# 以患者为中心的药物临床试验设计

# 技术指导原则（试行）

July 2023

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## I. Overview

### (1) Background

"Patient-centered" drug development refers to drug development based on the patient's perspective.

process of product development, design, implementation and decision-making, aiming at efficient research and development that is more in line with

Clinically valuable drugs that patients need.

Patients are the direct feelers and experiencers of disease states and drug treatments.

In the entire process of drug development and decision-making, patients should be regarded as active participants.

share with patients their experiences, opinions, needs and preferences regarding the disease and related treatments

Experience data as a key consideration in the design and implementation of drug development, and

Incorporate benefit-risk assessment systems into valuable drugs that meet patient needs

Provide scientific evidence for R&D and marketing.

The entire process of drug research and development should fully consider the needs of patients and put patients at the center

Three techniques for careful drug clinical trial design, trial conduct and benefit-risk assessment

Technical guiding principles will be adopted from different stages of drug development, implementation and evaluation.

Systematically explain how to fully consider patient needs and include patients in the early stages of research and development

Experience data for clinical trial design; how to ensure scientific reliability and test subjects

Optimize the experience of patients participating in clinical trials under the premise of patient safety and privacy;

And how to fully weigh the clinical benefits and risks of drugs from the patient's perspective, and

Make scientific decisions.

Patient-centered drug clinical trial design requires attention to and collection of patient data

patients' experiences and needs of illness and treatment and will be reliable, meaningful and representative

The science of representational patient experience data as a key element in clinical trial design

The basis for consideration fully reflects the clinical benefits and risks from the patient's perspective. at the same time,

Fully consider patients' feelings about participating in clinical trials in clinical trial design to

Promote patients to actively participate in clinical trials and obtain high-quality clinical trials efficiently

data.

(2) Purpose and scope of application

This guideline aims to clarify the patient-centered design of drug clinical trials.

The overall principles and key elements of planning, describing how to collect and analyze patient experience data

Incorporate data into the overall clinical development plan and trial design, as well as communicate with review agencies

important contents of communication, etc., to help sponsors carry out patient-centered drug clinical trials.

Provide technical reference for R&D.

This guideline only represents the current views and understanding of the drug regulatory authorities.

Not legally binding. With the progress of scientific research, this guide

The relevant content in the Guidelines will be continuously improved and updated. Apply these guidelines

When doing so, please also refer to the Good Clinical Practice (GCP) and National

International Conference on Harmonization (ICH) and other relevant published guidelines

guiding principles.

2. General principles

Patient-centered drug clinical trial design should still meet the needs of drug clinical trials

General principles of clinical trial design. It is recommended to refer to both ICH E8(R1) and national

"Guiding Principles for General Considerations in Drug Clinical Trials" issued by the Food and Drug Administration, and

Technical guiding principles for drug development for specific diseases, etc. From patient-centered

From a psychological perspective, we should focus on the following principles:

(1) Incorporate patient needs throughout the entire process of drug development

Encourage sponsors to start early in drug development and throughout the entire development life cycle

During the term, continue to listen and absorb patients' opinions, and collect data based on actual needs.

Study of patient experience data to understand unmet clinical needs and important

clinical outcomes.

(2) Clinical trial design reflecting patient needs

Research purpose, target population, control, safety and effectiveness of clinical trials

The selection of elements such as evaluation indicators and methods should be based on the patient's perspective. exist

In clinical trials, a design consistent with the research purpose is adopted, and patient experience data are

Incorporate into consideration of key elements of clinical trial design. The overall research design should

Fully reflect the patient's physical and mental feelings, quality of life, function and survival status, etc.

clinical benefits, thereby providing a basis for R&D and regulatory decisions.

(3) Improve subjects' experience and reduce subjects' burden

Clinical trial design should fully consider the experience of clinical trial subjects and adopt

Use a design that is easily accepted by subjects. While ensuring scientific validity, data quality and completeness

On the premise of integrity, by optimizing the design of clinical trials (such as administration methods

and frequency, sampling/inspection time point arrangements) and the application of new technologies and methods

or new trial models (such as remote visits) to improve the convenience of clinical trials,

Reduce the burden on subjects, thereby enhancing their initiative to participate and improving

Improve subject compliance, reduce dropout rate and subject selection bias, etc.

Purpose.

(4) Strengthen early and full-process communication

It should be emphasized that in all drugs and at different stages of their development, compliance with Patient-centered clinical trial design is an important principle. But clinical Elements of the overall R&D plan and trial design, as well as disease characteristics and existing treatments methods, target population characteristics and other factors. Sponsors are encouraged to consider specific circumstances. Communicate promptly and fully with the review agency. Communication focuses on clinical trial facilities Whether the plan is consistent with disease characteristics and drug treatment goals, patient experience and Whether opinions can be fully expressed and adopted, and whether clinical outcome assessment is experienced The rationality and rationality of applying clinical outcome assessment to the primary endpoint of clinical trials and key clinical trials Feasibility etc.

3. Considerations for patient-centered clinical trial design

(1) Patient-centered overall clinical research and development plan

Drugs are developed to maximize therapeutic benefit for patients with minimal risk The ultimate goal, the overall clinical research and development plan should start with the end in mind, and The "patient-centered" principle runs through the plan. Importantly, from clinical practice Uncover the unmet clinical needs of specific diseases and, based on existing information, identify Evaluate whether research is needed to collect patient experience data based on the survey and research content to address important scientific questions in clinical development. For example, For some rare diseases with low incidence, complex phenotypes and limited knowledge of clinical diagnosis and treatment diseases, it is encouraged to conduct research on the indications to be developed at the beginning of drug research and development. Clinical investigations and studies of the natural history of disease.

Adopt phased research decision-making considerations and dynamics in the overall R&D plan

Adjustment. For example, to support more accurate selection of populations during key study phases,

Near-clinical target populations (such as adults with co-morbid indications in adults and children)

The study also includes adolescents aged 12 years and above) and needs to be combined with

Clinical needs and drug characteristics, and obtain corresponding non-clinical and clinical evidence. example

For example, tools intended to be used in later clinical outcome assessments (including effectiveness and safety

Exploration and preliminary verification should be completed at an early stage. Furthermore, if in the early stages

It is discovered at this stage that the clinical benefits of specific groups of people are more significant, and subsequent research can be adjusted in a timely manner.

development plan and include appropriate populations in pivotal studies.

In line with scientific principles, optimize clinical research and development strategies to improve

High R&D efficiency. For example, extrapolation and modeling of pediatric indications based on adult data

Simulation assists drug development, adaptive design, etc. to avoid unnecessary patient exposure

dew.

(2) Research on collecting patient experience data

Patient experience data (PED) refers to all

Information provided by patients, their families, guardians, caregivers about the disease and related

information about experiences, opinions, needs and preferences regarding treatment.

Studies that collect patient experience data are studies that collect patient information as described above,

To provide support for drug research and development, which is different from specific drug clinical trials.

1. Objects for patient experience data collection

In studies that collect patient experience data, who the data is collected for depends on

The research purposes of clinical trials of drugs that they support. The research purpose determines the purpose

Detailed characteristics of the target population, such as disease characteristics, treatment methods, treatment-induced

complications and other factors, appropriate and detailed patient experience data collection should be designed accordingly.

The sorting criteria for set objects. should be combined with the purpose and science of specific drug clinical trials.

Academic considerations should be used to maximize the representativeness of data collection objects. argument generation

Important factors of representation include: demographic and socioeconomic characteristics (e.g., age,

gender, race, socioeconomic status), cultural background and language, education level

(such as academic qualifications, reading and writing skills, narrative skills, and numeracy skills), clinical

bed characteristics (e.g., disease severity, course, symptoms, and/or functional impact,

Comorbidities, concomitant medications, physical and cognitive abilities), etc. At the same time, attention should be paid to

Whether the sampling method and sample size can ensure sufficient representativeness.

2. Content of patient experience data

Sponsors should focus primarily on gathering the following: Patient perceptions of the disease

knowledge (symptoms and signs that patients are most concerned about, impact on quality of life, etc.), patients

Perspectives on existing treatments (limitations in accessibility, safety, and effectiveness

(e.g., gender, compliance, preference information, etc.), unmet clinical needs, patients'

Expected benefits and acceptable risks of potential treatments, subject participation in drug clinical trials

The burden of clinical trials (including psychological, financial, and social aspects) and participating drugs

R&D methods, etc.

3. Research methods for collecting patient experience data

After determining the objects and content of data collection, according to the research

Purpose Select appropriate qualitative, quantitative or semi-quantitative research methods. Qualitative method

Methods generally include in-depth interviews, open questions, qualitative questionnaires, etc., which can

Via face-to-face or online meetings (video and voice), telephone, Internet link,

Collect through appropriate methods such as email; quantitative methods usually include questionnaire surveys,

Scale surveys, big data analysis and other data generated using structured tools, automatic

However, medical history research, etc. If you need to study the impact of multiple backgrounds and different factors,

A joint study using quantitative and qualitative methods may be required. For example, first pass

Survey patients through questionnaires to gain an overall understanding of their experience with the disease or condition.

and then conduct in-depth interviews to obtain more information. Early clinical development

Patient experience research can focus on open-ended questions to help determine follow-up research

A more focused range of issues and assessment tools.

The design of survey questions should comply with general principles and requirements, such as avoiding incomplete,

Leading or unclear questions and avoid including multiple questions in the same question.

When collecting patient experience data, prioritize obtaining direct reports from the patients themselves.

description, and appropriate research methods can be used for special groups, such as through drawings

or games to capture the experiences of the pediatric patient population, through caregiver observations

Observed patient behavior reflects the experiences of a patient population who are unable to self-report.

For people with different cultural backgrounds, appropriate language and writing should be used, focusing on

Examining the impact of cultural differences on communication.

For more advice on collecting patient experience data, see Organizing Patient

Guiding principles for general considerations involved in drug development.

(3) Patient-centered clinical trial design elements

1. Research purposes oriented to patient needs

The essence of clinical trials is to raise important scientific questions and

plan to answer these questions. When determining the purpose of research, the nature of the disease needs to be considered

clinical history, treatment goals of experimental drugs, patient preference information, etc. For example, treat

Drugs used to treat chronic cholestatic liver disease generally aim to improve disease progression;

However, the disease is often accompanied by symptoms of itching, and severe itching significantly affects the patient's life.

quality of life, in this case with improvement of pruritus symptoms as the target indication

Research and development of new drugs can also bring clinical benefits to patients. early research collection

Patient experience data can be used to select options closer to patient needs for late-stage clinical trials

Provide support for research purposes.

2. Choose the right target group

During the drug research and development process, sponsors should combine disease characteristics, drug

Mechanism of action, known safety and efficacy characteristics, and existing treatments, etc.

Recruit subjects with the best benefit-risk ratio, and try to promote the generation of the subject population

Expressive. On the one hand, including patients who are most likely to benefit from the trial ensures

Protect the safety and rights of subjects. For example, for the lack of effective back-line treatments

For diseases that require treatment, if the efficacy of the trial drug is not yet clear, patients should be treated later

Patients are more likely to benefit from it than first-line treatments. For example, if the mechanism of action or

There are already data showing that experimental drugs are effective in patients with positive biomarkers.

Significant curative effect, but less curative effect or even no curative effect in marker-negative patients

If there is an effect, patients with positive markers are most likely to benefit from the trial; while in use

Insufficient control of markers in enriched subjects and treatment of marker-negative patients

When treatment options are limited, marker-negative patients may also be considered. Other

On the one hand, certain groups of people, such as children, should not be excluded without any scientific justification

Children, the elderly, pregnant women, patients with liver and kidney dysfunction, etc., if the same

Clinical needs should be included as much as possible based on the support of preliminary research data, except

Unless there is an obvious safety risk, or there is evidence that it is unlikely to benefit. forward

Prospective accumulation of necessary supporting data can avoid the need for late-stage clinical trials

Unnecessary restrictions on the study population. For example, for patients who may have combined liver function

Incomplete indications for chronic liver disease or the disease itself often have a negative impact on the patient's liver function.

Rare diseases that affect the development of liver function, supported by preliminary liver function impairment research data

Under this circumstance, patients with hepatic impairment may be considered in late-stage clinical trials. right

For drugs expected to be widely used in the elderly, preliminary data prove that there is no

When there are additional risks, a sufficient number of elderly patients should be included in clinical trials to adequately

Points represent the group of people who will be treated with the drug. If necessary, consider using

Adaptable design, pre-set the timing to adjust the entry criteria.

Sponsors should use a variety of methods to promote subject diversity, including

Including but not limited to: setting up adequate clinical trial risk management mechanisms to protect subjects

experimenter safety, and adopt clinical trial design and implementation methods that are easily accepted by patients.

to reduce the burden on subjects participating in clinical trials and strengthen patient communication and training.

training, selecting research centers in areas with high coverage of the target population, etc. Build more

For discussion, please refer to the "Technical Guidelines for the Implementation of Patient-Centered Drug Clinical Trials"

but".

3. Select the best and accessible control for the subject

The selection of control groups in clinical trials should fully ensure that subjects receive treatment

rights and interests, in line with ethical principles. As accepted standard treatments continue to

Revised, anticipating that appropriate control group selection will change over time

change. Therefore, it is recommended to select current clinical practice based on patient experience data.

Based on the best and accessible treatment, focus on other available treatments and evaluate

Dynamic changes in treatment needs over the coming period and prospective selection of controls

Group. In general, suboptimal treatments should be avoided as comparators that influence subjects

treatment options. If during the clinical trial, the target indications are

If the quasi-treatment changes, the subjects should be informed promptly to ensure that the subjects are fully

Understand other optional treatment methods and ensure that subjects can choose whether to withdraw

The right to experiment.

4. Effectiveness evaluation based on clinical outcome assessment

Patient-centered effectiveness evaluation should not only focus on the effects of the experimental drug on

In addition to the improvement of objective indicators such as survival time, we should also pay attention to the patient's feelings,

Gains in functional and survival status. Clinical outcome assessment can be used

(clinical outcome assessment, COA) tool for effectiveness evaluation.

4.1 Definition of clinical outcome assessment

Clinical outcome assessments are derived from patients, their caregivers, physicians, or other reviewers

Assessment by an evaluator to evaluate an individual patient's feelings, functioning, or survival status

Tools or means that usually require subjective evaluation rather than direct presentation of facts. root

According to different reporters, clinical outcome assessments were divided into physician-reported outcomes (clinician-

reported outcome (ClinRO), patient-reported outcome (patient-reported outcome)

outcome, PRO), observer-reported outcome (observer-reported

outcome, ObsRO), also includes functional outcomes based on test assessment of patient performance.

Performance-based outcome (PerfO); for details, please refer to the "PerfO"

Technical Guidelines for Patient-Centered Drug Benefit-Risk Assessment. For example, use

Numeric Rating Scale (NRS) or Verbal Rating Scale (VRS) to evaluate the patient's symptom severity,

Use the 6 minute walking test (6MWT) to measure

Measure patients' exercise capacity, assessed using frequency of cardiovascular event-related hospitalizations

The impact of cardiovascular events, etc.

Variables that can be measured in clinical trials based on clinical outcome assessments (e.g.

COA score) is accurately defined and used as an endpoint in clinical trials, thereby

Statistical analysis is used to answer specific research questions. Such endpoints are referred to as clinical

Outcome assessment endpoints. Precise definitions of endpoints generally include specific assessment categories

type, assessment time point, assessment method and other relevant information (such as the

integrated multiple assessment methods). For example: People with atopic dermatitis often have

Significant subjective symptoms, a certain measure of subjective symptoms can be used in clinical trials

scale to assess the severity of symptoms, and the scale score is precisely defined based on

The "average change of a certain scale score at a certain time point from the baseline" can be used as an evaluation

One of the end points of effectiveness.

4.2 Positioning of clinical outcome assessment endpoints in effectiveness evaluation

The sponsor should combine the research purpose with the patient experience data collected in the early stage.

, disease characteristics of target indications, drug action mechanism and clinical positioning, etc.

Taking all factors into consideration, clinical outcome assessment endpoints are used in key clinical trials.

as primary endpoint, coprimary endpoint, key secondary endpoint, or simply as

Exploratory endpoint. For different diseases, the positioning of clinical outcome assessment endpoints can

There may be different considerations, and as the understanding of the disease deepens and the existing

Changes depending on the degree of resolution of the treatment. Therefore, it should be combined with the specific circumstances and review

discussion with the review agency. Generally speaking, for the patient's function and living status

For diseases with a greater impact, the clinical outcome assessment endpoint may be selected as the primary endpoint.

Point (single, composite or co-primary endpoint). In addition, when evaluating drugs for

When objective indicators such as patient survival time are improved, the objective indicators can be combined with the same

Such important clinical outcome assessment endpoints are also used as co-primary endpoints or composite

end. For some diseases, laboratory tests or other objective indicators have been established as

surrogate endpoints to evaluate clinical efficacy. In this scenario, it may be possible to use clinical outcomes

The Bureau evaluates the data to provide additional background information or supporting data. especially for

Drugs that require long-term use, when similar products have similar improvements in objective indicators

At this time, clinical outcome assessment can provide more basis for evaluating the overall benefit.

Table 1 Examples of positioning of clinical outcome assessment endpoints in different application scenarios

| Application scenario COA positioning | | COA endpoint example |
|---|---|---|
| Adult constipation and intestinal disease<br>irritation syndrome | primary endpoint<br>(complex) | Overall improvement in IBS-C symptom severity<br>Response (including abdominal symptom severity rating<br>Partially improved and completely spontaneous defecation frequency changes<br>good) |
| eosinophilic esophagus<br>inflammation | primary endpoint<br>(common) | Reach the peak number of eosinophils in the esophageal epithelium<br>Proportion of patients with values ÿ6 per high-power field;<br>Patient-Reported Dysphagia Symptom Questionnaire<br>(DSQ) score change from baseline |
| Amyotrophic lateral sclerosis as primary | from randomization to an | ALSFRS-R score of at least |

| | | |
|---|---|---|
| disease | Time to drop 12 points or die in one of the endpoints | |
| Anti-HIV viral infection secondary endpoint | HIV symptom index (HIV Symptom Index, HIV-SI) score change from baseline | change |

Note: With the continuous in-depth understanding of the disease and the accumulation of patient experience data, COA positioning may

Something has changed.

Table 2 Examples of positioning of different clinical outcome assessment endpoints in the same application scenario

| Atopic dermatitis COA endpoint examples | | WITH THE type | WITH THE position |
|---|---|---|---|
| Researchers overall assessment (AGE) | At a certain point in time, IGA reaches complete skin lesions Clearance (0) and skin lesions almost complete Cleared (1) and decreased by ÿ2 from baseline proportion of patients | ClinRO | Co-owner Want the end one |
| Eczema area and severity degree index (EASI) | EASI score at a certain point in time compared with baseline Proportion of patients with ÿ75% improvement | ClinRO | Co-owner Want the end one |
| Itching severity number word rating scale ÿNRSÿ | Itching peak NRS at certain time points change from baseline | PRO | secondary end point |

Note: With the continuous in-depth understanding of the disease and the accumulation of patient experience data, the design and development of COA

Positioning may change

4.3 Select clinical outcome assessment tools that are consistent with the purpose

First, consider using existing literature and data resources to fully explore the established

An independent clinical outcome assessment tool should be analyzed to see whether it can meet the needs. Attention should be paid to

Historical details of the development of clinical outcome assessment tools for use in the originally developed

scene, directly used in new scenes, or improved for use in new scenes.

For example, rare diseases often require more sensitive measurement tools to quantify disease characteristics.

symptoms, clinical outcome assessments that are appropriate in many other therapeutic areas may not be appropriate

Used for certain rare diseases. Therefore, sponsors should consider validating and applying with caution

Clinical outcome assessment tools developed in other patient populations. If not available yet

clinical outcome assessment tools, and the development of new clinical outcome assessment tools can be considered.

Clearly define the assessment content of clinical outcome assessment tools, including concepts,

Dimensions and items and their interrelationships. It is recommended to evaluate the nuclear factors related to the target disease.

Cardiac symptoms/signs, pay attention to the impact of the core symptoms/signs of the disease, and pay attention when necessary

Multiple dimensions and items can be included if necessary. For example: constipated bowel

People with irritable syndrome (IBS-C) are often troubled by bowel symptoms related to bowel movements (such as abdominal

diarrhea, hard stools that are difficult to pass, tenesmus) and abdominal symptoms (such as bloating and

Abdominal discomfort). Based on this, the clinical outcome assessment tool DIBSS-C

Taking the core symptom "Severity of IBS-C symptoms" as the concept evaluated, including

It contains two dimensions: "defecation-related symptoms" and "abdominal symptoms". The former includes frequent defecation.

4 items including rate, stool hardness, tenesmus, and difficulty defecation, the latter including abdominal

There are 3 items for pain, abdominal discomfort, and bloating.

Select appropriate clinical outcomes based on the intended assessment content and application scenarios

Assessment type. For conditions with symptoms or functional impairment, PRO is generally used

Assessments because they provide direct evidence of the patient's sensory and functional experience.

However, when patients are unable to provide self-report, observation-based

reports of symptoms, events, or behaviors that reflect the patient's feelings and functioning (e.g.
Such as ClinRO, ObsRO), it is not encouraged to let others replace the patient. From the patient's perspective
Indirect measurement methods for reporting. When clinical judgment is required to interpret observations
ClinRO should be used to evaluate if there are any serious consequences, such as plaque psoriasis
psoriasis area and severity index (psoriasis area and severity index)
severity index, PASI). PerfO measurements can be used to pass one or a series of
Standardized tasks to assess patient functioning in a standardized way (e.g.:
Measuring motor function and cognitive function, etc.). In addition, where appropriate,
A composite clinical outcome assessment tool that includes multiple types of clinical outcome assessment tools is used.
Bureau Assessment Tool. Digital Health Technologies,
DHT) can be used to collect clinical outcome assessment data, and sponsors should
The application scenarios for outcome assessment justify the use of DHT. DHT specifics
For application, please refer to the "Technical Guidance for the Implementation of Patient-Centered Drug Clinical Trials"
in principle".

Different methods may be used to establish the final assessment of clinical outcomes in clinical trials.
Points include but are not limited to: ÿ Take the form of multiple end points/composite end points. right
For many diseases, we focus on more than one symptom, sign, function or living condition.
status, for example, "achieving both symptomatic and endoscopic remission (achieving clinical remission)
"proportion of subjects with solution" as an indicator of efficacy in ulcerative colitis; hereditary
Relief of acute exacerbations in patients with angioedema by composite visual analogue scale
(Visual Analogue Scale, VAS), including for non-laryngeal attacks
3 symptoms (abdominal pain, skin pain, skin edema) and 5 symptoms of throat attack

symptoms (skin swelling, skin pain, abdominal pain, difficulty swallowing, and vocal

sound changes). ÿ Convert clinical outcome assessment endpoints for different concepts into a single

A binary classification (event) endpoint. For example, using the Multidimensional Respondent Index

(multidomain responder index, MDRI) method to evaluate type VII mucopolymer

Clinical improvement in patients with glycostoria, based on different clinical outcome assessment endpoints,

Improvement, maintenance, and deterioration are classified according to preset response thresholds and assigned points respectively.

values (+1, 0, and -1), aggregated to form each subject's overall MDRI to support

Overall evaluation of effectiveness. Attention should be paid to the rationality and lack of response thresholds and scores.

issues such as handling of lost data. ÿDifferent subjects use different types of clinical results

measurement results from bureau assessment tools, such as the use of PROs and

The combined forms of ObsRO should be analyzed separately. ÿThe end point of individualization,

That is, in the same clinical trial, different individuals may have different endpoints.

Often a descriptive exploratory endpoint. For example, in medical practice, for critical

For patients with the disease, doctors may provide treatment based on the pathophysiology and other characteristics of each patient.

Each patient develops individualized treatment and care goals. Build personalized endpoints

The process should be standardized, and the criteria for evaluating results should be

Be consistent between heart and patient. ÿ Use different methods to collect the same clinical results

Measurement results assessed by the bureau, for example, through electronic devices, paper, interviews

Mode. If clinical outcome assessment is used as the primary endpoint of a pivotal trial, care should be taken to

Evaluate whether measurements collected in different ways are consistent and interpretable.

4.4 Other considerations

To interpret results for clinical outcome assessment endpoints, appropriate thresholds should be set

(e.g. range of score changes) to reflect clinically significant changes in the target population

Changes at the individual level, not just statistically significant. this threshold

The value needs to be scientifically demonstrated based on existing evidence. In addition, clinical results

Timing and frequency of assessment of endpoints, handling of concomitant events, and number of missing events

Aspects such as data and multiplicity issues need to be considered during clinical trial design.

To consider. If clinical outcome assessment is used as the primary endpoint of a pivotal trial, clinical

Key elements of outcome assessment should be clearly defined in advance in the trial protocol, including

Concepts, tools, collection methods, measurement methods, endpoint types and clinical significance

defined thresholds, etc.

The measurement performance of clinical outcome assessment includes its reliability, content/structural validity

and the ability to detect changes, useful for redeveloping or adapting established clinical

Outcome assessment is important, especially for clinical outcome assessment for primary endpoints

or co-primary endpoint. Exploratory studies examine clinical outcome assessment

The best time to measure tool performance to better select and/or refine clinical

Outcome assessment tools so that they can be brought into pivotal trials.

5. Incorporate patient experience data into safety monitoring

Drug safety risks are an important factor for patients to consider when choosing drugs

one. Through the results of early collection of patient experience data, patients can be understood

Perceptions of and tolerance for specific adverse effects in clinical trial design

Focus on collecting events that patients are concerned about and have poor tolerance for, thus affecting their compliance.

Especially for drugs with high toxicity and long course of medication. Under appropriate circumstances,

Clinical outcome assessments can also be used to assess the safety and tolerability of investigational drugs.

evaluate. For example, in evaluating the safety risks of drugs that treat anemia in chronic kidney disease

major adverse cardiovascular events (cardiovascular death, myocardial infarction and

stroke) as a safety endpoint. Focus on the assessment of symptomatic adverse events (e.g.

Nausea, pain, etc.), you can choose PRO measurement to directly reflect the patient's feelings.

by. For example, using the SF-36 health survey scale, the Depression Self-Rating Center

ÿÿÿcenter for epidemiologic studies depression scaleÿCES-

D) Etc. To assess the neuropsychiatric response and response of patients receiving combination anti-HIV infection therapy

Sleep status, etc.

Effective risk management should be reflected in clinical trial design to protect subjects

or safety. Especially for special groups and subjects with higher safety risks,

When necessary, consider formulating targeted risk management measures, including improving necessary

Assess and examine, set appropriate monitoring items and frequency during medication administration and follow-up

rates (or unplanned surveillance if necessary), and targeted prevention/treatment

methods and follow-up plans, etc. For example, patients with liver and kidney impairment may need

Adjusting the dose of the trial drug and setting a more stringent monitoring schedule and discontinuation of the drug

standard. For another example, HIV-infected patients need to be fully and dynamically evaluated

Its immune function, etc.

4. Communication

In order to better conduct patient-centered clinical trials, in drug research and development

During the process, especially in the early stages, the sponsor should actively discuss key issues with the review agency.

Communicate on big issues. The following points should be noted:

(1) Whether patients' experiences and opinions can be fully expressed and adopted

If you plan to conduct a study that collects patient experience data and report the results

be incorporated into key elements of clinical trial design, and sponsors are encouraged to cooperate with review agencies

Communicate with the organization on key issues such as how research is designed, implemented and analyzed, including

Including the objects, content, research methods, etc. of patient experience data collection to ensure

The patient's voice can be fully expressed and adopted to achieve reliable and meaningful

and representative data.

(2) The validity of the application of clinical outcome assessment to the primary endpoint of key clinical trials

rationality and feasibility

If a clinical outcome assessment endpoint is proposed as the primary endpoint, the sponsor

Strategies for the application of clinical outcome assessments should be discussed with review agencies as early as possible. Pass the early stage

Patient preference information and other data collected, or clinical results from exploratory phases

The bureau evaluates the preliminary evaluation results and demonstrates the application of clinical results to the primary endpoint of the key trial.

The rationality and feasibility of the bureau's assessment. Sponsors are encouraged to submit their proposals to the review agency as early as possible

Critical information for clinical outcome assessment, obtained before the start of pivotal clinical trials

Review agency feedback, including description of intended use and trial endpoints, clinical results

assessment tools, evidence supporting content validity and other measure performance, clinical

Scoring information and scoring explanations for outcome assessment, etc.

(3) Development and validation of clinical outcome assessment

Sponsors are encouraged to communicate with the review agency on the following key issues: ÿClinical results

Bureau evaluates suitability for intended use. Objectives should be fully communicated to the review agency

Characteristics of the disease and description of the planned assessment content using clinical outcome assessments. ÿ

Whether clinical outcome assessments can effectively and reliably assess clinically relevant, patient-related

an important indicator. The intended application scenarios for clinical outcome assessment should be described, including including the study phase, expected benefits and risks of the experimental drug, target population, and Control group selection, trial endpoint, etc. ÿWhether clinical outcome assessment data can be used as a in a way that is accurate, interpretable, and non-misleading (i.e., well-defined) Present. An evaluation of the performance of the clinical outcome assessment measure should be provided to the review agency. assessment, including confirming the content validity, construct validity, and reliability of clinical outcome assessments and the ability to detect changes, etc.

## 5. References

[1] ICH. E8(R1) Guideline on General Considerations for Clinical Trials. (2021).

[2] ICH. E11 (R1) Clinical Investigation of Medicinal Products in the Pediatric Population. (2017).

[3] ICH. E10 Choice of control group and related issues in clinical trials. (2000).

[4] FDA. Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders (Draft Guidance). (2022).

[5] FDA. Discussion Document for Patient-Focused Drug Development Public Workshop on Guidance 4. (2019).

[6] National Medical Products Administration. Technical Guidelines for Clinical Research and Development of Rare Disease Drugs

Guiding Principles (2021).

[7] National Medical Products Administration. Patient-reported outcomes in drug clinical development Guiding Principles for Application in (2022).

[8] ICH. E7 Studies in Support of Special Populations: Geriatrics.(1993)

[9] FDA. Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry. (2020).

[10] FDA. Cancer Clinical Trial Eligibility Criteria: Brain Metastases. (2020).

[11] FDA. Cancer Clinical Trial Eligibility Criteria: Patients with HIV, Hepatitis B Virus, or Hepatitis C Virus Infections. (2020).

[12] FDA. Cancer Clinical Trial Eligibility Criteria: Patients with Organ Dysfunction or Prior or Concurrent Malignancies. (2020).

[13] State Drug Administration. Drug clinical trial enrichment strategy and design Planning Guiding Principles (Trial) (2020).

[14] Kartolo A, Gyawali B. Should the control arms of randomized trials have an expiry date? [J]. Nat Rev Clin Oncol, 2022,19(7):425-426.

[15] State Food and Drug Administration. Anti-HIV infection drug clinical trial technology

Technical Guiding Principles (2021).

[16] FDA. DDT COA #000005: Diary for Irritable Bowel Syndrome Symptoms – Constipation (DIBSS-C). (2021).

[17] Drug Evaluation Center of State Food and Drug Administration. Clinical treatment of ulcerative colitis drugs Testing Technical Guidelines (2021)

[18] FDA. Eosinophilic esophagitis: developing drugs for treatment guidance for industry. (2020).

[19] Iwashyna T. J. & Deane A. M. Individualizing endpoints in randomized clinical trials to better inform individual patient care: the TARGET proposal[J]. Crit Care, 2016, 20 (1):1-8.

[20] Zhang Fujie, Xie Feng. Patient-reported outcomes in human immunodeficiency virus infection Application progress in clinical research and practice of infectious diseases [J]. Chinese Miscellaneous Infectious Diseases Chi, 2021,39(03):129-135.

[21] Basch E. The missing voice of patients in drug-safety reporting[J]. N Engl J Med, 2010, 362(10): 865-869.

[22] Di Maio M., Basch E., Bryce J. & Perrone F. Patient-reported outcomes in the evaluation of toxicity of anticancer treatments[J]. Nat Rev Clin Oncol,2016,13(5): 319-325.

[23] Dueck A. C. et al. Validity and Reliability of the US National Cancer Institute's Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-

CTCAE) [J]. JAMA Oncol, 2015,1(8):1051-1059.