Clinical Trial Application (CTA) for Drugs in China

August 2022

Committed to your Success

From Concept to Market

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General Requirements for CTA in China

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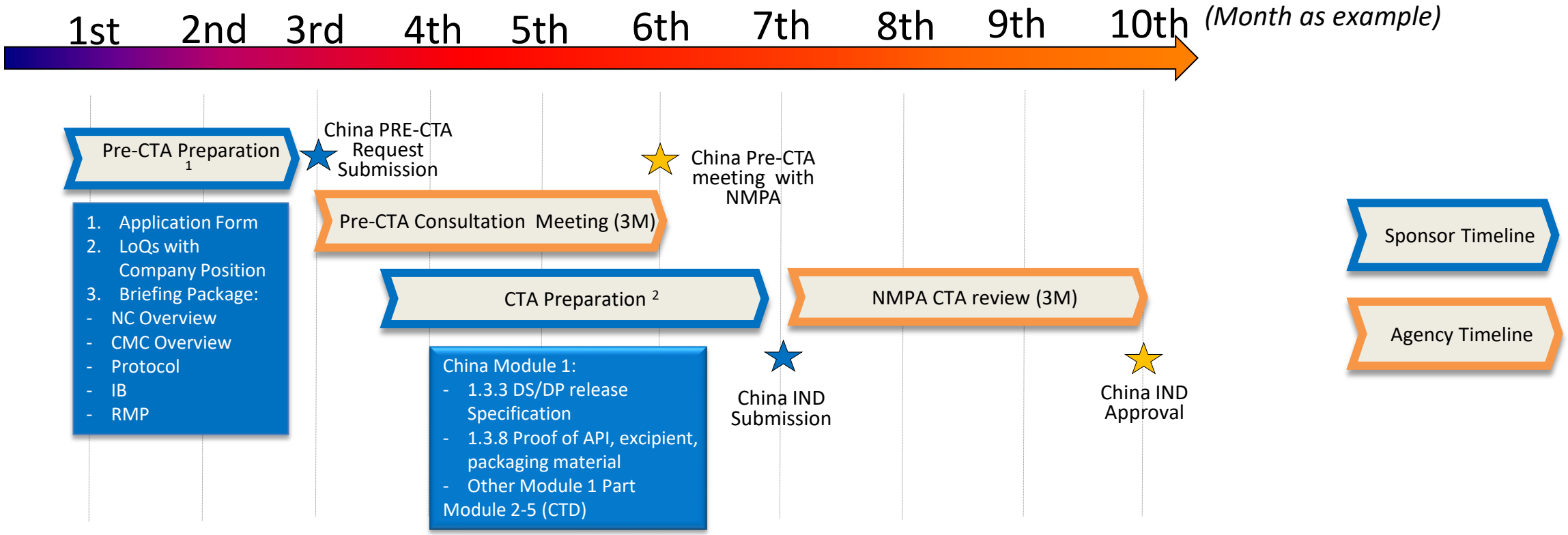
- CTA (Clinical Trial Application) : is required before the start of any clinical trial in China.
- Consultation meeting with NMPA before CTA submission “Pre-CTA Consultation Meeting” (Type II meeting) is mandatory for novel products (Cat.1 for chemical/biologics).
- Content of CTA consultation meeting package should include : application form, M2.3/2.4/2.5, M4 NC reports, clinical study protocol, RMP (Risk Management Plan), List of questions for CDE, CDE meeting presentation and sponsor positions.
- Content of China CTA Application: follows ICH CTD standards for Module 2, Module 3, Module 4 and Module 5. However, Module 1 is specific to China.
- CTA application and related documents should be translated in Chinese .
- Clinical Trial Registry – Sponsor should register their clinical trial in NMPA platform of clinical trails that is equivalent to “ClinicalTrails.gov”.
- CTA Maintenance – Protocol Amendment, Safety Reporting (DSUR & SUSAR) , Suspend, Termination mechanism etc. need to be done in timely manner

CTA Regulatory Process in China



Note:

- China PIND is currently mandatory for FIH study without any precedent IND/CTA approval around the globe
- It normally takes **6.5-7.5** months from PIND request to China IND approval as the current industry benchmark
- #1/2 – Refer to China PIND/IND dossier list for more details
- China PIND/IND submission dossier shall be written in simplified Chinese
- EC approval is in-parallel with IND approval or after IND approval

CTA Content (1/5)

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Module 1

Module 1 Sections
1.0 Explanation letter
1.1 Table of content
1.2 Application Form
1.3 Product related information
1.4 Application status (if applicable)
1.5 Accelerate marketing registration process application (if applicable)
1.6 Communication meeting (if applicable)
1.7 Clinical trial process management information (if applicable)
1.8 Risk management (if applicable)
1.9 Post-marketing research (if applicable), Including phase IV and research with specific research purposes.
1.10 Changes after marketing (if applicable)
1.11 Applicant/production enterprise supporting documents
1.12 Certification documents for small and micro enterprises (if applicable)

CTA Content (2/5)

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Module 2

Module 2 Section
2.2 Introduction
2.3 Quality Overall Summary
2.3 Introduction
2.3.S Drug Substance
2.3.S.1 General Information
2.3.S.2 Manufacture
2.3.S.3 Characterisation
2.3.S.4 Control of Drug Substance
2.3.S.5 Reference Standards or Materials
2.3.S.6 Container Closure System
2.3.S.7 Stability
2.3.P Drug Product
2.3.P.1 Description and Composition of the Drug Product
2.3.P.2 Pharmaceutical Development
2.3.P.3 Manufacture
2.3.P.4 Control of Excipients
2.3.P.5 Control of Drug Product
2.3.P.6 Reference Standards or Materials
2.3.P.7 Container Closure System
2.3.P.8 Stability
2.3.A Appendices
2.3.A.1 Facilities and Equipment
2.3.A.2 Adventitious Agents Safety Evaluation
2.3.A.3 Novel Excipients <Excipient Name>
2.3.R Regional Information

Module 2 Section
2.4 Nonclinical Overview
2.5 Clinical Overview
2.6 Nonclinical Written and Tabulated Summaries
2.6.1 Introduction
2.6.2 Pharmacology Written Summary
2.6.3 Pharmacology Tabulated Summary
2.6.4 Pharmacokinetics Written Summary
2.6.5 Pharmacokinetics Tabulated Summary
2.6.6 Toxicology Written Summary
2.6.7 Toxicology Tabulated Summary
2.7 Clinical Summary
2.7.1 Summary of Biopharmaceutics and Associated Analytical Methods
2.7.2 Summary of Clinical Pharmacology Studies
2.7.3 Summary of Clinical Efficacy <Indication>
2.7.4 Summary of Clinical Safety
2.7.5 References
2.7.6 Synopses of Individual Studies

CTA Content (3/5)

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Module 3

Module 3 Section
3.2.S Drug Substance
3.2.S.1 General Information
3.2.S.1.1 Nomenclature
3.2.S.1.2 Structure
3.2.S.1.3 General Properties
3.2.S.2 Manufacture
3.2.S.2.1 Manufacturer(s)
3.2.S.2.2 Description of Manufacturing Process and Process Controls
3.2.S.2.3 Control of Materials
3.2.S.2.4 Controls of Critical Steps and Intermediates
3.2.S.2.5 Process Validation and/or Evaluation
3.2.S.2.6 Manufacturing Process Development
3.2.S.3 Characterization
3.2.S.3.1 Elucidation of Structure and Other Characteristics
3.2.S.3.2 Impurities
3.2.S.4 Control of Drug Substance
3.2.S.4.1 Specifications
3.2.S.4.2 Analytical Procedures
3.2.S.4.3 Validation of Analytical Procedures
3.2.S.4.4 Batch Analyses
3.2.S.4.5 Justification of Specifications
3.2.S.5 Reference Standards or Materials
3.2.S.6 Container Closure System
3.2.S.7 Stability
3.2.S.7.1 Stability Summary and Conclusions
3.2.S.7.2 Post-approval Stability Protocol and Stability Commitment
3.2.S.7.3 Stability Data

Module 3 Section
3.2.P Drug Product
3.2.P.1 Description and Composition of the Drug Product
3.2.P.2 Pharmaceutical Development
3.2.P.2.1 Components of the Drug Product
3.2.P.2.1.1 Drug Substance
3.2.P.2.1.2 Excipients
3.2.P.2.2 Drug Product
3.2.P.2.2.1 Formulation Development
3.2.P.2.2.2 Overages
3.2.P.2.2.3 Physicochemical and Biological Properties
3.2.P.2.3 Manufacturing Process Development
3.2.P.2.4 Container Closure System
3.2.P.2.5 Microbiological Attributes
3.2.P.2.6 Compatibility
3.2.P.3 Manufacture
3.2.P.3.1 Manufacturer(s)
3.2.P.3.2 Batch Formula
3.2.P.3.3 Description of Manufacturing Process and Process Controls
3.2.P.3.4 Controls of Critical Steps and Intermediates
3.2.P.3.5 Process Validation and/or Evaluation
3.2.P.4 Control of Excipients
3.2.P.4.1 Specifications (1 document for all compendial excipients)
3.2.P.4.2 Analytical Procedures (1 document for each non-compendial excipients.)
3.2.P.4.3 Validation of Analytical Procedures (1 document for each noncompendial excipients.)
3.2.P.4.4 Justification of Specifications (1 document for each noncompendial excipients.)
3.2.P.4.5 Excipients of Human or Animal Origin
3.2.P.4.6 Novel Excipients

Module 3 Section
3.2.P.5 Control of Drug Product
3.2.P.5.1 Specification(s)
3.2.P.5.2 Analytical Procedures
3.2.P.5.3 Validation of Analytical Procedures
3.2.P.5.4 Batch Analyses
3.2.P.5.5 Characterization of Impurities
3.2.P.5.6 Justification of Specification(s)
Justification of Specification(s)
3.2.P.6 Reference Standards or Materials
3.2.P.7 Container Closure System
3.2.P.8 Stability
3.2.P.8.1 Stability Summary and Conclusion
Stability Summary and Conclusion
3.2.P.8.2 Post-approval Stability Protocol and Stability Commitment
3.2.P.8.3 Stability Data
3.2.A Appendices
3.2.A.1 Facilities and Equipment [name, manufacturer]
3.2.A.2 Adventitious Agents Safety Evaluation [name, dosage form, manufacturer]
3.2.A.3 Excipients
3.2.R Regional Information
3 batches COA
Chromatogram
3.3 Literature References

CTA Content (4/5)

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Module 4

Module 4 Sections
4.2 Study Reports
4.2.1 Pharmacology
4.2.1.1 Primary Pharmacodynamics
4.2.1.2 Secondary Pharmacodynamics
4.2.1.3 Safety Pharmacology
4.2.1.4 Pharmacodynamic Drug Interactions
4.2.2 Pharmacokinetics
4.2.2.1 Analytical Methods and Validation Reports
4.2.2.2 Absorption
4.2.2.3 Distribution
4.2.2.4 Metabolism
4.2.2.5 Excretion
4.2.2.6 Pharmacokinetic Drug Interactions
4.2.2.7 Other Pharmacokinetic Studies

CTA Content (5/5)

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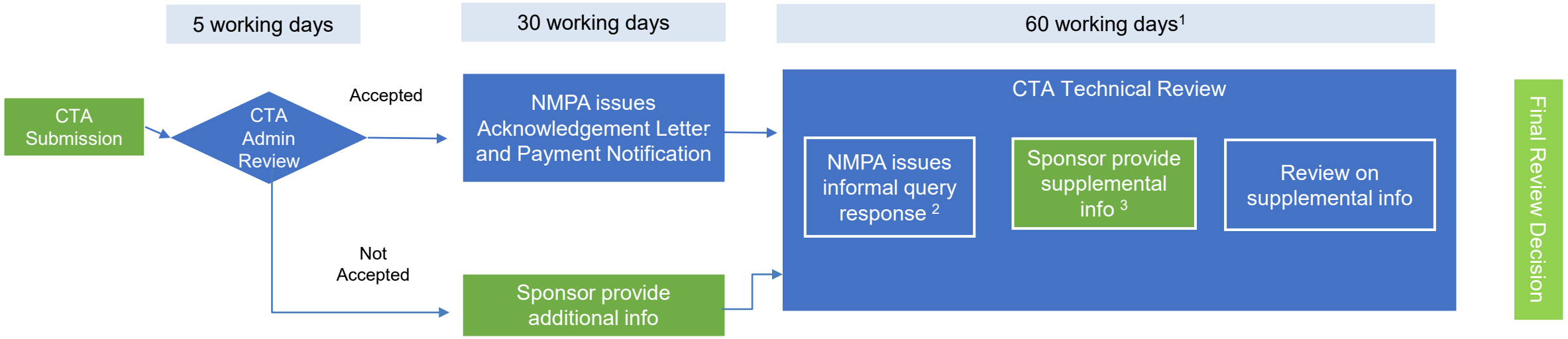
Module 5

Module 5 Sections
5.2 Tabular Listing of All Clinical Studies
5.3 Clinical Study Reports (Study Identifier Required)
5.3.1 Reports of Biopharmaceutic Studies
5.3.2 Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials
5.3.3 Reports of Human Pharmacokinetic (PK) Studies
5.3.4 Reports of Human Pharmacodynamic (PD) Studies
5.3.5 Reports of Efficacy and Safety Studies
5.3.6 Reports of Post-Marketing Experience
5.3.7 Case Report Forms and Individual Patient Listings
5.4 Literature References

CTA Submission and Review Process



1. 60 working days review duration is required by the latest Drug Registration Regulation effective from 2020
2. The informal query response will be issued anytime during technical review, ad-hoc queries (phone call) will be communicated to sponsors.
3. Sponsor must provide the supplemental information within 60 working days review cycle.

Clinical Trial Registry Requirements

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Register the study in Chinadrugtrials.org.cn

- Clinical Trial Registry Form contains all required clinical trial information to be posted according to regulations on clinical trial disclosure.
- Initial study registration submission and disclosure should be completed before Patient First Visit (FPFV) date and after clinical trial approval is obtained.
- All Changes to a clinical study should be reported **within 20 business days** of their occurrence.
- If clinical trial is suspended or terminated for safety reasons, the study status shall be updated **within 10 business days**.
- Clinical trial result should be reported w**ithin 12 months** after study completion date;
- Reason for withdrawal of trial registration information which is already disclosed. Resubmission would be approved if supporting documents could be provided.
- If no study information changes **in 1 year** after the initial study registration and information publication, brief reasons need to be submitted to the registration form on the CDE registration website.
- If IND is approved and clinical trial nor registered in the platform **within 1 year** , sponsor has to provide explanation for the delay.

Clinical Trial Registry Procedure

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- Request Public Disclosure for a New Trial granted with IND by NMPA
- Collect and Entry Data for full registration
- Review and Approve Registration Form
- Submit and Disclose Initial Full Registration by NMPA
- Maintain Disclosure Update
- Submit and Disclosure Study Result Information

CDE online Registry Platform

NMPA Registration Fees

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Category	Local Product (RMB)	Imported Product (RMB)
CTA	192,000	376,000
Supplemental Information (Technical Review waived)	9,600	9,600
Supplemental Information (Technical Review required)	99,600	283,600

References

- Drug Administration Law of the People's Republic of China (2019 Revision);
- Provisions for Drug Registration;
- Guidelines for Acceptance of Technical Review of Chemical Drug Substances (Trial Implementation), issued on Feb 2022;
- Announcement No. 146 of CFDA, 2017: Announcement of Adjustment on the Review and Approval Procedure of APIs, Pharmaceutical Excipients and Packaging Materials

Thank you

For additional information please contact us at:

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