Patient Engagement Guide for Drug Development

~What Patients Need to Know About Drug Development~

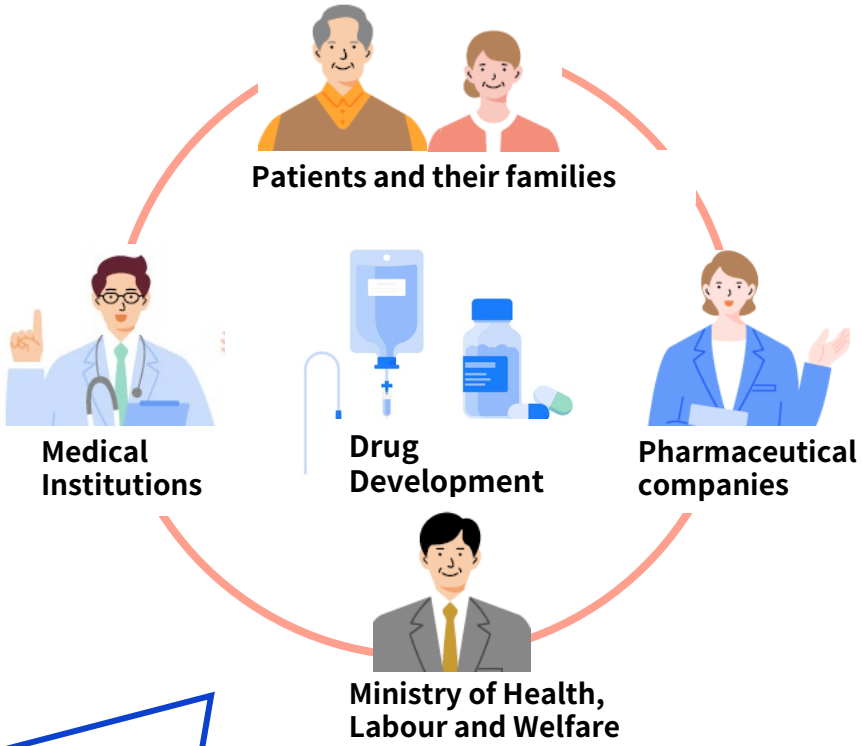
CHUGAI PHARMACEUTICAL CO., LTD.

Created in December 2025

Chugai Pharmaceutical's thoughts

Chugai considers patients and their families to be part of the drug development team, and has created this guide for everyone who is a member of the team.

We aim to achieve even more fulfilling collaboration by deepening the overall picture of drug development and the basic knowledge of clinical trials, and by knowing that your experience can be an important hint for advancing drug development.



We believe that drug development that reflects the perspectives and voices of patients will lead to the development of "Medicine" that patients will genuinely satisfy. We aim to develop drugs that patients, medical institutions, pharmaceutical companies, and the Ministry of Health, Labour and Welfare work together as a team*.

*Quote source: Chugai Pharmaceutical website "Drug development together with patients"

When pharmaceutical companies and patients work together in clinical trials

The road to the development of medicines (see p. 6 for details)

basic research (2-3 years)	Non-clinical trials (3-5 years)	Clinical Trials (3-7 years)	Approval Application and Review (about 1 year)	Post-Marketing Survey
Discovery and development of Novel Drug Candidates	Researching the efficacy and safety of novel substances	Efficacy and safety testing in humans	Application for approval to the Ministry of Health, Labour and Welfare and review by insepectorts	Check safety and usage after release

Process from before the start of the clinical trial ~ during the clinical trial ~ after approval (see p. 18 for details)

Listening to the experiences of patients and their families → **Preparation of clinical protocol / Informed consent form** → **Conducting and administering clinical trials** → **Disclosure of clinical trial results Post-approval response**

Patient voices and experiences are delivered to pharmaceutical companies in every aspect of clinical trials and are utilized!

From before clinical trials initiation to after approval is obtained, there are opportunities for pharmaceutical companies and patients to collaborate in a variety of situations.
For example, we listen to patients' experiences and use them to prepare clinical trial protocols, exchange opinions on what they felt during clinical trials, what they would like to improve, and how to disclose clinical trial results.

Composition of the " Patient Engagement Guide for Drug Development "

This document is a guide for patients who are not familiar with clinical trials and drug development to understand the basic overview, and consists of the following three parts.

1. Overview of Drug Development

- ✓ First, to deepen the understanding of the overall picture of drug development and the preparation and implementation process of clinical trials, this consists of two sections: "1. Overview of drug development" and "2. What is a clinical trial?
- ✓ This section introduces the general content of drug development.

2. What is a clinical trial?

3. Collaboration with patients in drug development

- ✓ **This guide aims to help patients understand when and why pharmaceutical companies seek their perspectives during the drug development process.**
- ✓ Specific examples of collaboration are described in "3. Collaboration with Patients in Drug Development".

Explanation of terms (attached) The explanation of the terms that appear in this document is posted at the very end. Please refer to it when reading the materials.

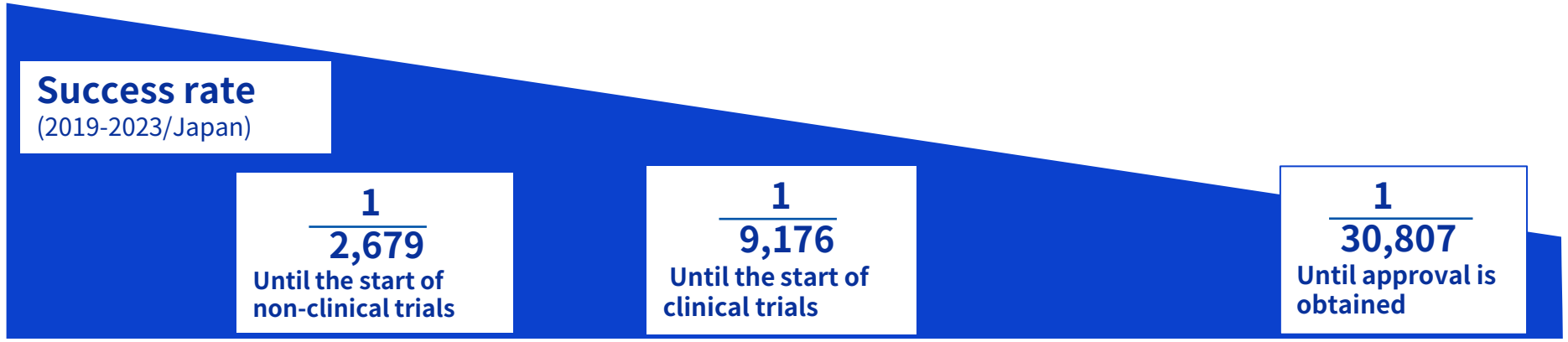
table of contents

The journey to the development of medicines* and success rates**

It takes more than 10 years for a drug to be born, but the success rate is said to be extremely low.

In addition, even after being reviewed and approved, post-sales investigations are repeatedly conducted to properly confirm efficacy and safety.

basic research (2-3 years)	Non-clinical trials (3-5 years)	Clinical Trials (3-7 years)	Approval Application and Review (about 1 year)	Post-Marketing Survey
Discovery and development of Novel Drug Candidates	Researching the efficacy and safety of novel substances	Efficacy and safety testing in humans	Application for approval to the Ministry of Health, Labour and Welfare and review by insepectorts	Check safety and usage after release



* Quote source: Japan Pharmaceutical Manufacturers Association website "Drug discovery and drug development"
**Source: Japan Pharmaceutical Manufacturers Association website "DATA BOOK 2025 A-7-9 Number of compounds by development stage and number of approvals obtained (Japan)"

table of contents

Clinical trial rules and their necessity*

- **Since clinical trials also have a research aspect, there are rules such as the "Declaration of Helsinki", "Good Clinical Practice (GCP)", and "Pharmaceuticals and Medical Devices Act" to protect the rights and safety of those participating in clinical trials.**
  - Explanations of terms such as the Declaration of Helsinki, GCP, and the Pharmaceuticals and Medical Devices Act are posted at the very end, so please refer to them.
- **All clinical trials are planned and conducted according to these rules.**
  Compliance with these rules protects the human rights, safety, and privacy of those who participate in clinical trials.

*Quote source: Chugai Pharmaceutical website "Drug development together with patients"

Phases of the trial and its objectives*

Clinical trials usually proceed in three steps.

Phase I

- **In a small number of healthy adults**, the dosage of " candidate for medicine" will be increased little by little from a very small amount to investigate its safety.
- By measuring the amount of "candidate for medicine" present in blood, urine, etc., we also examine how quickly it is absorbed into the body and how long it takes to be excreted from the body.

Phase II

- **For a relatively small number of patients** who are expected to be effective as a "candidate for medicine", we will examine what kind of effect it exerts depending on the degree of disease (efficacy), how many side effects it has (safety), and how it should be used (dosage, interval, duration, etc.).
- When examining the effect and usage, several dosages are usually used to compare, but a placebo is commonly added at that time. If there is a standard medicine currently in use, it may be compared with it.

Phase III

- **For a large number of patients**, the efficacy, safety, and usage of the " candidate for medicine" obtained from the results of the phase II study will be finally confirmed.
- The method of confirmation is mainly to compare the standard medicine currently used, if there is one, and to the placebo when there is no standard medicine.
- Apart from this, we may also examine the effectiveness and safety of long-term use.

After completing the three steps, the pharmaceutical company developing medicine compiles all the data and applies to the Ministry of Health, Labour and Welfare to approve it as Medicine. Only by passing the strict inspection of the Ministry of Health, Labor and Welfare and being approved can a "candidate for medicine" become a "medicine".

*Quote source: Japan Pharmaceutical Manufacturers Association website "Three steps of clinical trials"

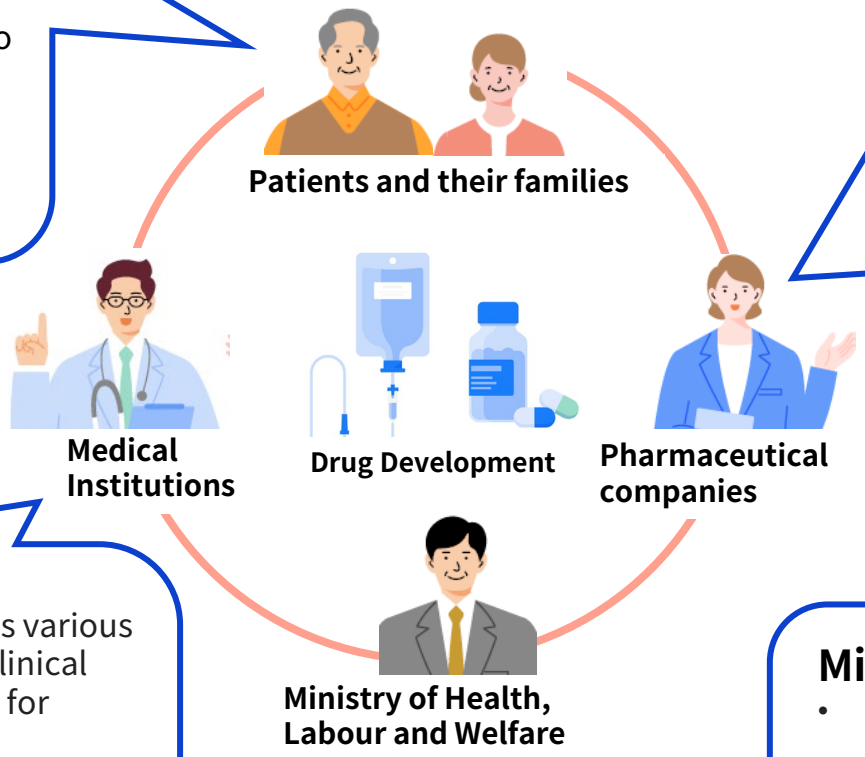
The role of people involved in clinical trials

Patients participating in clinical trials

- Understand the contents of the "Informed consent form", come to the clinic according to the schedule, undergo examinations, and use the "Candidate for Medicine" correctly.
- If there is any change in your physical condition, report it to your doctor.

Pharmaceutical companies

- In order to confirm that the human rights of those who participated in the clinical trial are being protected, that the clinical trial is being conducted in the correct procedures, and that no side effects have occurred, we will directly check the medical records of those who participated in the clinical trial and meet with the person in charge of the medical institution.
- It is also responsible for reporting the latest information to medical institutions and the Ministry of Health, Labour and Welfare.



Medical Institutions

- The doctor in charge of the clinical trial provides various explanations to those who participated in the clinical trial, confirms safety, and evaluates candidates for medicine.
- If any side effects occur in the participants, we will provide the best treatment.
- There are doctors, nurses, pharmacists, and other staff and clinical trial coordinators (CRCs).
- The study will report the status of the study to the Institutional Review Board and be reviewed to see if the study can be continued.

Ministry of Health, Labour and Welfare

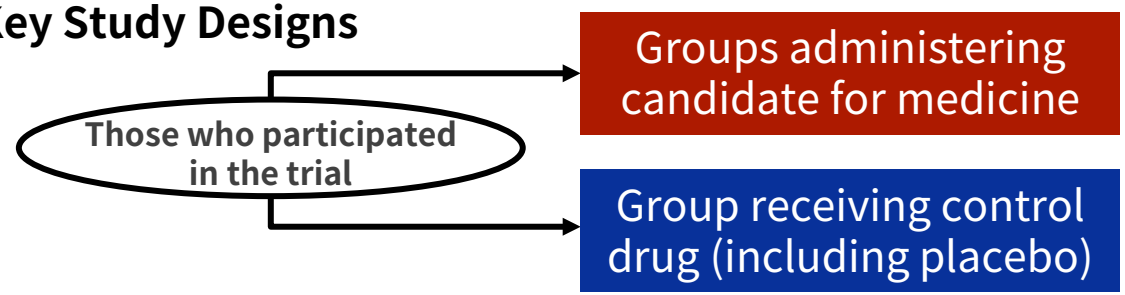
- When we receive new information or changes to plans related to " Candidate for Medicine " from companies, we will review them from time to time and, if necessary, provide appropriate instructions such as terminating the study, revising the study protocol, or adding additional tests.

*Quote source: Chugai Pharmaceutical website "Drug development together with patients"

Clinical Trial Protocol

- **What is a clinical protocol?**
  - **Patients who are eligible for the trial**
  - **Amount of candidate for medicine and number of uses**
  - **It is a document created by a pharmaceutical company that describes the type and number of tests required to assess safety and efficacy.**
- **What are the key points when creating a clinical protocol?**
  - **We consider whether the safety of the participants in the trial is ensured, whether the burden is minimized, and how data is collected to confirm the characteristics of the investigational drug.**

Key Study Designs



In comparative trials of “candidate for medicine", it is often used to prevent patients and doctors who are conducting the trial from knowing whether a "drug candidate", a placebo, or a standard "medicine" is used. This is to objectively evaluate the Efficacy and safety of the medicine without preconceived notions*.

Example of confirming the characteristics of "candidate for medicine" (evaluation method)

Example (1) Cancer: Percentage of patients with complete cancer disappearance
→ to evaluate efficacy

Example (2) When side effects from " candidate for medicine " appear, strength
→ to assess safety

Example (3) Pharmacokinetics of " candidate for medicine "
→To be useful for subsequent clinical trial planning and conduct

*Quote source: Japan Pharmaceutical Manufacturers Association website "Medicine" and "clinical trials"

Informed Consent Form

It is the most important document for patients to decide whether to participate in a clinical trial or not of their own free will. The benefits of participating in the trial, the risks of the investigational drug, and the schedule of the study are described, and the doctor explains the study using the Informed Consent Form.

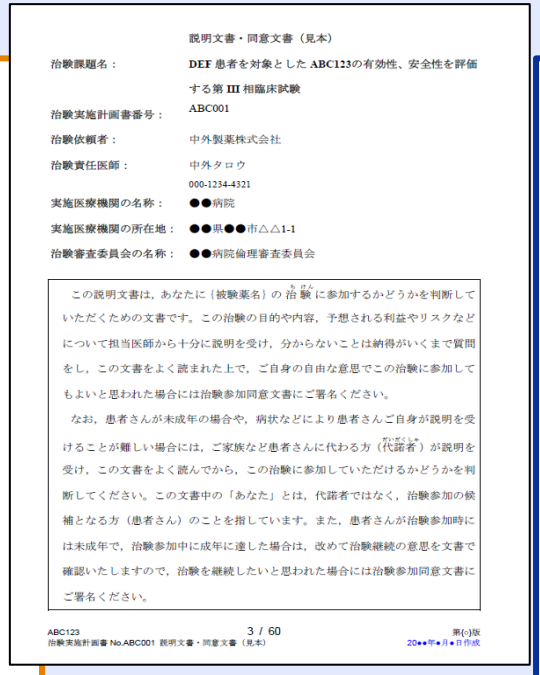
Structure of the Informed Consent Form

Trial Description

1. Overview of the clinical trial
- What is a clinical trial?
- Overview of the Investigational drug
- Expected Benefits and Risks
- Clinical trial flow
- Cost of the trial

2. Details of the clinical trial
- What I want you to protect
- Trial Targets patients
- Trial Withdrawal
- What to do in the event of a health hazard
- Risks from investigational drugs and tests

3. Clinical trial schedule



説明文書・同意文書（見本）

治験課題名： DEF 患者を対象とした ABC123の有効性、安全性を評価する第 III 相臨床試験

治験実施計画書番号： ABC001

治験依頼者： 中外製薬株式会社

治験責任医師： 中外タロウ 000-1234-4321

実施医療機関の名称： ●●病院

実施医療機関の所在地： ●●県●●市△△1-1

治験審査委員会の名称： ●●病院倫理審査委員会

この説明文書は，あなたに｛被験薬名｝の治験に参加するかどうかを判断していただくための文書です。この治験の目的や内容，予想される利益やリスクなどについて担当医師から十分に説明を受け，分からないことは納得がいくまで質問をし，この文書をよく読まれた上で，ご自身の自由な意思でこの治験に参加してもよいと思われた場合には治験参加同意文書にご署名ください。

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ABC123 治験実施計画書 No.ABC001 説明文書・同意文書（見本） 3 / 60 第(○)版 20●●年●月●日作成

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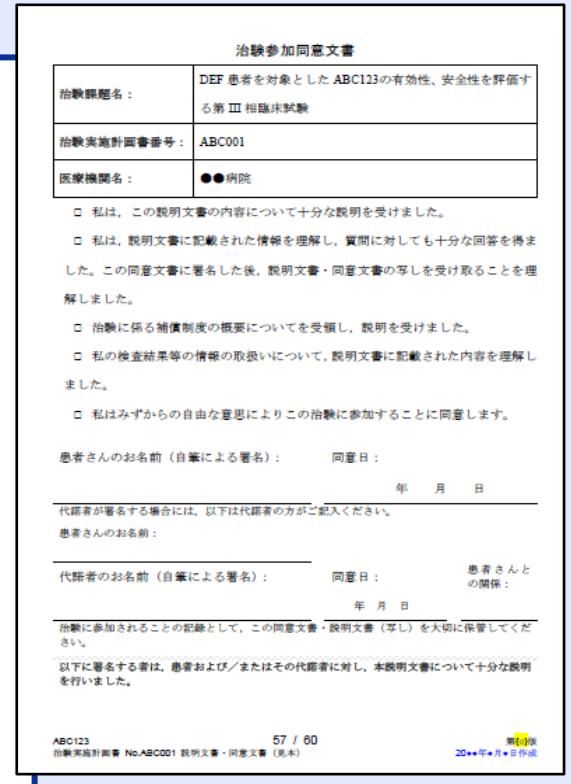
Consent Verification

1. Agreement/Confirmation
- Understanding of the content of the explanation
- Opportunity for questions and answers
- Provision of other necessary materials
- Voluntary consent

2. Participant's signature
(Consent of the Representative if necessary)

3. Signature of the doctor explaining the explanatory document



治験参加同意文書

治験課題名：	DEF 患者を対象とした ABC123の有効性、安全性を評価する第 III 相臨床試験
治験実施計画書番号：	ABC001
医療機関名：	●●病院

□ 私は，この説明文書の内容について十分な説明を受けました。

□ 私は，説明文書に記載された情報を理解し，質問に対しても十分な回答を得ました。この同意文書に署名した後，説明文書・同意文書の写しを受け取ることを理解しました。

□ 治験に係る補償制度の概要についてを受領し，説明を受けました。

□ 私の検査結果等の情報の取扱いについて，説明文書に記載された内容を理解しました。

□ 私はみずからの自由な意思によりこの治験に参加することに同意します。

患者さんのお名前（自筆による署名）： 同意日： 年 月 日

代諾者が署名する場合には，以下は代諾者の方がご記入ください。

患者さんのお名前：

代諾者のお名前（自筆による署名）： 同意日： 年 月 日 患者さんとの関係：

治験に参加されることの記録として，この同意文書・説明文書（写し）を大切に保管してください。

以下に署名する者は，患者および／またはその代諾者に対し，本説明文書について十分な説明を行いました。

ABC123 治験実施計画書 No.ABC001 説明文書・同意文書（見本） 57 / 60 第(○)版 20●●年●月●日作成

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Conditions for those who participate in the clinical trial

In order to verify the effectiveness of the "candidate for medicine" and ensure the safety of those who participate, the criteria for participating people are set for each clinical trial, and the doctor in charge will ultimately determine whether they can participate in the clinical trial.

In general, those who fall under the following conditions can participate

- Those who have been diagnosed with a disease that is eligible for "candidate for medicine"
- Those who are judged by a doctor to be able to comply with the trial schedule

In general, those who fall under the following conditions are not eligible to participate.

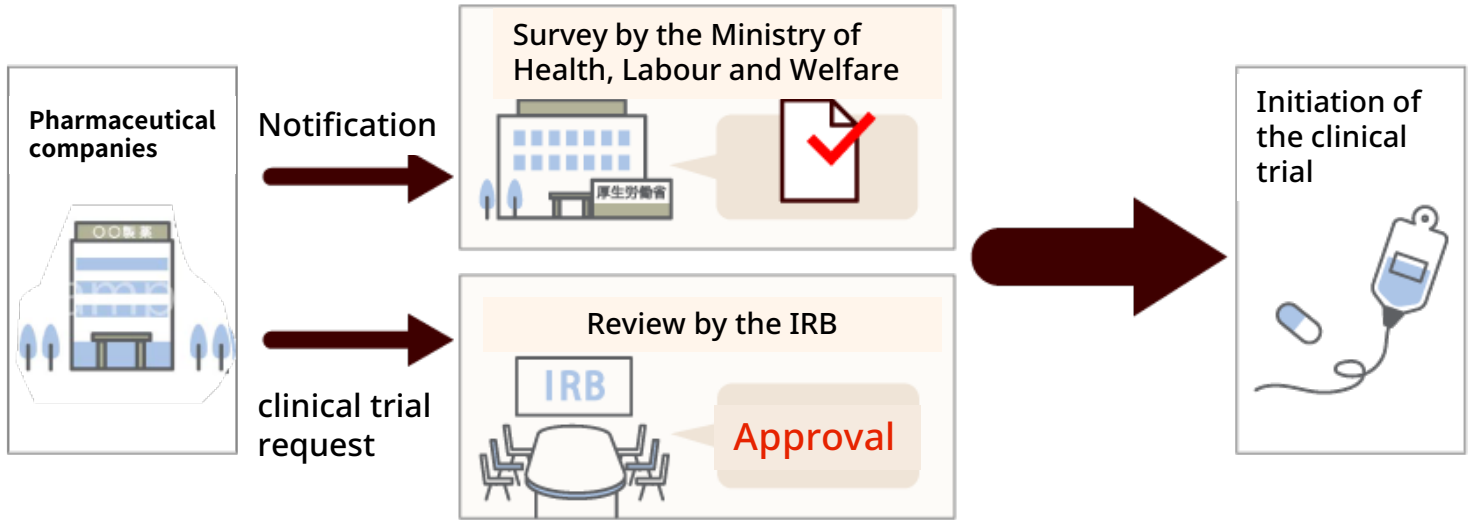
- Those who use drugs that have same mode of action as “candidate for medicine"
- Those who have serious myocardial infarction, arrhythmia, lung disease, or suspected infection
- Breastfeeding and pregnant (including those who wish)
  - ✓ If the "candidate for medicine" may affect reproductive function or fetus

Review of clinical trial plans

The Ministry of Health, Labour and Welfare and the medical institution conducting the clinical trial will deliberate on the "clinical trial protocol" and “informed consent form", respectively.

① The Ministry of Health, Labour and Welfare conducts preliminary investigations based on clinical trial protocols and other information submitted by pharmaceutical companies from the perspectives of "clinical trial rules," "whether the human rights and safety of participants in clinical trials are being protected," and "whether they are scientifically valid."

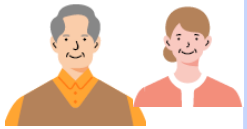
② The medical institution will ask the Institutional Review Board (IRB) to review whether or not to conduct a clinical trial. The Institutional Review Board will review whether it is appropriate to conduct the clinical trial, whether it is ethically and scientifically safe for the person participating in the clinical trial, and whether there are any disadvantages.



General flow when participating in a clinical trial

Clinical trials are generally conducted in the following steps:

Duration of investigational drug administration

	Explanation and Informed consent	Screening Tests	Start of investigational drug administration	Examination and administration	Follow-up
 **To the patient Cooperation**	After listening to the explanation of the clinical trial, **you will be asked to decide to participate of your own free will.** **You can also stop participating at any time after participating in the trial.**	**After you agree to participate in the trial,** you will be asked to undergo any necessary tests and investigations **before participating in the study.**	**Patients who meet the conditions in the screening test** is enrolled in the trial After that, the investigational drug will be started.	You will be asked to undergo tests and investigational drug administration **according to the schedule set by the protocol.**	Even after the investigational drug is administered, you will be **asked to check on any changes in your physical condition** through phone confirmation and visits.
			evaluation		
 **In a medical institution to be implemented**	It explains the purpose and content of the trial, as well as the expected benefits and risks.	Tests and survey results **will determine whether a patient is suitable for participation in the trial.**	• We will review and evaluate the following: ✓ The effect of the investigational drug (evaluated by the treating physician based on the test results, etc.)) ✓ Changes in physical condition		

Disclosure of information on clinical trials

You can check information and results of clinical trials in the following ways:

- **Clinical trial information registration site** (click on the icon to open each website)

Site Name	explanation	QR code	Reference materials
jRCT Japan Registry of Clinical Trials	• A public site where you can find information on clinical trials (including corporate trials) and clinical research in general in Japan. • Companies and researchers conducting clinical trials and clinical studies are required to post trial information in jRCTs, which cover domestic clinical trial and clinical research information.		How to find a clinical trial ~The way of jRCT~ (Prepared by the Japan Pharmaceutical Manufacturers Association)
ClinicalTrials.gov Clinical Trials.dot Gab	• English notation • Public sites where you can find clinical trials that are mainly conducted in the United States		Mikata of ClinicalTrials.gov (Prepared by the American Association of Research and Pharmaceutical Industries)
☆ Please refer to other information sites as they are also listed on the "Pharmaceutical Association website" and "Introduction of information sites other than jRCT".			

- **Academic Papers and Conferences**
- **Pharmaceutical companies (official websites of each company)**

*Quote source: Japan Pharmaceutical Manufacturers Association website "Clinical trial information site" "How to find a clinical trial ~jRCT method~"

table of contents

Situations where you want to collaborate with patients in drug development

We think of patients and their families as "part of a team" in drug development. Your opinions are very valuable information in drug development.

[What we would like to hear]
・From "the life/thoughts of patients and their families"
Opinions on evaluation items and evaluation methods in clinical trials

[What we would like to hear]
・What did you feel while participating in the clinical trial?
・What do you want to improve?

Listening to the experiences of patients and their families

Preparation of clinical protocol / Informed Consent Form

Conducting and administering clinical trials

Disclosure of clinical trial results Post-approval response

[What we would like to hear]
・Is it a test that is usually conducted?
・Is the schedule available for participation compared to daily medical treatment?
・What are the concerns about dealing with side effects and emergency systems?
・Do you feel uncomfortable with the conditions for participating?
・Is the informed consent form understandable?

[What we would like to hear]
・What kind of content and how do you want to know the results of the clinical trial?

How to collaborate with patients

We take appropriate methods according to the content and purpose of the collaboration, and listen to the opinions of patients and their families throughout the trial period.

Face-to-face/web interview between the Person in charge of development and the patient

- Ask for your opinion on the trial plan during the preparation stage of the clinical trial
- Regardless of whether the trial is conducted, we ask for patients' experiences and opinions on the disease and treatment

Confirmation of materials by the patient and meeting between the person in charge of development and the patient

- Ask for your opinion on the text of the materials that convey the results of clinical trials in easy-to-understand language to patients.

Listening to the experiences of patients and their families → **Preparation of clinical protocol / Informed Consent Form** → **Conducting and administering clinical trials** → **Disclosure of clinical trial results Post-approval response**

Conducting Questionnaires

- Ask patients who participated in the trial for their opinions on "problems during participation in the study" and "materials for patients to be used during the study and their contents" (during and after the study).

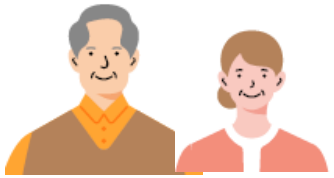
Awareness in collaboration with patients (1)

What are patients paying attention to in their daily lives?

Chugai drug development personnel listened to current treatments and opinions on diseases from patients with a certain disease, and worked to utilize them in the development of " candidate for medicine ".

Chugai drug development personnel

< Question to patients>
What has been the most concerning side effect during your treatments so far?



Patients

< Patient's opinions>
I'm concerned about the swelling of my face, but I want to **avoid going out as much as possible because there is a risk of worsening symptoms due to "sun exposure".**

Chugai drug development personnel

< What I noticed after listening to the voices of patients >
Not only the side effects, but also the fact that they are exposed to sunlight in their daily lives. We will consider reducing the number of visits to the hospital and making use of it in the clinical trial plan!

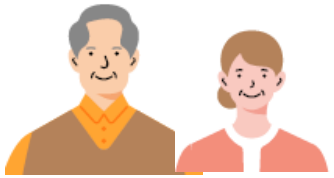
Awareness in collaboration with patients (2)

What is the goal of treatment for the patient?

Chugai drug development personnel listened to current treatments and opinions on diseases from patients with a certain disease, and worked to utilize them in the development of " candidate for medicine ".

Chugai drug development personnel

< Question to patients>
What do you expect from the treatment plan with Drug B?



Patients

< what patients value >
I primarily expect pain relief. Therefore, even if there is a possibility of side effects, I would like to use a dosage that is effective.

Chugai drug development personnel

< What I noticed after listening to the voices of patients >
It seems necessary to investigate what kind of symptoms patients are experiencing by each dose of treatment B in the clinical trial data and share it with patients!

Supplementary Information

Protection of personal information of those participating in clinical trials

Protecting Information

- Clinical trials have implemented a number of safety measures to protect the privacy of study participants in accordance with laws that set out applicable privacy protections and rules to be followed when conducting clinical trials.
- To ensure the confidentiality of study participants' medical and personal information, study data and specimens collected from study participants (e.g., blood) are assigned unique numbers.

Use and Sharing of Information

- Chugai Pharmaceutical and others may analyze uniquely numbered clinical trial data and use it for research purposes. It may also be shared with independent researchers and government agencies.
- In addition, the results of this trial may be published in medical journals or presented at academic conferences, but no trial participants will be identified.

Supplementary Information

Explanation of terms (1/2)

The glossary* used in this document is shown in the table below.

term	explanation
Non-clinical trials	It is a test that collects necessary data such as the efficacy, safety, and pharmacokinetics of a drug using cells or animals, not on humans. The results of this trial will be important information for clinical trials.
Clinical Trials	A clinical trial is a test that examines the efficacy and safety of a drug in humans.
Approval Application	This is an application to obtain permission to manufacture and sell as a drug. In order to obtain approval, we submit information related to development, such as non-clinical trials (effects and toxicity in cells and animals), clinical trials, and manufacturing methods, to the Ministry of Health, Labour and Welfare for review.
Investigational drug	This is a drug used in clinical trials. There are drugs to be developed and drugs to be used as comparisons and contrasts, or placebos (fake drugs). ***In this document, the term "candidate for medicine" is used to indicate the drug to be developed in clinical trials.**
Placebo	Although it does not contain the ingredients of the drug to be evaluated, it is made exactly the same as the drug to be evaluated in terms of appearance, such as color, shape, and size. It is also called a fake drug. This is a comparison to evaluate the efficacy and safety of the investigational drug.
Adverse events	It refers to any undesirable symptoms, signs, diseases, etc. that occur when using a drug, regardless of whether it is caused by investigational drug or not.

*Quote source: Chugai Pharmaceutical website "Patients and the general public – glossary"

Supplementary Information

Explanation of terms (2/2)

The glossary* used in this document is shown in the table below.

term	explanation
Side effect	It is an undesirable reaction that occurs due to the use of investigational drugs. There are acute side effects (such as allergic reactions) and chronic side effects from long-term use. The GCP (Standards for the Conduct of Safety Studies for Pharmaceuticals) defines adverse events that cannot be denied as adverse events with a causal relationship with investigational drug.
GCP	Good Clinical Practice: Standards for conducting clinical trials of pharmaceutical products. It is a law that respects the human rights of those who participate in clinical trials and stipulates that clinical trials on humans must be conducted scientifically. All pharmaceutical companies, medical institutions, etc. involved in clinical trials must follow this.
Institutional Review Board（IRB）	This committee examines the protection of human rights and safety of people participating in clinical trials, as well as whether the tests are scientifically valid and whether there are any problems with the contents. The members of the review committee must include not only medical personnel, but also people who have no interest in the hospital and people other than medical and pharmaceutical experts.
Pharmacokinetics	It refers to the way drugs enter the body, appear in the blood, and leave the body. When a drug is absorbed into the body, some of it is broken down and eventually excreted. We investigate the process, route, time, etc., and use it for efficacy and safety information.
Declaration of Helsinki	Ethical principles for medical research involving human beings, adopted at the World Medical Association General Assembly in 1964.
Drugs and Medical Devices Act	Act on Ensuring the Quality, Efficacy, and Safety of Pharmaceuticals, Medical Devices, etc. In addition to ensuring the quality, efficacy, and safety of pharmaceuticals and medical devices as determined by the national government (Ministry of Health, Labour and Welfare), the law stipulates manufacturing, labeling, sales, distribution, advertising, etc.

*Quote source: Chugai Pharmaceutical website "Patients and the general public – glossary"

INNOVATION BEYOND IMAGINATION

CHUGAI PHARMACEUTICAL

Roche A member of the Roche group