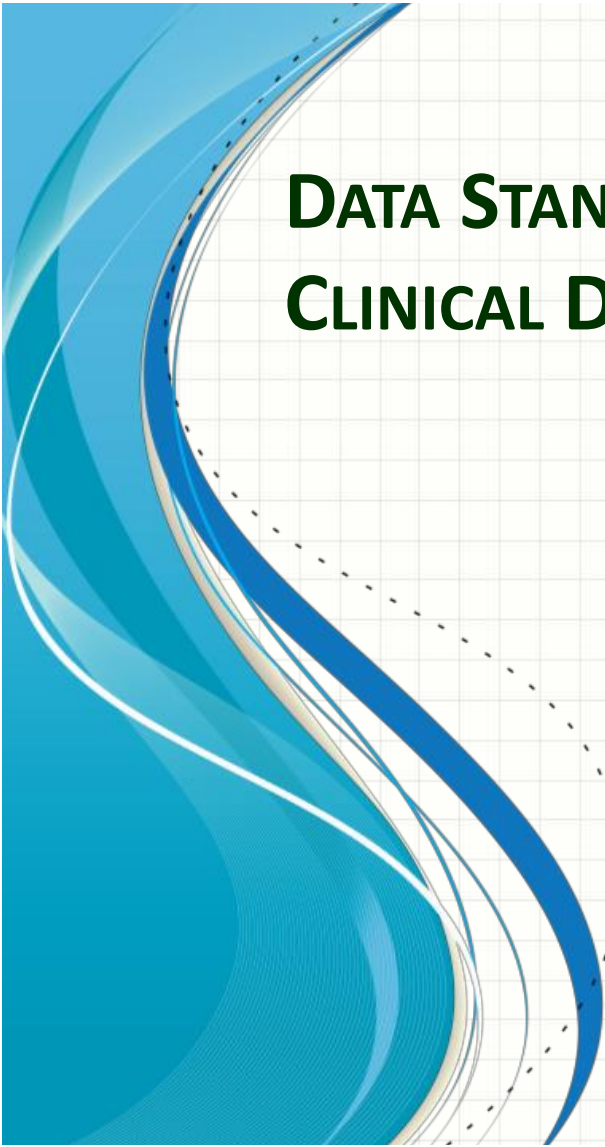
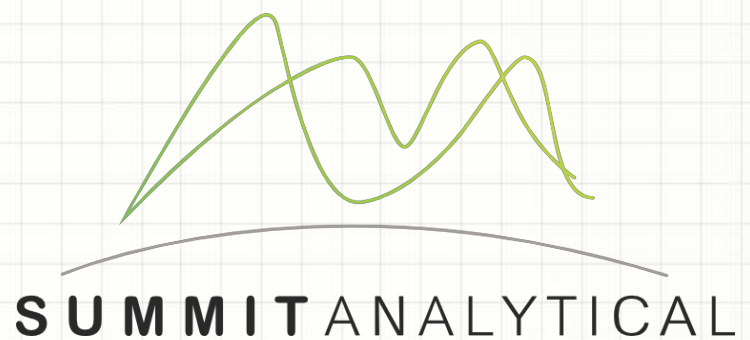




DATA STANDARDIZATION PLANNING FOR CLINICAL DEVELOPMENT PROGRAMS



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Summit Analytical, LLC
2014-10-12



Welcome

Overview of Topics in Presentation

1

- Clinical Development Plan & Data Standards Compliance

2

- Recent Guidance: Study Data Standardization

3

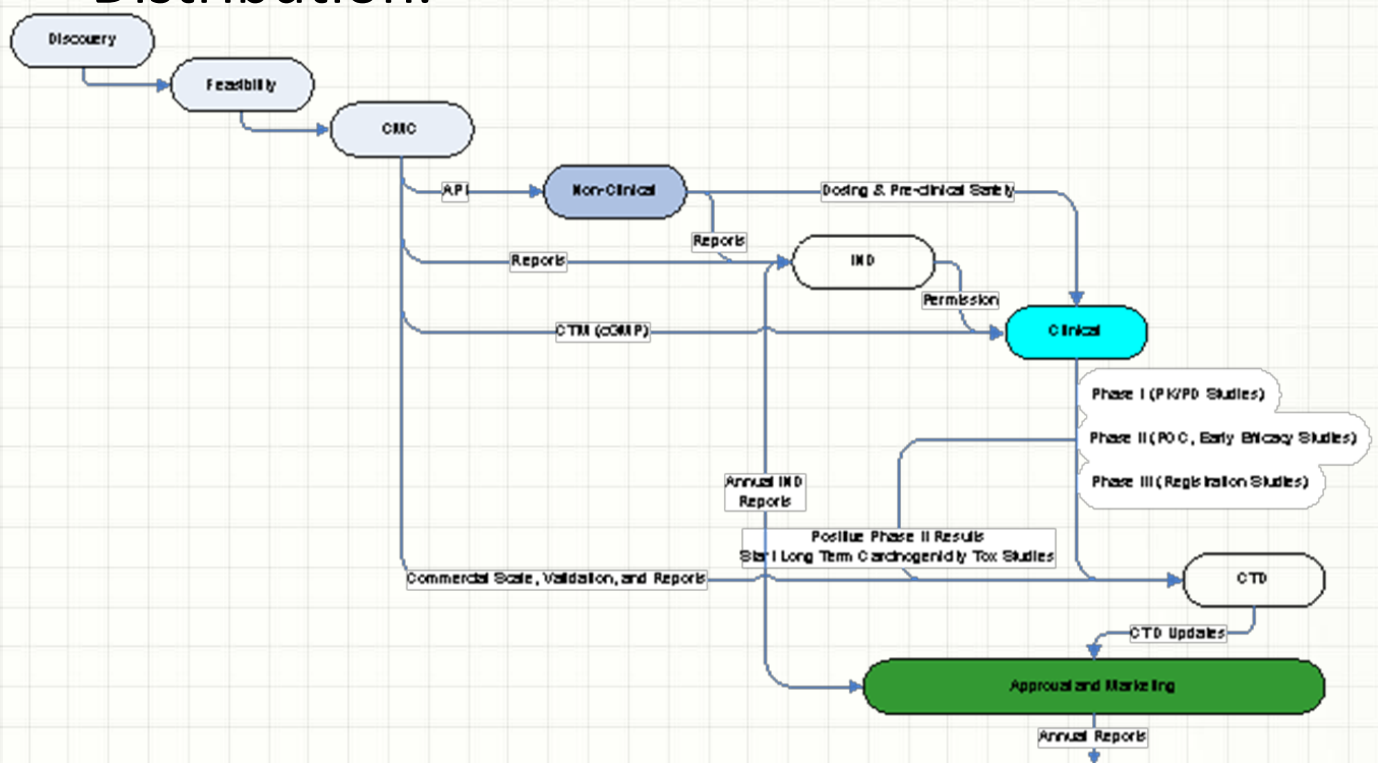
- Relationships: CDP/SDSP and the IB and Annual Reporting

Disclosure

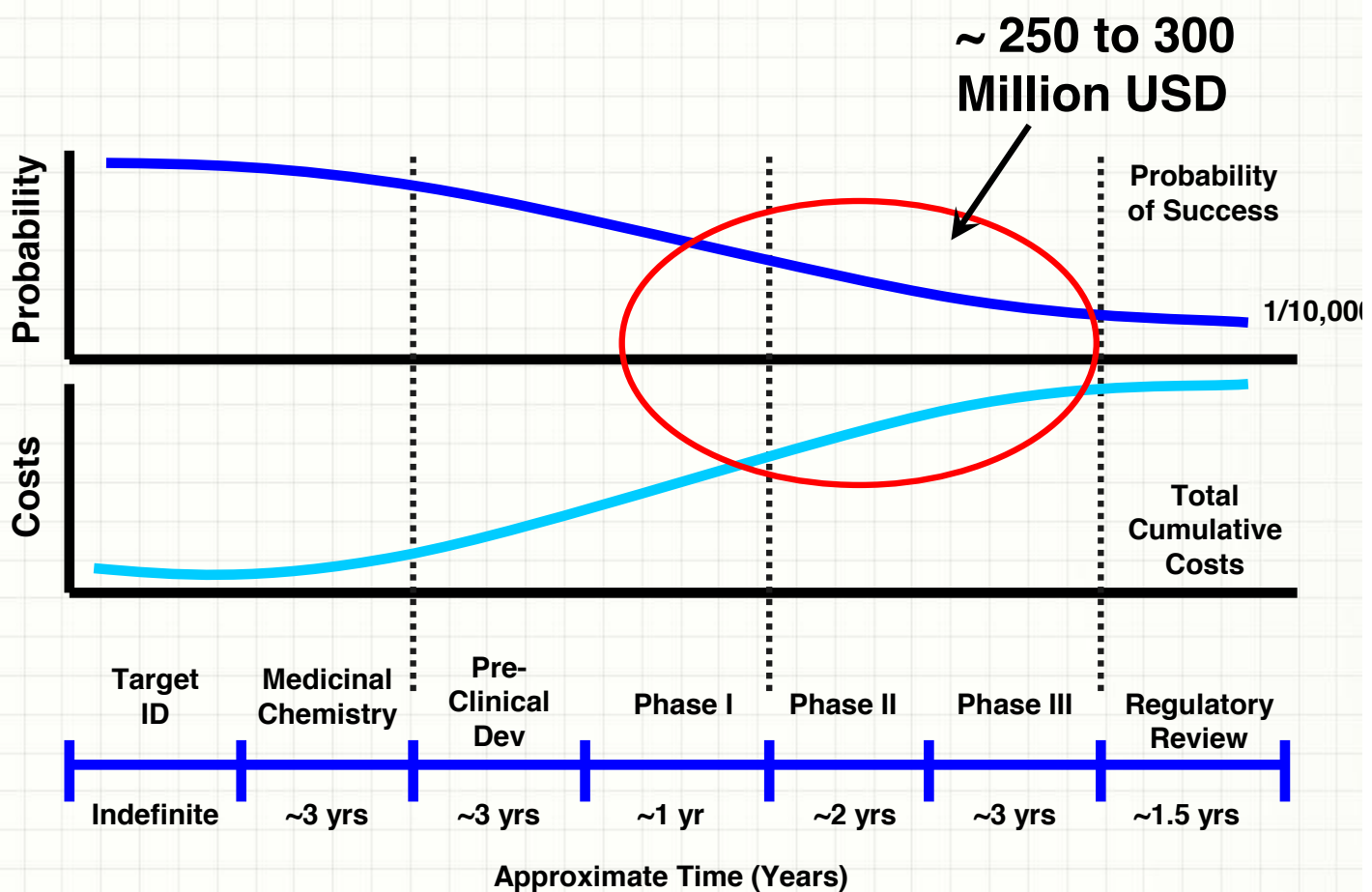
- Materials in this presentation come from the following sources:
 - FDA Draft Guidance Documentation
 - ICH Guidance (E8, E9)
 - EMEA Points to Consider Documentation
 - Multiple sponsor FDA Meeting Minutes from Consulting Practice

Roadmap-Molecule to Market

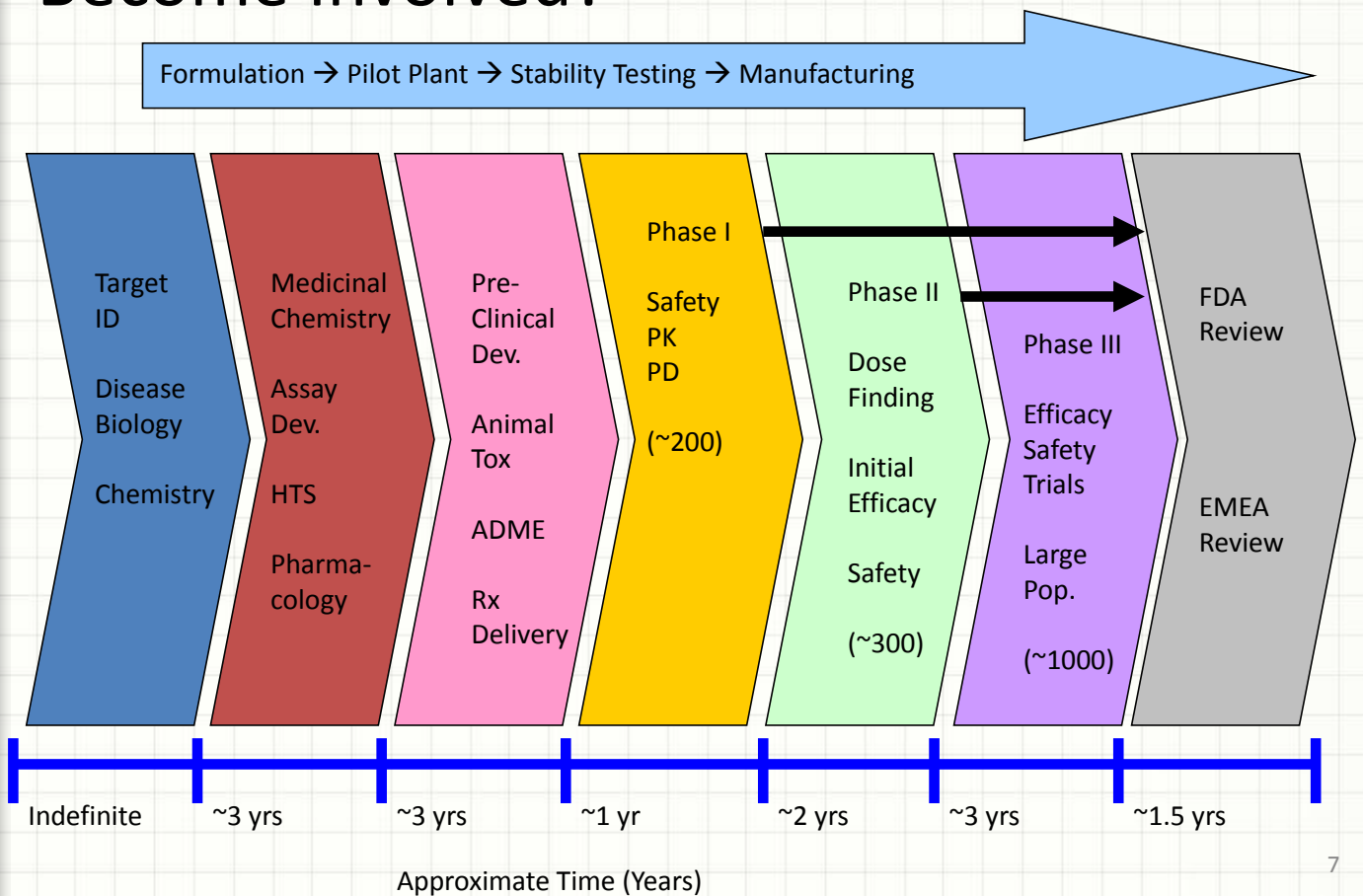
- Well defined steps for development of an NCE from Molecular development to Market Distribution.



Economics and Probability



When Does a Regulatory Authority Become Involved?



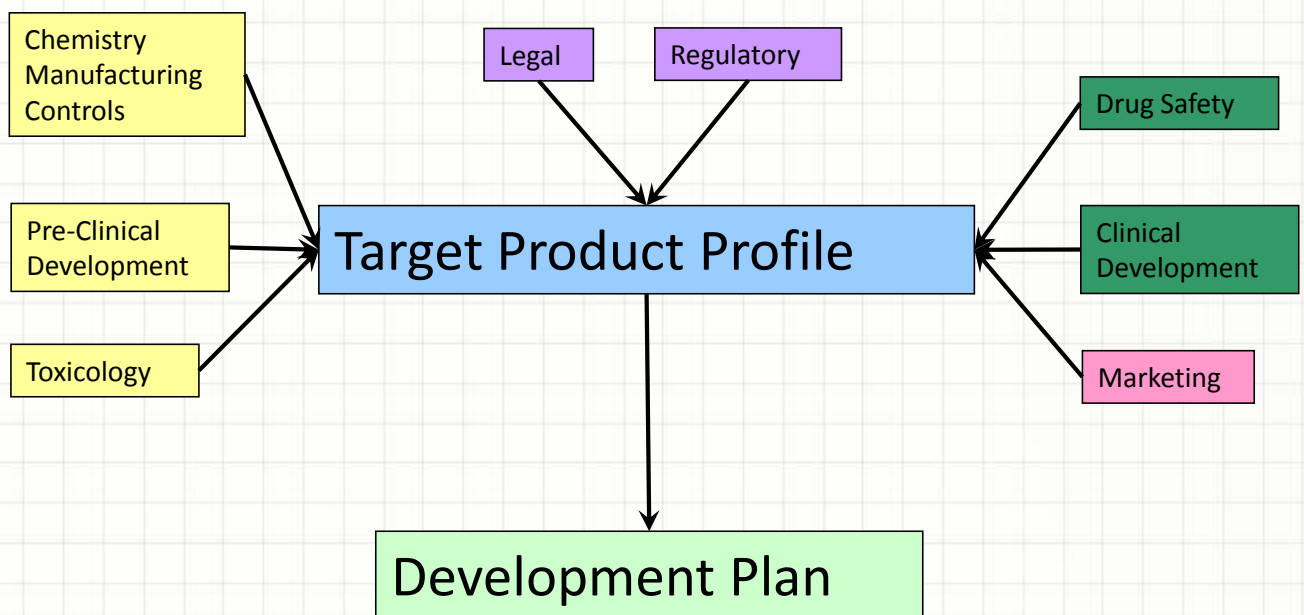
Regulatory Authorities ARE Involved When....

- Sponsors:
 - test drugs or biologics in animals or cells (GLP)
 - seek permission to test a drug or biologic in Humans (IND, IMPD, GCP)
 - want to set up pilot and/or production manufacturing of a drug or biologic (GMP)
 - seek permission to market (NDA)
 - market and monitor the safety of a drug or biologic in clinical use (post-marketing surveillance)
- At ALL stages of the process

Regulatory Agencies

- Harmonization
 - All agencies have been engaged in ICH
 - Agencies are accepting cross-referenced applications
- Sharing of Safety data
 - Agencies now requiring reporting of data intra- and inter-agency
 - Pooling of data for better safety reporting (reduce risk)
- Manufacturing Quality
 - Agencies inspecting cross-boarders to ensure quality in Drug Substance and Drug Product

Regulatory Authorities ARE involved at ALL stages



http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/ucm368613.htm

PhUSE | PhUSE Wiki | Roadrunner | TING | Alaska Cruisetours: 13... | NC RV Rentals

U.S. Department of Health & Human Services

a A A



U.S. Food and Drug Administration
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Data Standards

Study Data Standards

▶ Study Data Standards for Regulatory Submissions

[CDER/CBER Position on Use of SI Units for Lab Tests](#)

[Janus Clinical Trials Repository \(CTR\) Project](#)

[Standard for Exchange of Non-Clinical Data](#)

[Study Design Standard](#)

[Study Participation Standard](#)

[Subject Data Standard](#)

Study Data Standards for Regulatory Submissions

Position Statement

FDA recognizes the investment made by sponsors over the past decade to develop the expertise and infrastructure to utilize Clinical Data Interchange Standards Consortium (CDISC)[1] standards for study data. The submission of standardized study data enhances a reviewer's ability to more fully understand and characterize the efficacy and safety of a medical product.

The Prescription Drug User Fee Act (PDUFA V)[2] Performance Goals state that FDA will develop guidance for industry on the use of CDISC data standards for the electronic submission of study data in applications. In the near future, FDA will publish guidance that will require study data in conformance to CDISC standards.[3]

FDA envisions a semantically interoperable and sustainable submission environment that serves both regulated clinical research and health care. To this end, FDA will continue to research and evaluate, with its stakeholders, potential new approaches to current and emerging data standards. FDA does not foresee the replacement of CDISC standards for study data and will not implement new approaches without public input on the cost and utility of those approaches.

September 13, 2013

[1]www.cdisc.org

[2]<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm>

Target Product Profile

- Drives strategy for Development of Compound
- Product Description (mirrors the labels)
- Describes the Regulatory Assessment
 - Regulatory Plan (International)
 - Regulatory Risks
- Describes Requirements to achieve corporate and regulatory goals
- FDA Guidance on TPP
<http://www.fda.gov/cder/guidance/6910dft.htm>



Clinical Development Plan

- Target indication
- Rationale for clinical development
 - Background information
 - Overview on therapeutic area, current/future therapies and competitors
 - Summary of development status
 - Describes opportunities and potential hurdles in clinical development
 - Describes Safety and Efficacy, Pharmacokinetic and Pharmacodynamic endpoints (and now standards)
 - Market Access and Clinical Effectiveness strategy



Clinical Development Plan

- Clinical Development
 - Clinical pharmacology, pharmacokinetics (Phase I)
 - Dosage forms / dose definition (Phase I and II)
 - Efficacy variables / Efficacy trials (Phase III)
 - Safety Monitoring and Reporting (Phase I, II, III)
 - Clinical Trial Supplies
 - Statistical Plan (Includes Endpoints and Methods)
 - Phase IIIb, IV (Post-Marketing Trials)
 - Post-Marketing Safety Surveillance
 - Pharmaco-economics, Epidemiology



Clinical Development Plan

- Budget and capacity
 - Basis for budget planning
 - Integration into overall project budget
 - Planning for Clinical Team Resources
 - Clinical Pharmacologists
 - Clinical Trial Managers
 - Clinical Program Medical Scientists
 - Clinical Research Associates
 - Statisticians / Programmers
 - Data Managers
 - Medical Writers
 - Epidemiologists
 - Other Specialists Identified

Clinical Development Plan

- Trial outline of main trials, including main primary and secondary variables
- Statistical considerations for efficacy trials
- Clinical pharmacology strategy
- Clinical safety strategy
- Milestones, High level timelines
- Contingency Plans
- Regulatory Meetings for Clinical Discussion
- Study Data Standardization Plan





Clinical Development Plan

- Adaptable, and updated at least on an Annual basis
 - Generally updated when the IB and Annual reporting are completed
- Important on-going reference for all disciplines on the drug development team
- Required as part of US IND Item 4 (General Investigational Plan)
- Identifies “Go/No Go” decision points
- Integrated, International, and Comprehensive
- Defines activities, regulatory information, competitor information, and steps to develop product

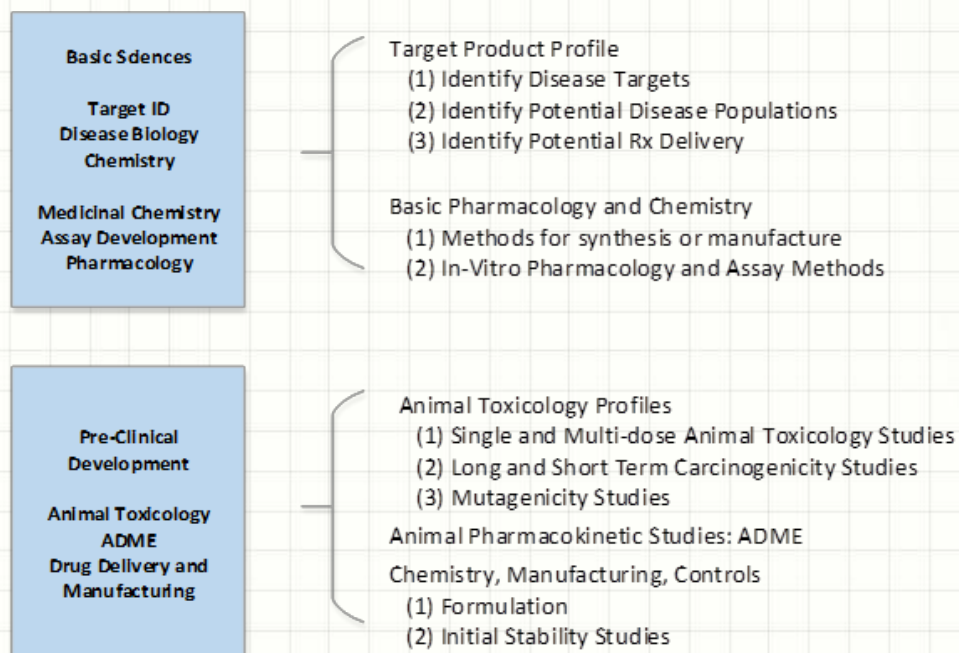


Regulatory Milestones TPP / CDP Updated

- IND Submission
- End of Phase I (Meeting/ Consultation)
- End of Phase II Meeting
- Pre-NDA meeting
- Annually with the IB and Annual Reports to the IND or IMPD

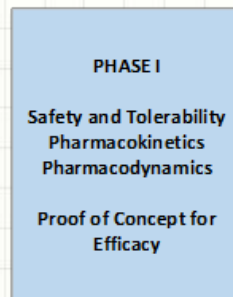
Planning Documentation

- Early Development



Planning

- Elements for Data Standardization

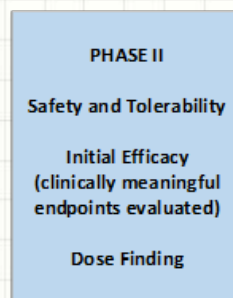


Phase I Clinical Development Plan Information

- (1) Initial PK Single and Multi-Dose Studies
- (2) Identify Pharmacodynamic surrogates
- (3) Initial proof of concept of efficacy in small population sample

Identify for SDSP

- (1) Potential Endpoints for Safety, PK/PD, and Efficacy
- (2) Document and Standardize Methods for Assessment and Analysis of Endpoints

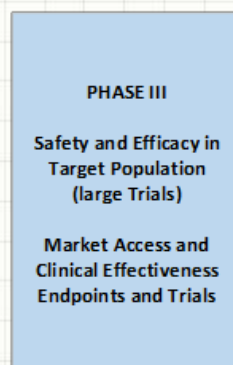


Phase II Clinical Development Plan Information

- (1) Dosage form, Dose Definition and Finding Studies
- (2) Drug-Drug, Drug-Food, Drug-Disease PK Studies
- (3) Safety Assessments: Initial TEAE of Interest
- (4) Efficacy Endpoints: Initial Testing, Identify clinically meaningful differences to evaluate

For SDSP

- (1) Update with New Information
- (2) Refine and Document Methods for Assessment and Analysis of Endpoints



Phase III Clinical Development Plan Information

- (1) Registration Safety and Efficacy Studies for each Indication to be submitted.
- (2) Population PK Studies
- (3) Long Term Safety Assessments
- (4) Efficacy Endpoints: Confirmation of labelled efficacy endpoints and methods for analysis.
- (5) Identify Clinical Effectiveness/ Market Access variables for assessment.

For SDSP

- (1) Update with New Information for Efficacy Endpoints
- (2) Add Clinical Effectiveness/Market Access Endpoints

References

- FDA Guidance on Target Product Profile: <http://www.fda.gov/cder/guidance/6910dft.htm>.
- FDA Guidance on Providing Regulatory Submissions in Electronic Format – Standardized Study Data: <http://www.fda.gov/downloads/Drugs/Guidances/UCM292334.pdf>
- FDA Guidance. Study Data Technical Conformance Guide, Technical Specifications Document: <http://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM384744.pdf>
- FDA Web Page: CDER Study Data Standards Resources. <http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm>
- FDA Web Page: Study Data Submissions to CBER. <http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/ucm209137.htm>
- FDA Study Data Standards for Regulatory Submissions Position Statement. <http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/ucm368613.htm>
- PhUSE Wiki, Optimizing Data Standards Working Group: Study Data Standardization Plan. [http://www.phusewiki.org/wiki/index.php?title=Study_Data_Standardization_Plan_\(SDSP\)](http://www.phusewiki.org/wiki/index.php?title=Study_Data_Standardization_Plan_(SDSP))

Thank You – Questions/Discussion



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