Camargo
PHARMACEUTICAL SERVICES
Farther. Faster. Together.℠

CMC FOR 505(b)(2) APPLICATIONS

Lynn Gold, PhD, Ken Phelps, Kathryn Wekselman, PhD, RN, and Karen Seta-Aust, PhD
Camargo Pharmaceutical Services, LLC | Cincinnati, OH 45242

LEARNING OBJECTIVE

The Chemistry, Manufacturing, and Control (CMC) Section (Modules 2 & 3 of the Common Technical Document [CTD]) of any application to the FDA will be the cornerstone for demonstrating the quality of any drug product. A clear document that complies with the ICH Harmonized Tripartite Guideline per the ICH Steering Committee Meeting (9 Nov 2000) is instrumental to that process. The objective of this presentation is to outline the variations that can occur from application to application depending on the dosage form, drug product, and type of file under construction, specifically a 505(b)(2) application.

ICH HARMONIZED TRIPARTITE GUIDELINE

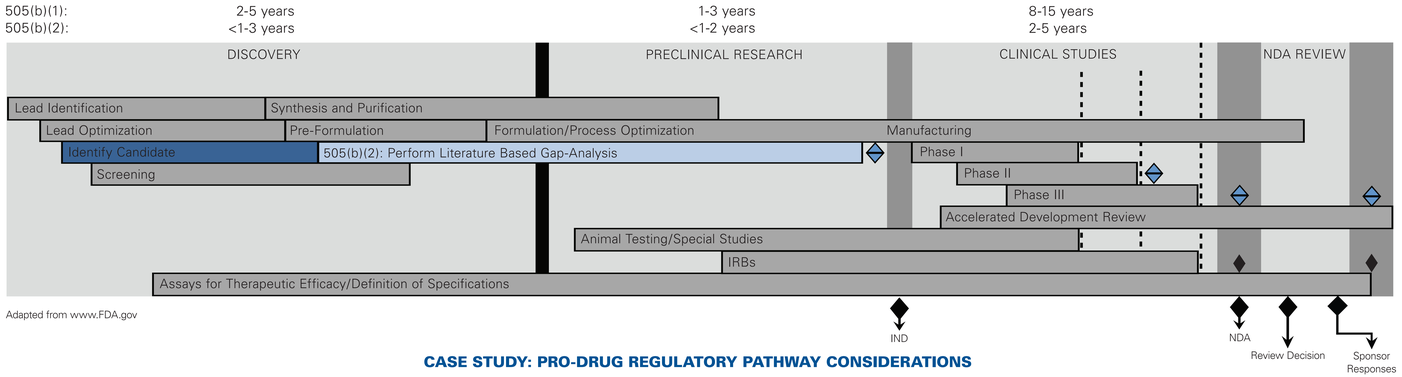
M4Q (R1): Quality
Module 2: Quality Overall Summary (QOS)
Module 3: Quality
The section of the application covering chemical and pharmaceutical data including data for biological/ biotechnological products.

Re-edited with numbering and section headers changes, September 2002

The Quality section of the Common Technical Document (M4Q) provides a harmonized structure and format for presenting CMC information in a registration dossier. The table of contents includes sections on Drug Substance and Drug Product. There are also sections for regional specific information, as well as some appendices. Due to the fact that many CMC topics have not yet been the subject of ICH guidelines (e.g., drug substance synthesis, drug product manufacture, container closure), the content of M4Q is not totally harmonized. A new section on Pharmaceutical Development has been included to replace the Development Pharmaceutics Report (currently a part of the EU submission requirements). Also, a new CMC summary document, the Quality Overall Summary, has been developed.

http://www.ich.org/cache/compo/276-254-1.html

505(b)(1) VS 505(b)(2) DRUG DEVELOPMENT PROGRAMS



Adapted from www.FDA.gov

- Industry Time
- FDA Review Time
- Go/No-Go Descision
- Sponsor/FDA Meetings Encouraged
- Advisory Committees

CASE STUDY: PRO-DRUG REGULATORY PATHWAY CONSIDERATIONS

Pro-drug found in human plasma PK profile different from RLD → **505(b)(1) NME**
Full Clinical Development Plan
- Patent Protection
- Full Nonclinical Studies
- Full Phase I Studies
- Full Phase II Studies
- 2 Well-Controlled Phase III Studies

Pro-drug found in human plasma PK profile similar to RLD → **505(b)(2) NME**
Modified Clinical Development Plan
- 5 Years Marketing Exclusivity
- Limited Nonclinical Studies
- Full Phase I Studies
- Full Phase II Studies
- 1 Well-Controlled Phase III Study

Pro-drug not found in human plasma PK profile different from RLD → **505(b)(2)**
Limited Clinical Development Plan
- 3 Years Marketing Exclusivity
- Nonclinical from Public Domain
- Limited Phase I Studies
- No Phase II Studies
- 1 Well-Controlled Phase III Study

Pro-drug not found in human plasma PK profile similar to RLD → **505(b)(2)**
Pharmacokinetic Program
- No Marketing Exclusivity
- Nonclinical from Public Domain
- Limited Phase I Studies
- No Phase II Studies
- No Phase III Studies

CMC CRITICAL ISSUES

- Short, concise summaries
- Well-developed product development history
- Justification of specifications
  - Impurities
  - Residual solvents
  - Stability

FULL CMC DEVELOPMENT PROGRAM

Quality Overall Summary (Module 2)
- Drug Substance (Summary)
- Product (Summary)
- Regional Information

Drug Substance (Module 3S)
- Manufacturing Process and Validation
- Analytical Methods and Validation
- Characterization of Starting Materials
- Release Specifications
- Stability Specifications and Studies
- Bulk Container Closure

Drug Product (Module 3P)
- API Supplier
- API Specifications
- Excipient Suppliers
- Excipient Specifications
- Final Drug Product Specifications
- Final Drug Product Stability and Study
- Final Drug Product Manufacturing
- Process, Controls, and Validation Container Closure

505(b)(2) REGULATION

505(b)(2) application is one for which one or more of the investigations relied upon by the applicant for approval "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted" (21 U.S.C. 355(b)(2)).

POTENTIAL 505(b)(2) CANDIDATES

- Racemates
- New excipients
- New dosage form
- Pharmacokinetic alteration
- New indication
- New combination
- Pro-drug of approved drug

Camargo
PHARMACEUTICAL SERVICES
Farther. Faster. Together.℠

1.888.451.5708 **www.camargopharma.com**