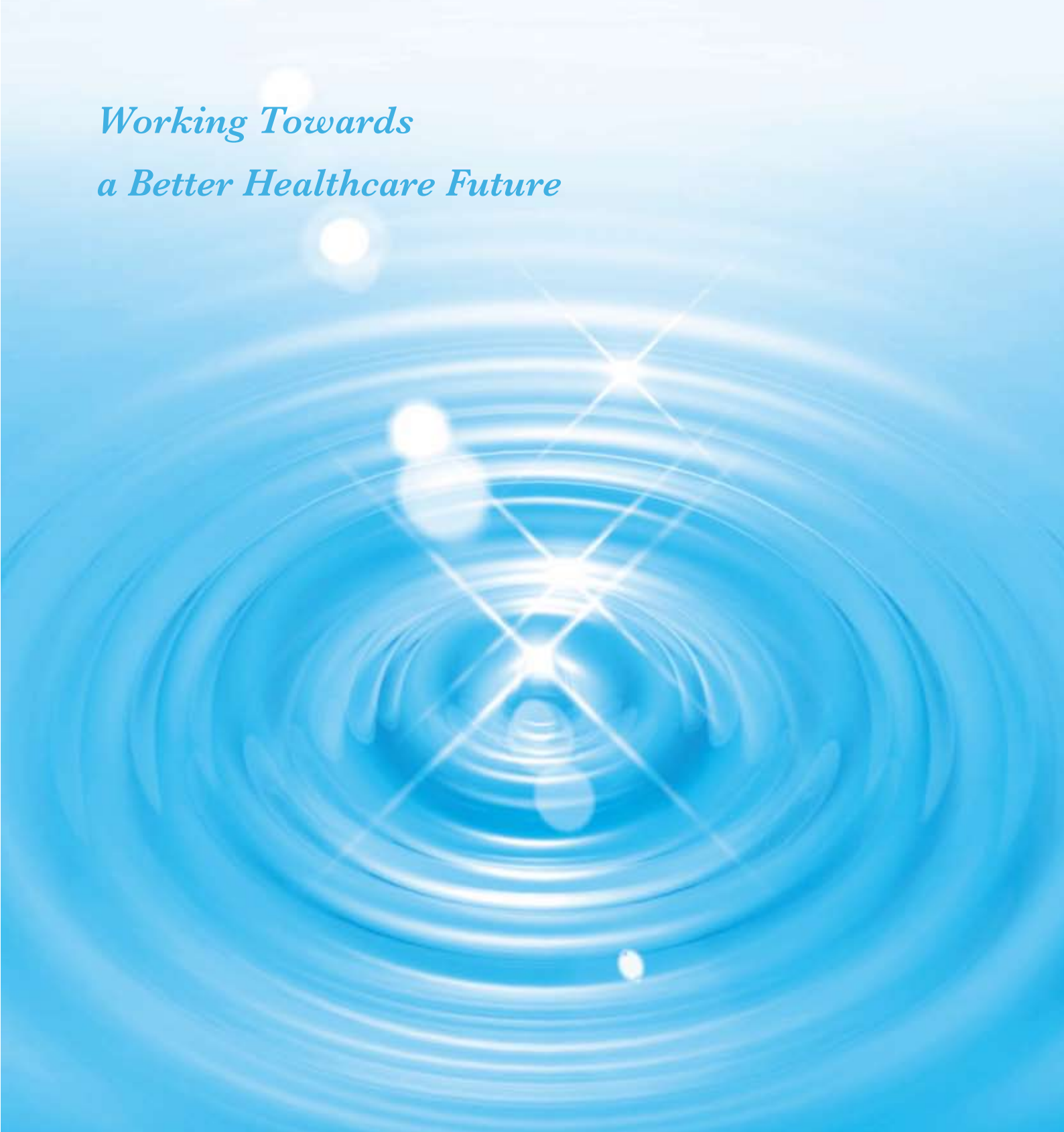




The Japan Medical Association

# Center for Clinical Trials

*Working Towards  
a Better Healthcare Future*



# Table of Contents

- JMACCT's business outline ..... 3
- Investigator-initiated clinical trials (IITs)
  - Current situation of IITs (What is an IIT?/ Implementation Structure/ Achievements/ Implementation Process) ..... 4
  - Outline of JMACCT's support (Data management/ Handling of safety data/ Preparation of Clinical Trial Notification) ..... 6
- Clinical trials networks
  - Massive Network for Clinical Trials (MNCT) ..... 8
  - Regional clinical trials networks ..... 10
- Dissemination of clinical trial information and provision of educational support ..... 12
- Project for Promoting Clinical Research for New Medicine ... 13
- Clinical trial registration and disclosure of the results ..... 13
- Contribution to the New 5 Yearly Clinical Trial Activation Plan ... 14
- Organizational information ..... 15

# Contributing to improving the infrastructure for clinical trials in Japan

The Japan Medical Association Center for Clinical Trials (JMACCT) conducts Large Scale Clinical Trial Network Project subsidized by the Ministry of Health, Labour and Welfare (MHLW) and supported by Health and Labour Sciences Research Grants.

## Objectives of Large Scale Clinical Trial Network Project

Large Scale Clinical Trial Network Project is designed to:

- Contribute to the development of innovative drugs and other medical products by improving the environment for clinical trials in Japan and by establishing a system that enables the smooth conduct of high-quality clinical trials
- Contribute to the advancement of health and welfare related measures by conducting Large Scale Clinical Trial Network Project and Program for Promoting Large Scale Clinical Trial Network Project

## Outline of the Project



### Revitalization of clinical trials in Japan



#### Large Scale Clinical Trial Network Project

- Supporting investigator-initiated clinical trials
- Promoting regional clinical trials networks

Aims of this project are: to organize medical institutions into a clinical trials network in order to expeditiously provide the public with medically necessary or innovative drugs and medical devices; and to conduct model clinical trials to improve the infrastructure for clinical trials.

#### Promotion of Large Scale Clinical Trial Network Project

- Organizing / managing a nation-wide network of clinical sites (MNCT: Massive Network for Clinical Trials)
- Supporting coordination among leading sites (i.e., core research centers / major trial institutions designated by MHLW)
- Implementing education projects to disseminate clinical trial knowledge

The promotion activities include management and maintenance of the Japan Medical Association Center for Clinical Trials, management of MNCT and other services related to the conduct of clinical trials and regulatory submissions.



JMACCT also conducts the promotion project of Clinical Research for New Medicine subsidized by MHLW, by providing support for researchers who are funded by this project.

Brief history	Aug.	FY2003	FY2004	FY2005	FY2006
IIT	Establishment of JMACCT	3 trial grants awarded	5 trial grants awarded	4 trial grants awarded	Fentanyl citrate filed for approval H5N1 influenza vaccine filed for approval
CT network		Started development of MNCT	Grant awarded to 10 CT networks	Grant awarded to 4 CT networks	Grant awarded to 8 CT networks
Dissemination			Industry-Government-Academia Joint Forum for Clinical Trial Promotion Distribution of educational posters	Symposium for Clinical Trial Promotion Distribution of educational DVDs and videos	Symposium for Clinical Trial Activation 'Rinsho shiken no ABC (The ABC's of Clinical Trials)' (extra number of 'The Journal of The Japan Medical Association') published
Other			Started providing DM services Launched a safety information management system	Launched a Web site for clinical trial registration and disclosure	Clinical Research on Pediatric Diseases (Current Project: Clinical Research for New Medicine)

# To help provide patients with new drugs sooner

## Investigator-initiated clinical trials

After the 2003 amendment to the Japanese Pharmaceutical Affairs Law (PAL), clinician investigators have become able to plan and conduct a clinical trial under the Clinical Trial Notification (CTN).

JMACCT supports investigator-initiated clinical trials through several grant schemes subsidized by MHLW. Specifically, the grant program is designed to accelerate clinical development of high priority drugs/medical devices recommended by the member societies of the Japanese Association of Medical Sciences (JAMS) that are:

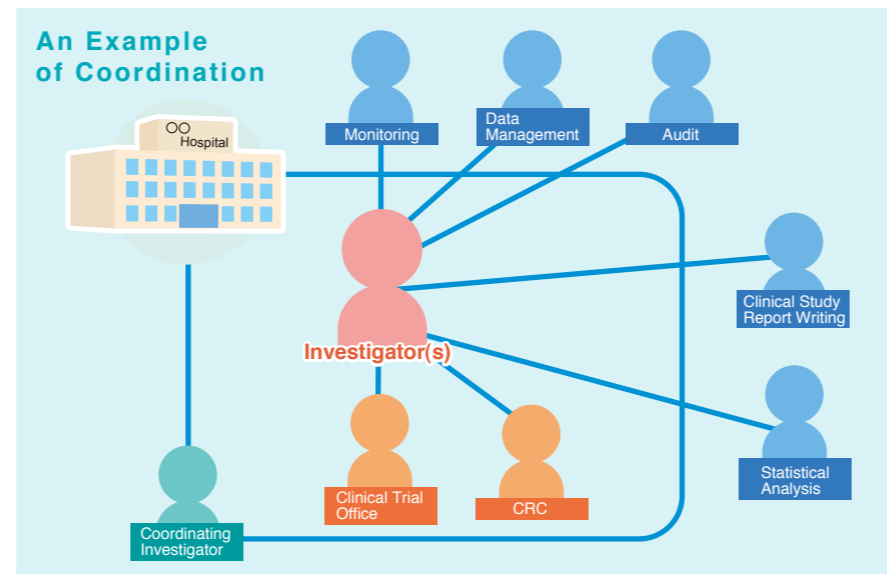
- Widely used as standard treatment in the US or Europe but not yet approved in Japan.
- Already marketed in Japan and commonly used for off-label indications.

JMACCT's support focuses on urgently needed new drugs or existing drugs with new indications for which regulatory approval is not being pursued due to a lack of financial incentives.



## Implementation Structure

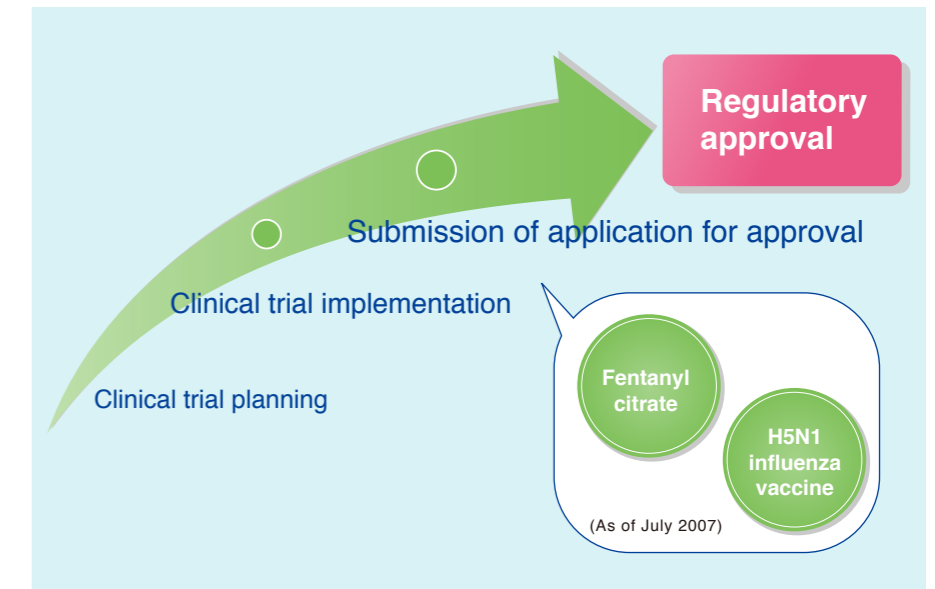
A sponsor-investigator (clinician) alone can never conduct an investigator-initiated clinical trial. As described below, in order to perform a successful clinical trial, it is essential for an investigator and other specialists in different areas to work closely as a team and perform to the best of their expertise.



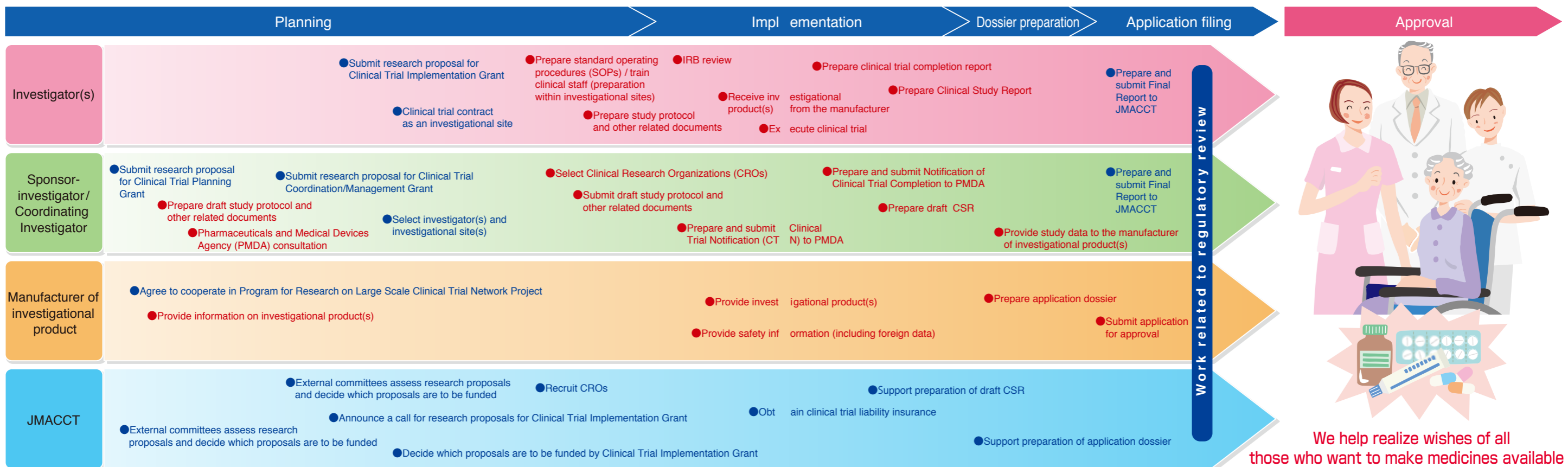
## Achievements

A list of awarded researches and up-to-date information on research progress is provided on our Web site.

<URL>  
<http://www.jmacct.med.or.jp/ct/subject.html>



## Implementation Process



We help realize wishes of all those who want to make medicines available to the patients as fast as possible.

●Process of investigator-initiated clinical trials ●Process of Large Scale Clinical Trial Network Project

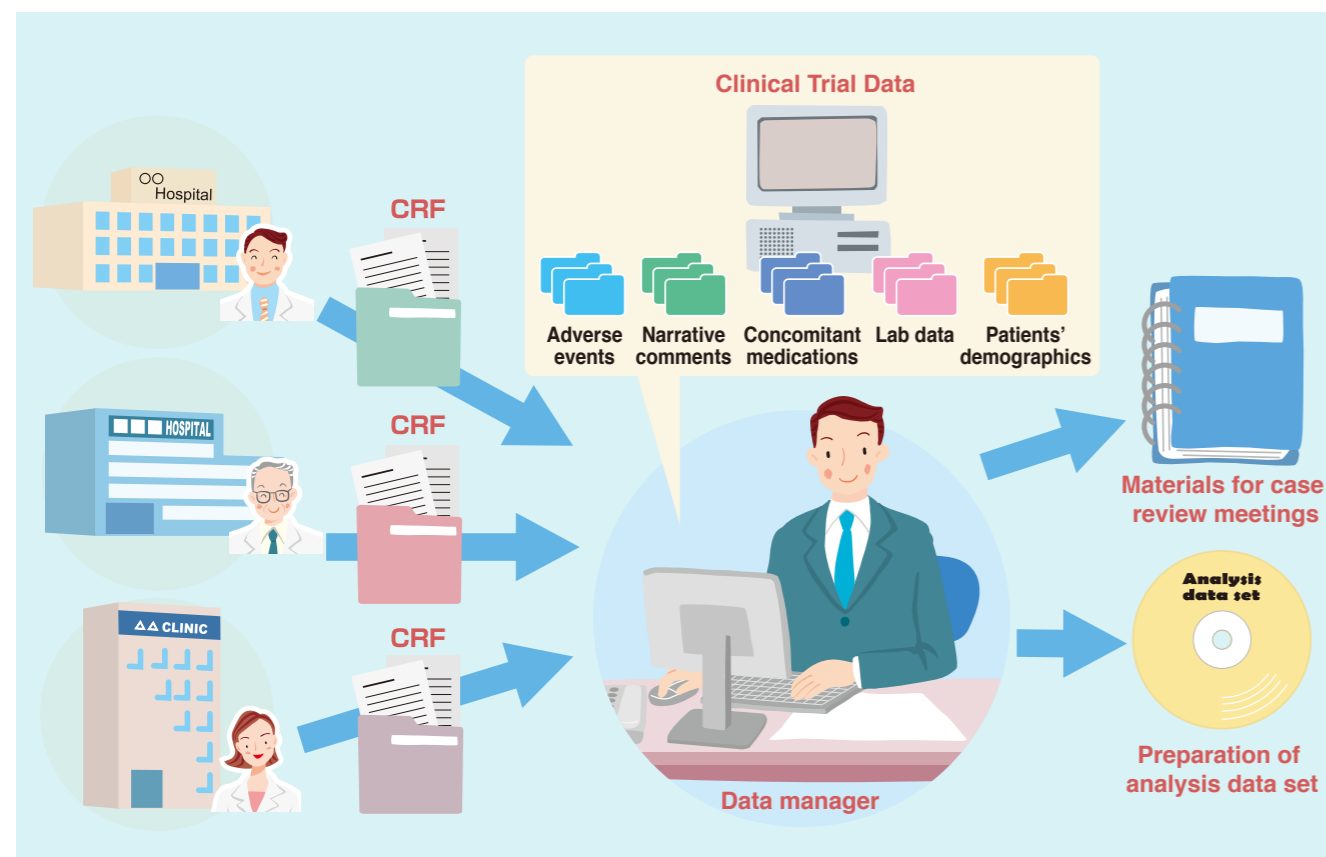
# To help provide patients with new drugs sooner

## ● More efficient data management

The proper management of data is crucial to the accurate assessment of the efficacy and safety of the investigational products. Since sponsor-investigators are required to control and assure the quality of data generated from their clinical trials, JMACCT provides the following services in support of data management:

- Support for draft Case Report Form (CRF) preparation
- Data center management
- Preparation of data management plan
- Storage and management of CRFs and related documents
- Database management
  - Study progress management
  - Security management
  - Data coding
  - Electronic Data Capture (EDC) system development
  - Data input and cleaning
  - Preparation of analysis data set
- Logical check on the data and query generation
- Preparation of materials for case review meetings
- Support for CSR preparation

The focus of JMACCT's data management services includes providing support for physician / CRCs (e.g., consultation on data handling, workshops, etc.) as well as providing objective and statistical supervision. These services facilitate gaining a fuller perspective of the clinical trial, contribute to reducing the number of inquiries from study monitors and enable proper monitoring of the trial, thereby improving the quality of data and reducing the cost and time associated with processing clinical trial data.



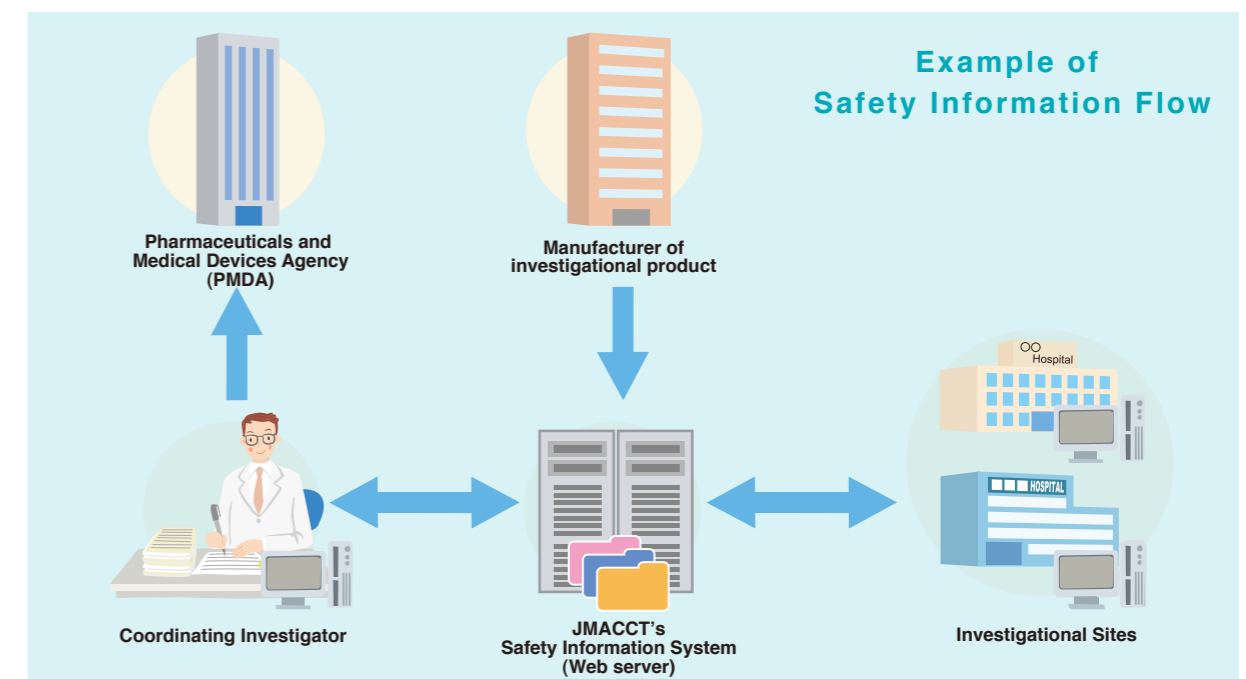
## ● Handling of safety data (Safety Information System)

Serious adverse events (SAEs) reported during clinical trials, foreign adverse event reports, literature/research reports and reports on foreign regulatory actions must be reviewed and determined, within the limited timeframe, whether they are to be reported to PMDA, and relevant reports must be prepared and submitted if necessary. To fulfill this requirement, it is particularly important for multicenter trials to have an organized system in place, because the views of many investigators need to be harmonized before making a decision.

JMACCT developed a safety information system (Web server) and provides support for the handling of safety information in investigator-initiated clinical trials. Our support includes the following:

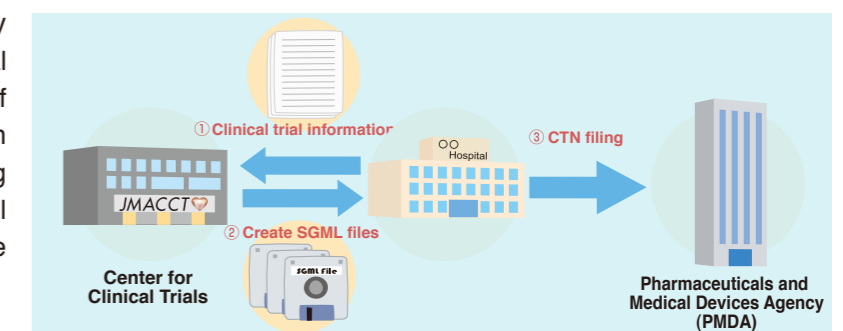
- Management of electronic documents including SAE reports
- Information sharing and exchange of views among medical institutions
- Follow-up of safety information handling
- Maintenance and management of computer networks including safety information system
- Preparation of clinical trial adverse drug reaction (ADR) reports

JMACCT's safety information system and its well-coordinated support ensure accurate and speedy information sharing among investigational sites and appropriate management and storage of safety information throughout the course of investigator-initiated clinical trials.



## ● Preparation of Clinical Trial Notification (SGML processing tools)

For the clinical trials supported by JMACCT, JMACCT prepares Clinical Trial Notification and Notification of Changes in Clinical Trial Protocol in SGML format using SGML processing tools based on the clinical trial information received from study site institutions.





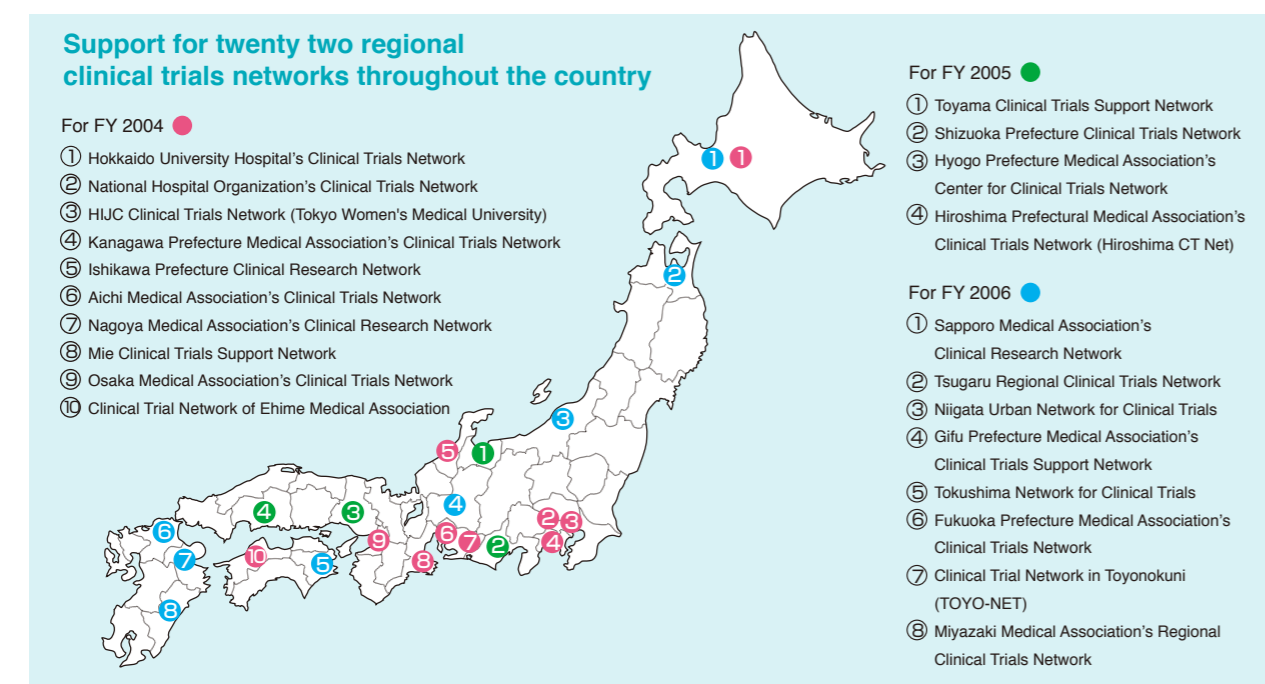
# Improvement of the infrastructure for clinical trials

## Support for regional clinical trials networks

The clinical sites registered with the MNCT have been developing regional clinical trials networks in the areas where they are located.

Since 2004, JMACCT has provided funding for 22 of such clinical trials networks under the MHLW's Project for Research on Establishment of Regional Clinical Trials Networks with the purpose of putting the necessary infrastructure in place, establishing an appropriate framework to perform high-quality clinical trials expeditiously and promoting clinical trials in Japan.

Apart from providing funding, JMACCT's support also includes disseminating information on the efforts made by relatively active clinical trials networks to other networks, promoting networks to pharmaceutical companies and offering forums for the sites registered with the network and corporate sponsors to exchange their views. Through its services, JMACCT will continue to help medical institutions to have more opportunities to participate in company-sponsored clinical trials utilizing their expertise.



## Roles and activities of regional clinical trial networks

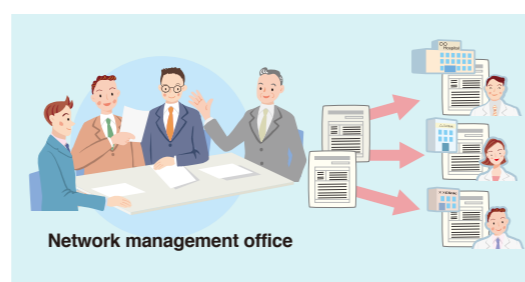
The clinical sites and investigators within a regional clinical trials network work together collaboratively and function as if they were a single institution. This results in a reduced burden on trial sponsors and more efficient and smoother conduct of clinical trials.

At the initiative of their management offices, the clinical trials networks have been making the following efforts.

### For efficient conduct of clinical trials

#### Development and provision of uniform SOPs and forms

Typically each medical institution has its own standard operating procedures (SOPs) and forms, and therefore the sponsor needs to take a case-by-case approach, such as creating different documents that meet the needs of each investigational site. To address this problem, each clinical trials network has uniform SOPs and forms that are used by its member sites, thereby contributing to the efficient conduct of clinical trials.



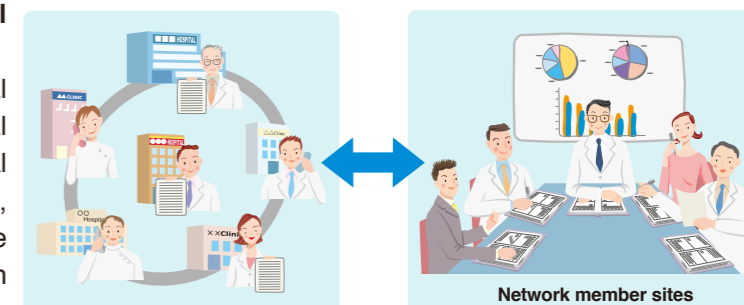
### Providing a single contact point for each clinical trials network

It would be inefficient if the sponsor had to directly contact each medical institution and visit sites one by one to select investigational sites. Instead, the management office of each network serves as a single contact point for study sponsors looking for investigational sites for their clinical trials, allowing for an efficient survey for site selection. Some networks have IT systems in place in order to speed up the exchange of information between the management office and medical institutions.



### Management of cooperative Institutional Review Board (IRB)

It may be difficult for small-sized medical institutions to have their own Institutional Review Board (IRB). To ensure the ethical and scientific conduct of clinical trials, clinical trials networks have cooperative IRBs in place and carry out reviews for such sites.



### Establishing and strengthening a system for clinical trial implementation

#### Establishment of cooperation system in case of emergencies

In some cases, it is difficult for small-sized sites to respond appropriately to the occurrence of unexpected adverse drug reactions by themselves. Therefore, by working in close cooperation with the other network member sites in their areas and having the necessary arrangements for securing the safety of the trial participants, such small sites can prepare themselves for emergencies and adequately conduct clinical trials.

#### Education and training of clinical trial staff

To perform a clinical trial successfully, the staff must maintain extensive up-to-date knowledge of ethical and statutory requirements as well as of medical and scientific information. Not only physicians who conduct clinical trials but all staff involved in the conduct of clinical trials, including CRCs and trial office staff, need to receive education and training. Clinical trials networks offer necessary trainings to the members on a regular basis.



### Provision of clinical trial information

Some clinical trials networks have their own Web sites. In addition to providing trial information for potential trial participants, they promote their network to corporate sponsors through the Web sites. The efforts made by the networks also include other education activities such as distributing brochures and offering open lectures to the public to encourage participation in clinical trials.

# Fostering a broader public understanding of clinical trials

## Dissemination of clinical trial information and provision of educational support

### Dissemination and education

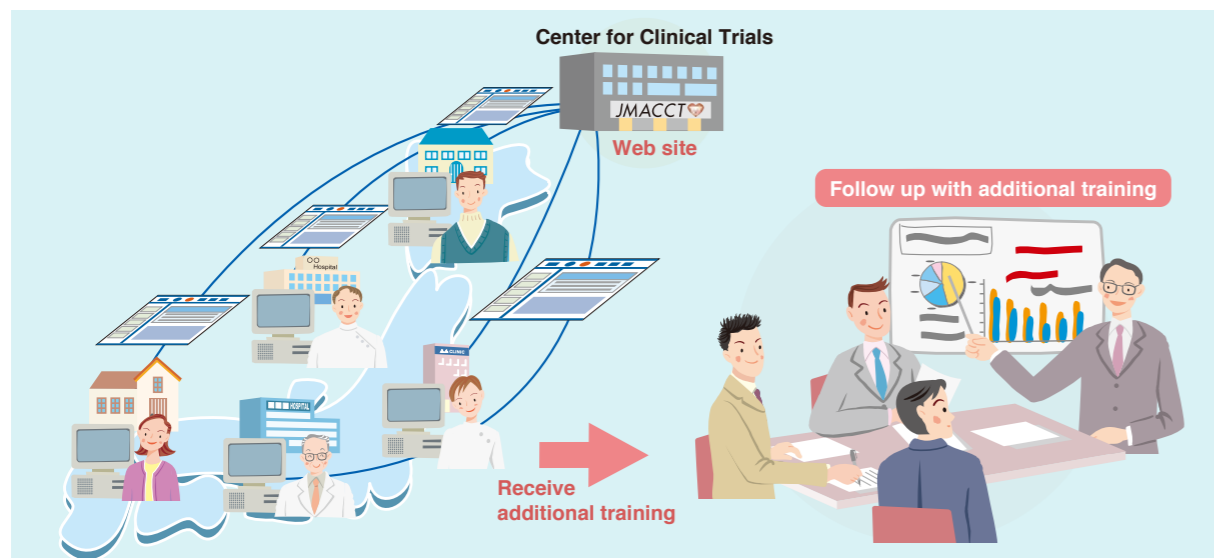
As well as providing educational materials including posters and videos for medical institutions, JMACCT organizes symposiums and seminars for conferences to promote public awareness of clinical trial as part of its dissemination and education efforts.



### E-learning program (expected to start in the second semester of FY 2007)

E-learning offers flexibility and allows users to learn in their own environment and at their own pace and level.

Using e-learning technologies, JMACCT is developing a clinical trial education program that is designed to improve and maintain the quality of clinical trials. This program will provide learning opportunities for all professionals involved in the conduct of clinical trials. All e-learning questions are categorized by subject area (e.g., Clinical Trial/GCP standards, Adverse Events, Statistical Analysis) so that the learners can efficiently gain the knowledge they need, and self-check tests allow the learners to know where their weaknesses are. JMACCT will continue to improve its e-learning program by adding and updating the questions and providing follow-up training and contribute to the development of skilled personnel who are capable of handling problems related to clinical trials.



# Promotion of Clinical Trial

## Project for Promoting Clinical Research for New Medicine

JMACCT runs the following three programs to support researches awarded by Health and Labour Sciences Research Grants and conducted under the MHLW's project of Clinical Research for New Medicine.

<URL> <http://www.jmacct.med.or.jp/pediatric/index.html>

### Program for the invitation of foreign scientists to Japanese institutes

JMACCT invites excellent foreign researchers to Japanese institutes and helps stimulate research cooperation with other countries in order to support the promotion of Clinical Research for New Medicine.

### Program for sending Japanese researchers to overseas institutes

JMACCT sends young researchers with Japanese nationality who reside in Japan to overseas countries. The achievements made in their researches performed at foreign universities or research institutions will contribute to the promotion of Clinical Research for New Medicine.



### Program for dissemination of research results

For the purpose of presenting the results of Clinical Research for New Medicine, JMACCT organizes meetings and workshops for the public and the researchers who conduct researches in the related subject areas. Also, JMACCT provides information on the initiatives taken for the promotion of Clinical Research for New Medicine through brochures and on its Web site, thereby fostering the public understanding of issues in new technologies including the researches conducted under the project of Clinical Research for New Medicine.



## Clinical trial registration and disclosure of the results

To encourage registration of clinical trials and public disclosure of trial results in the effort to improve transparency in clinical trials, JMACCT has developed a web-based clinical trial registry that meets the WHO standards. The registry focuses on investigator-initiated clinical trials of drugs and medical devices; however, it also accepts other types of clinical researches. Trial data can be downloaded in XML format from the Web site.

<URL> <https://dbcentre3.jmacct.med.or.jp/jmacctr/>

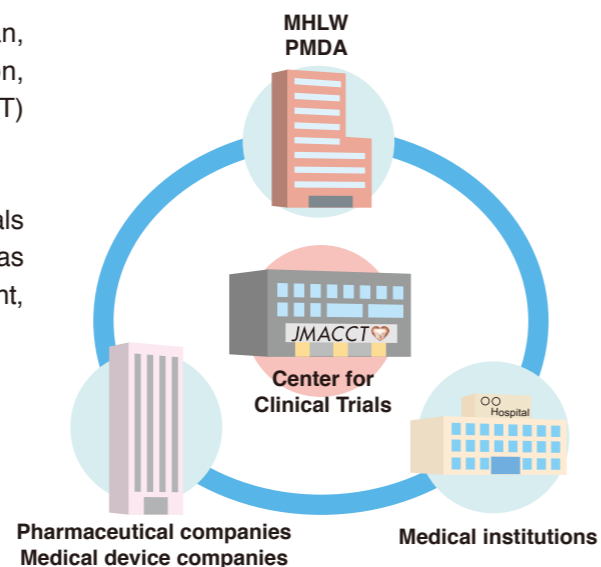


# Further revitalization of clinical trials

## Contribution to the New 5 Yearly Clinical Trial Activation Plan

The New 5 Yearly Clinical Trial Activation Plan, developed jointly by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) and MHLW, has been implemented since FY2007.

JMACCT actively contributes to achieving the goals of the Plan by conducting the following activities as well as by promoting cooperation among government, businesses and medical institutions.

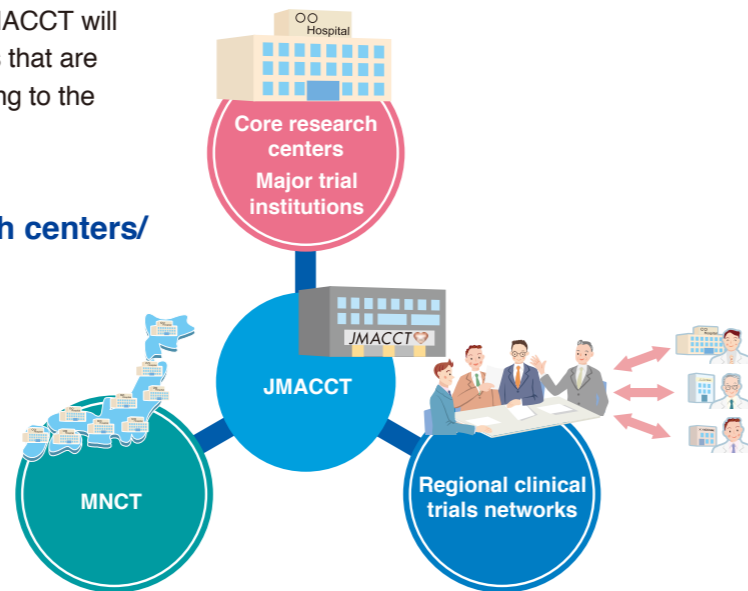


### To ease the burden on sponsors: support for standardization of clinical trial documents

A large amount of documents, such as contractual documents and safety reports, generated during clinical trials are exchanged between companies sponsoring clinical trials and clinical sites. Currently, trial sponsors need to process many different forms that are specific to each individual site. Based on input from both clinical sites and corporate sponsors, JMACCT will prepare and propose templates of documents that are necessary for clinical trials, thereby contributing to the efficient conduct of clinical trials.

### Cooperation between core research centers/major trial institutions and MNCT/regional clinical trials networks

JMACCT supports cooperation between core research centers/major trial institutions and MNCT/regional clinical trials networks.



### Support for core research centers and major trial institutions

#### Promotion of cooperation among core research centers and major trial institutions

The main features of the New 5 Yearly Clinical Trial Activation Plan include 'core research centers' and 'major trial institutions.' Designated medical institutions will take initiatives in improving the framework and infrastructure for clinical trials and clinical researches. JMACCT will provide core research centers and major trial institutions with necessary support for effective cooperation and communication and strive to stimulate clinical trials in the nation.

#### Support for training conducted by core research centers and major trial institutions

With the constant advancement of science, relevant laws and regulations are often revised and updated. For the conduct of clinical trials/researches for medical products that are the fruits of medical and pharmaceutical progress, it is essential to be alert and updated with the latest developments in the related fields. JMACCT provides supports for necessary training conducted by medical institutions.

## Organizational information

### Organization name

Japan Medical Association Center for Clinical Trials



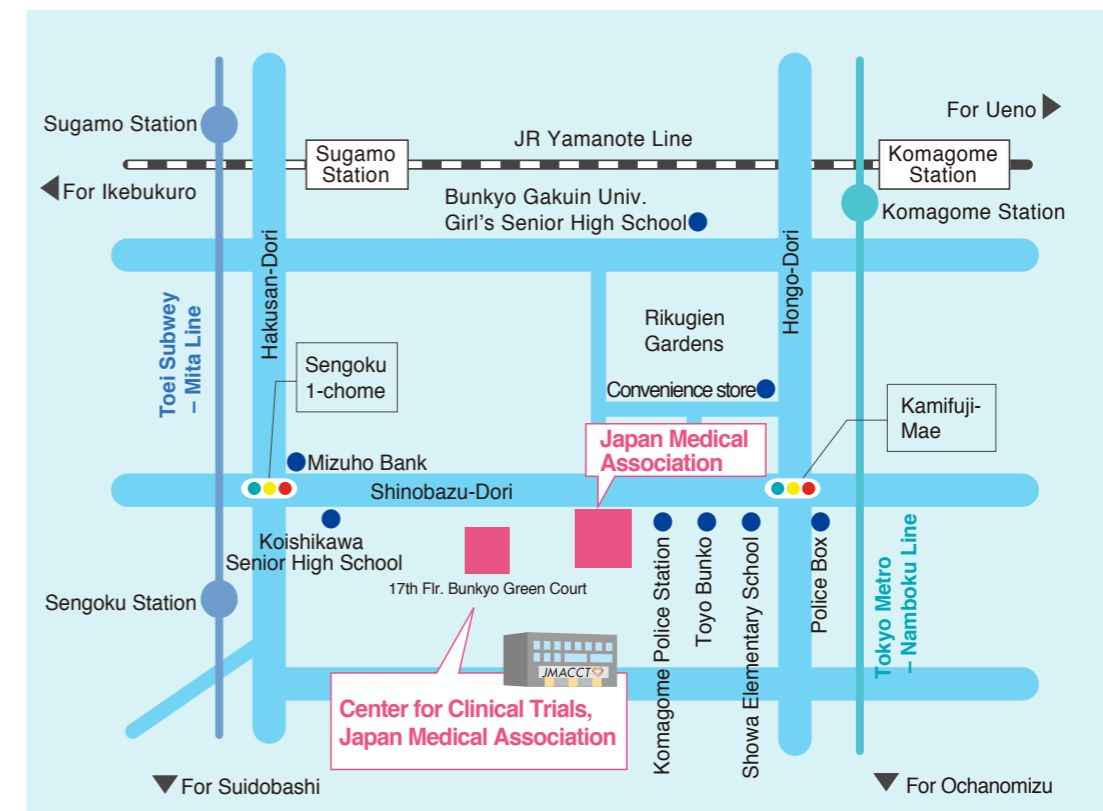
### Date of establishment

August, 2003



### Address

17th Flr. Bunkyo Green Court Center Office,  
2-28-8 Honkomagome, Bunkyo-ku, Tokyo 113-0021, Japan  
TEL : 03-5319-3781 FAX : 03-5319-3790  
URL : <http://www.jmacct.med.or.jp/>



### External Committees

To ensure fairness and transparency of the grant programs operated by JMACCT, there are external committees consisting of experts from different fields including health care, academia and pharmaceutical industry. These committees assess proposals and applications for the grant programs and decide which research proposals or applicants are to be funded.

<URL> <http://www.jmacct.med.or.jp/jma/outside.html>

