appendix

New Drug Phase I Clinical Trial Application Technical Guidelines

I. Introduction

In order to help new drug registration applicants (pharmaceutical companies, scientific research institutions and scientific researchers) apply for Phase I clinical trials, improve the efficiency of new drug development and review, protect the safety and rights of subjects, and ensure the quality of clinical trials, this technical guide is hereby issued. This guideline describes the information that needs to be provided to the Center for Drug Evaluation of the State Food and Drug Administration (hereinafter referred to as the Center for Drug Evaluation) when a new drug conducts its first clinical trial in my country.

The purpose of this guideline is to: clarify the technical requirements for phase I clinical trials of new drugs and improve the quality of application materials for phase I clinical trials; shorten the development cycle of new drugs and speed up the process of new drug listing by standardizing the data requirements of phase I clinical trials.

This guideline applies to both innovative and improved new medicines, including chemicals and treatments With biological products (except cell and gene therapy products).

2. Consultation and communication

If the applicant has any doubts in the process of R&D and application for clinical trials, he can inquire about the relevant guiding principles through the website of the Center for Drug Evaluation, or consult the relevant issues through the "Applicant's Window" on the website of the Center for Drug Evaluation in accordance with relevant norms.

Before submitting an application for a clinical trial of a new drug, the applicant may apply for a pre-clinical trial application meeting with the Center for Drug Evaluation in accordance with the methods and working procedures stipulated in the "Administrative Measures for Drug Development and Technical Review Communication and Exchange".

Communication between applicants and CDE helps improve the quality of clinical trial applications to speed up the process of follow-up research and review.

3. Technical Requirements for Phase I Clinical Trial Application

(1) Data format and content

The application materials for Phase I clinical trial applications should be submitted in paper materials and electronic materials, and electronic materials can be sent in the form of CD. The format and content can be organized and submitted with reference to the requirements of the International Council for Harmonization of Technical Requirements for the Registration of Drugs for Human Use (ICH) Common Technical Document (CTD).

(2) Introductory statement and overall research plan

The introductory statement should include the name of the new drug, all active ingredients, pharmacological action class, structural formula (if known), dosage form, formulation prescription, route of administration, purpose of clinical trials, etc. If there is experience with the investigational drug used in the clinic, a brief overview should be provided, including research and marketing experience in other countries; if not, write under the title "none".

The overall research plan should summarize the design basis of the application for the clinical trial program, mainly including the proposed indications, subject population, number of subjects, dosing regimen (dose, dosing interval, dosing duration, etc.), drug safety Evaluation methods, risk control plans, etc., risk justification for any safety expected based on available information (important identified risks, important potential risks, important missing data, etc.).

(3) Investigator Handbook

The Investigator's Brochure is a summary of the existing pharmaceutical, non-clinical and clinical research (if any) data about the investigational drug in human research.

When new important information becomes available, the sponsor should update the Investigator Brochure to include a summary of all important research information on the investigational drug. The updated Investigator's Manual should be submitted to the Center for Drug Evaluation in a timely manner. The format and content of the Investigator's Manual can be written with reference to the relevant chapters of ICH E6.

The investigator's handbook should include the following:

1. Cover page: including the name of the drug, the name of the applicant for registration, the date of completion or update date and version number;

2. Table of Contents: List all first-level titles, second-level titles and corresponding page numbers; 3. Confidentiality statement; 4. Overview: Introduction of drug types, proposed indications and pharmacological characteristics; 5. New drug name and physical and chemical properties: a brief description Name of the drug, chemical name (if any), molecular weight, molecular formula, structural formula (if any), physical and chemical properties, dosage form, temporary expiration date based on existing stability data, storage conditions, precautions for use, etc.;

6. Non-clinical research results 6.1

Pharmacological effects: The completed non-clinical test results used to indicate drug efficacy should be included. 6.2 Toxicological studies: safety pharmacology tests, single-dose toxicity tests, repeated-dose toxicity tests, genotoxicity tests, reproductive toxicity tests, carcinogenicity tests and other toxicity tests are listed separately. If some studies have not been carried out or need not be carried out, the reasons and basis need to be explained. 6.3 Non-clinical pharmacokinetic studies: should include drug absorption, distribution, generation

Excretion and Excretion (ADME). If some studies have not been carried out or need not be carried out, the reasons and basis need to be explained.

7. Existing clinical research or use data (if any): should include domestic or foreign current All clinical trial information and literature are available.

7.1 Human pharmacokinetics 7.2

Effectiveness 7.3 Safety 7.4 Listing 8.

Others If there is no new drug use

information, it should be based on

existing non-clinical and clinical research

A summary of the results, providing information that the applicant considers relevant: may include special populations, safety information, warnings and precautions, risk control plans, drug interactions, overdose, etc. 9. References

(4) Clinical trial plan

The clinical trial protocol should include the following information:

1. Research background, briefly describe the indications of the drug, and briefly describe the existing clinical trials of the drug Efficacy and safety data (if any); 2. The purpose

of the trial; 3. The number of subjects

expected to participate; 4. Description of

inclusion and exclusion criteria; 5. Description

of dosing schedule, including duration, starting dose, dose escalation regimen and termination conditions, dosing schedule, and describe the basis and method for determining the first dose;

6. Test indicators, relevant trial details that are critical to the subject's safety evaluation, such as the subject's vital signs and necessary blood biochemical monitoring;

7. Toxicity determination principles and test suspension criteria for study suspension.

(5) Pharmaceutical research information

The pharmaceutical research of new drugs continues to deepen with the progress of drug research, and there are different research purposes in different research stages. For the pharmaceutical research data of the Phase I clinical study of the new drug application, the rules of drug research and development should be followed, and the focus should be on the pharmaceutical research information related to the safety of the subjects planned for the study (such as analysis of impurity profiles based on existing knowledge, inspection of related substances) Methodological validation of specificity and sensitivity, analysis and control of potential genotoxic impurities, immunogenicity and immunotoxicity of new biological drugs, etc.).

According to the information provided in the pharmacy section, clinical trials should be suspended when there are concerns about safety or when data are insufficient for safety evaluation. Reasons for concern may include, but are not limited to, the following:

(1) The chemical structure of the new drug or the preparation excipients have known toxicity or are very likely to have toxicity;

(2) The new drug cannot maintain stability during the entire phase I clinical trial project planned to be implemented; (3) The impurity characteristics of the new drug show potential toxicity, or the impurities in the new drug whose content is above the identification limit have not been adequately identified and have not been identified. assessment of its potential toxicity;

(4) There are biosafety issues with animal-derived components; (5) The master cell bank or the working cell bank has not been fully identified.

The applicant should analyze whether the available pharmaceutical study information indicates potential human risks, discuss these potential risks, and describe the measures planned to control or monitor the risks.

For new drugs with biological toxicity, radionuclides, etc., or new drugs involving biosafety risks, relevant research materials, research plans and risk control measures should be provided in accordance with relevant international technical guidelines. 1. Chemical pharmaceutical research information New drug applicants should analyze and compare samples for animal research and samples to be used for human trials (can be listed in a list). Human trials provide support for safety. For chemical drugs applying for Phase I clinical research, the following pharmaceutical research materials need to be provided, and at the same time, the summary table of pharmaceutical research information for Phase I clinical trials of chemical drugs should be summarized and submitted according to the attached table and submitted electronically. 1.1 API information 1.1.1 The manufacturer should submit the complete address of the API manufacturer (including production and inspection). 1.1.2 Preparation process Information on the preparation process of the API should be provided, including the reaction flow chart, indicating the reagents, solvents and catalysts used in the process. For the preparation of peptides and small molecule nucleic acid drugs by fermentation process, extraction process, etc., more information on preparation process needs to be provided. For sterile APIs, sterilization/sterilization process and sterility assurance measures shall be provided.

1.1.3 Structural confirmation The methods, maps and a brief structural analysis summary used for structural confirmation should be provided. 1.1.4 The physicochemical properties should list the crystal form, dissolution, and dissolution of the drug substance that have been studied and may be related to the performance of the preparation.

Key physical and chemical properties such as degree, permeability, particle size, etc.

If possible, list specific solubility data in different media (eg, different pH). 1.1.5 Quality control should provide preliminary quality standards, explain inspection items, acceptable limits, analytical methods, and provide representative maps. In the early stage of drug development, it is not necessary to submit comprehensive and complete analytical method verification information, but at least key verification information such as method specificity and sensitivity should be provided.

A sample inspection report should be provided. Provides batch analysis data for key study batches (eg, for safety studies, stability studies, clinical studies, etc.). Preliminary impurity profile analysis results, potential genotoxic impurity control strategy should be provided and analytical information. Research and report can be submitted according to the ICH M7 guideline.

1.1.6 Stability The research data on the stability of the drug substance should be provided, and the analytical methods used should be listed. The preliminary data of representative samples and other supporting stability research data should be submitted in the form of a list, and the representative map of the key items should be provided. Stability data should support compliance with the physicochemical parameters of the new drug during the planned clinical study period, and limited supportive stability data may be provided if the planned trial period is extremely short. On the basis of ensuring the stability of the drug during clinical trials, gradually accumulate stability data to support further clinical development.

1.1.7 Packaging and storage

The direct contact packaging materials and storage conditions should be listed.

1.2 Preparation information 1.2.1 The dosage form and product composition should list the formulation composition and dosage of the preparation.

The final removed components should also be listed. The excipients in the preparation should meet the pharmaceutical requirements; for the brand-new excipients that have not been used in the preparations at home and abroad, related declarations should be made.

1.2.2 The name and address of the manufacturer

should be submitted to the manufacturer of the clinical trial preparation (including production, packaging, and inspection) 's full address.

1.2.3 Production process and process control The

production process information, including process flow diagram, shall be provided. Sterilization process and sterility assurance measures should be provided for sterile preparations; more detailed process descriptions should be provided for unconventional preparations.

1.2.4 Quality control should

provide preliminary quality standards. Explain the acceptable limits, analytical methods, and representative spectra of the inspection items. The reporting method of impurities can be referred to ICH Q3A and Q3B. Appropriate quality control items and analysis methods should be set according to dosage forms and product characteristics. The test items that are for the purpose of accumulating data, but not as conditions for the release of preparations, should be indicated. In the early stage of drug development,

it is not necessary to submit comprehensive and complete analytical method verification information, but at least verification information on key items such as method specificity and sensitivity should be provided. Provide inspection reports for

key study batches (such as for safety studies, stability studies, clinical studies, etc.). Preliminary research results on the degradation pathways and degradation products of the preparation should be provided. See ICH Q3B. 1.2.5 Stability should provide preparation stability research data, list the analytical methods used, and submit preliminary data and other support for representative

samples (such as animal pharmacology and toxicology research samples, samples to be used in clinical trials) in tabular

form Sexual stability research data should be provided

Provides a representative map of key projects. Stability data should support compliance with the physicochemical parameters of the formulation during the planned clinical study, and limited supportive stability data may be provided if the planned trial period is extremely short. 1.2.6 Packaging and storage conditions The information and storage conditions for direct contact with packaging materials should be listed. For pharmaceutical packaging materials with new materials, new structures, and new uses, information should be provided and related declarations should be made as required. 1.2.7 Other preparations that are compatible with clinical needs and have special requirements for use should be provided.

Provide relevant stability test results. 1.3 Placebo information If a placebo needs to be used in a clinical trial protocol, a prescription for the placebo, Research materials such as production process and production plant related information, quality control and inspection results.

2. The pharmaceutical research information of biological products provides a summary summary of the results of pharmaceutical research, and provides explanations for the quality control items that are lower than the basic requirements of pharmacopoeia control in the proposed quality standards, or lower than the requirements of general technical guidelines; The difficult issues that are found and need to be brought to the special attention of the reviewers will be highlighted.

2.1 Raw materials for production

2.1.1 The name, source, quality standard, safety and other information of the starting materials for production should be provided. The starting materials for production should meet the standards of the current version of the Pharmacopoeia of the People's Republic of China or the Pharmacopoeia of the People's Republic of China. The relevant requirements of the three "Quality Control Procedures for Raw Materials and Excipients for the Production of Biological Products" are classified according to the risk level and provide

Corresponding supporting documents and/or quality control test reports, etc.

2.1.2 Establishment and identification of engineered cells (bacteria)

For proteins expressed by gene recombination technology, the amino acid sequence should be provided.

The gene is remodeled or mutated, the applicant can combine the effect on the structure and function of the product

Make a preliminary description. Provide the name, source, structure and genetic properties of the expression vector,

The structure of the recombinant expression vector should be determined. Provide host cells (bacteria) and constructed

Name, source, safety, culture characteristics and biological characteristics of engineered cells (bacteria)

(genotype and phenotype), passage history (including domestication process), assay results, etc.,

Indicate whether genetic manipulation has been performed to introduce foreign gene sequences.

2.1.3 Establishment, verification, preservation and passage stability of seed bank

Research data on the establishment, verification, preservation and passage stability of seed banks should be provided.

Reference should be made to the Chinese Pharmacopoeia, European Pharmacopoeia, United States Pharmacopoeia and other international general pharmacopoeia, national

To verify the seed bank according to the relevant international requirements or other international general standards, and to provide

The verification report for the seed bank ensures that there is no risk of contamination by internal and external factors. established species

The sub-library should be able to support subsequent research and development.

2.1.4 Sources and quality standards of other raw materials used in production

Other raw materials used in production should be listed in tabular form according to the process flow

name, source, quality standard, usage steps, etc. Other raw materials used in production should also be

Comply with the current version of the "Pharmacopoeia of the People's Republic of China" standard or the "Pharmacopoeia of the People's Republic of China"

The relevant requirements of the three "Quality Control Procedures for Raw Materials and Excipients for the Production of Biological Products"

according to the risk level, and provide corresponding supporting documents and/or quality control inspections

test report, etc.

2.2 Stock solution

2.2.1 The manufacturer

should provide the complete address of the manufacturer of the raw solution (including production and inspection).

2.2.2 For the preparation process and process control of the stock solution, a flow chart shall be provided according to

the process steps, and the process parameters, production scale, and important production equipment shall be indicated, and the technical conditions and parameters of the key process steps shall be provided. For purification process, coupling process and other special treatment steps, the technical conditions and parameters used should be clearly defined; the key process steps of virus inactivation/removal should be verified. Research data on optimization of key process parameters should be provided. 2.2.3 The stock solution preparation process development summary should list the batch size, production time, production location of each batch of stock solution in the process

development, as well as the corresponding production process, production scale and sample use (such as quality research,

pharmacology and toxicology research, process stability). properties, stability studies, controls/references, etc.), and provide assay results. Quality comparability analysis of samples for animal pharmacology and toxicology research and samples to be used for Phase I clinical trials, so as to provide safety support for subsequent human trials. 2.3 Preparation 2.3.1 The manufacturer shall provide the name and address of the manufacturer of the sample preparation for clinical trials. 2.3.2 Dosage forms and formulation prescriptions should specify the specific dosage forms, and list the formulation composition of the unit dose product, explain the role of each ingredient in the formulation, and the standards for implementation. In case of excessive addition, an explanation should be given. If the special solvent is attached, please

refer to the above table to list the special solvent

's prescription. For brand-new excipients that have not been used in domestic and foreign preparations, related declarations should be made.

2.3.3 Preparation process and process control 2.3.3.1 Batch formula: List the batch formula composition of the samples for clinical trial in a table.

2.3.3.2 Process flow chart: The flow chart shall be provided according to the process steps, indicating the process parameters.

number and production equipment.

2.3.4 The summary of preparation preparation process

development should list the batch, production time, production location of each batch of preparation in process development, as well as the corresponding production process, production scale and sample use (such as quality research, toxicology research, process stability). , stability studies, reference/reference batches, etc.), and provide assay results. The list description should also include a pharmacological comparability analysis between the animal toxicology study samples and the samples to be used for Phase I clinical trials, so as to provide safety support for subsequent human trials. 2.4 Quality Research and Quality Control 2.4.1 Quality Research 2.4.1.1 Structure Confirmation In the early stage of research and development, preliminary structure confirmation of the samples should be carried out, and research data should be submitted.

Complete structural confirmation data can be submitted when applying for new drug marketing, including primary structure, secondary structure and advanced structure, etc.

The batch number of the sample for structure confirmation should be provided. If a reference substance is used, the source, batch number and quantity of the reference substance should be stated. 2.4.1.2 Physical and chemical properties Provide clear physical and chemical properties of products with reference to relevant guidelines.

2.4.1.3 Biological activity Provide

biological activity measurement methods and standards. 2.4.1.4 The

analysis of related substances/impurities includes starting raw materials,

product-related substances and process-related substances, and corresponding

Analysis. For impurities involving biological toxicity and immunogenicity, sensitive and specific detection methods should be provided, and strict control requirements should be formulated.

2.4.2 Quality control 2.4.2.1

The quality standard shall be

combined with the verification data analysis of multiple batches of trial products to determine the preliminary quality standard of the stock solution and preparation, and the quality standard of this stage shall be provided in the form of a list, which shall include inspection items, inspection methods and limit standards. At least the verification information of key items such as the specificity and sensitivity of the key quality

attribute detection method should be provided. 2.4.2.2 The batch inspection report shall provide batch analysis data of representative process and inspection of representative batch samples

Qualification reports, such as samples for non-clinical trials and samples for clinical trials, etc.

2.5. Stability The

research should be carried out with reference to the relevant guidelines for the stability research of biological products. stability The findings should support a phase I clinical trial. 2.6. Packaging

materials/containers and other direct contact materials shall list the intended packaging

and storage conditions. List the proposed packaging material/container

and other direct contact materials.

(6) Pharmacological and toxicological information

Pharmacological and toxicological information should include non-clinical research review, pharmacological action summary report,

Toxicology study summary report, pharmacokinetics summary report and various research reports. Applicants should submit all completed nonclinical trials, including exploratory nonclinical pharmacology and toxicology studies of the drug, so that the review department can make an overall evaluation at this stage. Study-related references and protocol revisions are also available as part of this information.

1. Non-clinical research reviews Non-

clinical research reviews should provide summary information on the completed non-clinical studies, each Items can be listed in the form of a list, the content should include the description of the following aspects. The format and content can be listed with reference to ICH CTD 2.4.

1.1 Outline the trial strategy of the non-clinical trial study and the trial implementation date. 1.2 Non-clinical study design compliance information and deviations from the design. 1.3 Quality comparability analysis results of the test substance and pharmaceutical research and clinical trial samples fruit.

1.4 List the general research items and numbers of non-clinical trials, research institutions, Study site, nonclinical study review should be signed and dated.

1.5 The results of animal toxicology studies and toxicokinetics are systematically presented, and special attention should be paid to information that may endanger human safety.

1.6 The results of non-clinical studies have supportive evidence for clinical trials. 1.7 Statement of adherence to Good Practice (GLP) for nonclinical research of pharmaceutical products. In the case of non-compliance with the above regulations, the reasons should be stated and an explanation should be provided that may have affected the test results.

2. Summary of pharmacological studies An

overview of in vitro and in vivo pharmacological effects and their mechanisms of action, as well as secondary pharmacodynamic information. Pharmacodynamic studies of new drugs should be carried out using recognized in vitro and in vivo test systems and indicators.

Newer in vivo models should be used as far as possible to carry out efficacy studies related to the mechanism of action and to provide information on the relationship between drug efficacy and exposure. Pharmacodynamic studies should inform the relevance and efficacy potential of new drugs to clinical disease treatment. Efficacy information is usually not the main reason for delaying clinical trials. However, it should be submitted at the time of the Phase I clinical trial application. 3. Summary of toxicological studies A summary report of toxicological studies should be provided. The extent, severity and duration of toxic effects, dose-relatedness, reversibility, species and gender differences should be described. Special attention should be paid to information on repeated dosing toxicity, animal death, pathological examination, local tolerance, and other issues requiring special explanation. Depending on drug characteristics and human study staging, special research information may be required, such as macromolecular drugs requiring in-depth studies to increase immunogenicity and immunotoxicity. The evaluation of toxicology findings should focus on the logical evaluation of the correlation of toxic responses and explain the risk predictions extrapolated to humans. Evaluation factors include animal species, number of animals, administration dose, administration period, exposure and its correlation with the maximum human exposure. The results of toxicity tests should clearly state the NOAEL, MTD and/or STD10, HNSTD dose and exposure. quantity information. It is recommended to state in tabular form.

In addition, for each toxicology study supporting the proposed clinical trial safety, applicants are encouraged to submit a full list of data suitable for detailed review. In order to be able to describe the contents of these listings, the following documents should also be provided with the listings:

(1) A brief introduction to the research (such as a technical report or abstract, including a method introduction section); (2) The overall plan for the toxicology research and development of the product and its revision instructions.

Repeated-dose toxicity test cycles supporting the proposed clinical trial protocol should refer to relevant guidelines. 4.

The pharmacokinetic summary

should address the feasibility of the analytical method, pharmacokinetic/toxicokinetic parameters, absorption and tissue distribution, metabolism, excretion, and physiological changes due to efficacy and toxicity issues, such as disease states effects, antibody production, cross-reactivity, etc. If there are existing human studies, the metabolism and exposure of animals and humans in non-clinical studies should also be compared, and the predictive effects of non-clinical study results on potential adverse reactions in humans should be described. For details, see Guidelines for Nonclinical Pharmacokinetic Technical Studies. 5. Each research report should provide the obtained pharmacological effect, toxicological research and pharmacokinetic research report. 6. Other summary reports are comprehensive summary reports of all test results, which should be accurate and consistent with the test results, and should fully reflect the test situation and data results, and a comprehensive technical evaluation can be made based on this.

If the final toxicology report for each study is not available when the Phase I clinical trial application is submitted, an audited draft report and a summary report based on the draft report can be submitted. The final report of each toxicology study should be submitted within 120 days after the initial submission of the clinical trial application. The final report should include a description of all changes and the necessary analysis of whether they would affect the original safety assessment.

(7) Description of past clinical experience

If there is previous clinical experience, the applicant should provide an overview of relevant information.

If the investigational drug has been clinically studied in China or other countries or has been marketed, detailed information on the safety of the proposed trial or the basis for the proposed trial should be provided. All published literature data related to the safety of the proposed trial or the efficacy evaluation data of the intended indication study of the investigational drug should be provided, including a reference list or important supporting literature related to the previous clinical experience of the investigational drug . In addition, the proposed clinical study should be comprehensively evaluated based on the available information, which will help support the selection of the dose, duration of medication, drug combination, and test population of the clinical study.

(8) Overseas research materials

For the relevant research that has been carried out or is being carried out abroad for the declared product, the relevant research shall be submitted. Provide original and Chinese translation materials. The Chinese translation should be consistent with the original content.

4. References

1. Technical Guidelines for Stability Research of Chemical Drugs (APIs and Preparations) ÿ20150205ÿ

2. Technical guidelines for the preparation and structure confirmation of chemical drug APIs ÿ20070823ÿ

3. Judgment criteria for the authenticity of chemical drug research data and maps ÿ20100510ÿ

4. Technical Guidelines for Drug Single-dose Toxicity Study (20140513) 5. Technical Guidelines for Drug Repeated Dosing Toxicity Study (20140513) 6. Q&A for Test Requirements for Non-clinical Safety Evaluation (20140513) 7. Drug Non-Clinical Safety Evaluation Technical Guidelines for Clinical Pharmacokinetic Research (20140513)

8. Guidelines for non-clinical safety evaluation of new pharmaceutical excipients (20120515)

9. Technical guidelines for drug non-clinical dependence research (20071121)

10. Technical Guidelines for Stability Research of Biological Products (Trial) (20150415)

11. Technical Guidelines for the Management of Process Changes in the Production of Biological Products ÿ20080904ÿ

12. General Principles of Validation Techniques for Analytical Methods for Quality Control of Biological Products ÿ20080904ÿ

13. General principles for non-clinical safety technical review of therapeutic biological products ÿ20100506ÿ

14. Guidelines for the Management of Phase I Clinical Trials of Drugs (Trial) (20111207)

15.ICH Q3AÿR2ÿ-Impurities in new drug substances 16.ICH Q3BÿR2ÿ-Impurities in new drug Products 17.ICH E6ÿR1ÿ-Guideline for good clinical practice 18.ICH E6ÿR2ÿ-Integrated addendum to ICH E6ÿR1ÿ

19.ICH M3ÿR2ÿ-Guidance on nonclinical safety studies for the conduct of human clinical trails and marketing authorization for pharmaceuticals

20.ICH M4- The Common Technical Document

21.ICH M7ÿR1ÿ-Assessment and control of DNA reactive ÿ mutagenic ÿ impurities in pharmaceuticals to limit potential carcinogenic risk

22.ICH S6-Preclinical safety evaluation of biotechnology derived pharmaceuticals

23.ICH S9 -Nonclinacal evaluation for anticancer pharmaceuticals

24.Content and format of INDs for phase I studies of drugs, including well-characterized, therapeutic, biotechnology-derived products.

25.Guidance for Industry Q&A on Content and format of INDs for phase I studies of drugs, including well-characterized, therapeutic, biotechnology-derived products.

5. Schedule

Summary table of pharmaceutical research information for chemical drug phase I clinical trial application

1. Basic information

Acceptance number API acceptance number:	Preparation acceptance number:
applicant	
Compound name application name (Chinese and English) or laboratory code	Has the current name been approved by the Pharmacopoeia Committee: Yes ÿ No ÿ
Stereoconfigurations of compounds with well-defined structures	
molecular formula	
molecular weight	
Dosage Form and Route of Administration	Remarks: Tentative Dosage Form for Phase I Clinical Study
Specification	Remarks: Tentative specifications for Phase I clinical studies
Indications proposed for clinical study	information. The clinical research project to be carried out, the number of subjects and the research period, etc.

2. API information

API Synthesis Chemistry	The reaction conditions, solvents, reagents, catalysts, etc. used should be indicated in the chemical reaction formula.
Reaction type, purification method	Provide information on manufacturers, synthesis processes and quality control of key materials.
and the current scale of trial production	Indicate the proposed location for the preparation of clinical batches.
Drug Substance Structure Confirmation	lists the methods used for structure confirmation and a brief summary of structure analysis.

<table>
<tr><td>Key physicochemical properties of APIs

characteristic</td><td colspan="3">List the crystal form, solubility, permeability, particle size, etc. of the API that may be related to the performance of the preparation

chemical properties.

If possible, please list specific solubility data in different media (eg, different pH).</td></tr>
<tr><td rowspan="7">API

Quality Control</td><td>project</td><td>method</td><td>limit</td></tr>
<tr><td></td><td rowspan="5">Brief method, such as HPLC</td><td></td></tr>
<tr><td></td><td></td></tr>
<tr><td></td><td></td></tr>
<tr><td></td><td></td></tr>
<tr><td colspan="3">For key items involving safety, specific inspection methods and methodological verification summaries should be listed.

For example, related substances, residual solvents, class I heavy metal inspection, etc.</td></tr>
<tr><td>critical batch

analyze data</td><td colspan="3">Submit pivotal study batches (including for safety studies, stability studies,

batch analysis data for clinical studies, etc.).

In addition, combined with the relevant research information of the preparation, submit the impurity profile analysis results in the form of Annex 1-3.</td></tr>
<tr><td>API

Stability Summary</td><td colspan="3">Provides an overview of the stability study, listing the batch, batch number, investigation conditions, (already

Completed) investigation time, change trend of the investigation project and preliminary conclusions. List the initial packaging and storage

save conditions.</td></tr>
</table>

3. Formulation information

<table>
<tr><td>Formulation, formulation, formulation

Art description and existing test

scale</td><td colspan="3">List the formulation composition of the preparation, provide a brief description of the process, and provide a detailed description for sterile preparations

The sterilization/sterilization process conditions of the unconventional process preparations need to provide a more detailed process description.

Indicate the proposed location for the preparation of clinical batches.</td></tr>
<tr><td rowspan="4">Formulation Quality Control</td><td>project</td><td>method</td><td>limit</td></tr>
<tr><td></td><td rowspan="3">Briefly describe the method of analysis, e.g.

HPLC</td><td></td></tr>
<tr><td></td><td></td></tr>
<tr><td></td><td></td></tr>
</table>

	For key items involving safety and formulation characteristics, specific inspection methods and Summary of methodology validation, such as related substance inspection, dissolution/release inspection, etc.		
critical batch analyze data	Key study batches (including those used for safety studies, stability studies, research, clinical studies, etc.) In addition, combined with the relevant research information of the API, submit the impurity profile analysis results in the form of Annexes 1-3.		
preparation Stability Summary	Provides an overview of the stability study, listing the batch, batch number, investigation conditions, (already Completed) investigation time, change trend of the investigation project and preliminary conclusions. Compatibility for clinical use and preparations with special requirements for use need to provide relevant stability data. test results. List the proposed packaging and storage conditions.		

Appendix 1-1

API batch analysis data

batch number	Trial production time	Trial production Place	Trial production scale	use Craft*	main equipment	use	key quality data (vs. such as related substances*, containing amount, particle size, crystal form, etc.)

Appendix 1-2

Formulation Batch Analysis Data

batch number	Trial production time	Trial production Place	Trial production scale	Where to use Square, Process*	main equipment	use	key quality data (vs. such as related substances*, containing amount, dissolution rate, etc.)

*If the formulation process is changed during the research process, please number them in sequence, fill in the numbers in the form, and list the numbers represented by the numbers below the form.

Specific prescription process

*For the provision of relevant substance data, the impurities of the identified structure are listed as a single known impurity.

Impurities that appear fixed are listed separately according to relative retention time.

Please mark the clinical batch samples.

Appendix 1-3

Impurity profile analysis

List the identified impurity structures in tabular form, describe their source and relative retention time, and indicate whether there is potential in combination with the process

of genotoxic impurities.

Impurity name or code	Impurity structure	source of impurities	relative retention time

If there is a potential genotoxic impurity, an initial control strategy should be provided.