in the Quality Assurance subdirectory are only policy documents related to the pharmaceutical company itself.<br>Note: access is controlled by QA to ensure appropriate version control |
| Drug Substance | • Process Description (a clean/brief description of the manufacturing process; older version and process changes are kept as a history of the process over time)<br>• Cleaning studies and methods<br>• Drug Substance Reports (includes: development reports, campaign summary reports, etc.)<br>• Stability (subdirectories for each stability protocol, as well as a master stability tracker of due dates for all stability data; each stability protocol subdirectory has subdirectories by pull point (1 mo, 3 mo....) which contain raw and summary data for that point)<br>• Drug substance packaging information<br>• Miscellaneous subdirectories (deuterated drug substance, metabolites, etc.) |

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| Drug Substance CMO | • Audits<br>• Contracts and Agreements (including RFPs, contracts, change orders, invoices, Quality Agreement)<br>• Specifications—Raw Materials<br>• Specifications—Drug Substance<br>• Specifications—Contact Materials<br>• Analytical methods—raw materials (with subdirectories for each method containing SOPs and validation reports)<br>• Analytical methods—intermediates (with subdirectories for each method containing SOPs and validation reports)<br>• Analytical methods—drug substance (with subdirectories for each method containing SOPs and validation reports)<br>• Lots (Each lot has its own subdirectory with separate subdirectories for each lot for: master batch records, executed batch records, analytical results, deviations, raw materials testing, correspondence related to the lot, certificates, release documents)<br>Note: each separate DS CMO has a subdirectory which appears in the Drug Substance Directory. The goal is to keep all documents from each site separate to the degree possible. |
| Formulation | • Contracts and Agreements (including RFPs, contracts, change orders, invoices)<br>• Vendor Reports (Pre-formulation, formulation, lyophilization, container closure, delivery device, etc.)<br>• Analytical methods<br>• Stability studies (initial storage studies and clinical in-use studies)<br>• Container closure and delivery device information<br>Note: assume that formulation development takes place at an independent development laboratory; after development is complete, the project is transferred to a CMO for GMP manufacturing of the DP. |
| Drug Product | • Process Description (a clean/brief description of the manufacturing process; older version and process changes are kept as a history of the process over time)<br>• Cleaning studies and methods<br>• Drug Product Reports (includes: development reports, campaign summary reports, etc.)<br>• Stability (subdirectories for each stability protocol, as well as a master stability tracker of due dates for all stability data; each stability protocol subdirectory has subdirectories by pull point (1 mo, 3 mo....) which contain raw and summary data for that point)<br>• Container closure information<br>• Miscellaneous subdirectories (deuterated drug product, etc.) |

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| Drug Product CMO | • Audits<br>• Contracts and Agreements (including RFPs, contracts, change orders, invoices, Quality Agreement)<br>• Specifications—RMs<br>• Specifications—DP<br>• Specifications—Contact materials<br>• Analytical methods—raw materials (with subdirectories for each method containing SOPs and validation reports)<br>• Analytical methods—drug product (with subdirectories for each method containing SOPs and validation reports)<br>• Lots (Each lot has its own subdirectory with separate subdirectories for each lot for: master batch records, executed batch records, analytical results, deviations, raw materials testing, container closure release info, correspondence related to the lot, certificates, release documents)<br>Note: each separate DP CMO has a subdirectory which appears in the Drug Product Directory. The goal is to keep all documents from each site separate to the degree possible. |
| Labeling and Packaging CMO | • Audits<br>• Contracts and Agreements (including RFPs, contracts, change orders, invoices, Quality Agreement)<br>• Label Design and Approval<br>• Batch Records By Labeling Run<br>• Retest and Expiry Documentation<br>• Note: each separate DP CMO has a subdirectory which appears in the Drug Product Directory. The goal is to keep all documents from each site separate to the degree possible. |
| Inventory and Shipping | • Inventory of drug substance and drug product which is in the hands of the pharmaceutical company's technical operations<br>• Shipping Records (each DS and DP shipment has its own subdirectory with customs information, invoice, end user letter...)<br>Note: DP disappears from the inventory as it is transferred to clinical inventory which is maintained by the clinical supplies management system of the CSM CRO. Shipping records in this subdirectory do not include shipments to clinical sites which are managed by the CSM CRO. |
| Safety | • Safety evaluations, MSDSs, and information from the Pre-Clinical and Clinical groups provided to the CMC group about DS and DP safety. |
| Miscellaneous | • CDAs, consulting agreements<br>• Meeting minutes with a subdirectory for each meeting series (CMC, Clinical Supply, each vendor...) |