Prospect of ICT Utilization at Core Clinical Research Hospitals

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One of Fujitsu's endeavors in healthcare is to develop coordinated solutions for medicine and pharmaceuticals, and is focusing on clinical trial research at medical institutions to enhance the development of drugs and medical equipment. Today, Fujitsu aims to develop a stronger system of medical cooperation by introducing the tsClinical DDworks21 series, developed for the pharmaceutical industry, into the existing healthcare product range including the Hope series. They will be used with electronic medical records and other medical information systems. It is also promoting the Fujitsu Healthcare Solution HOPE New Medical Good Clinical Practice (NMGCP), a clinical trial management solution to help trial implementations. Three systems are applied at medical establishments, namely the GCP Management System for managing clinical trials, the Electronic Data Capture (EDC) System for collecting case data, and a warning system for managing side-effect information. The coordinated solution for medicine and pharmaceuticals thus helps to improve the process efficiency in the development of drugs and medical equipment, and renders powerful support for quality management (validation), which is important and in fact essential in this field. This paper describes the development of Fujitsu's coordinated solution that focuses on the clinical trial research at medical practices. It describes its role, effects and future prospects, drawing on the social current in relation primarily to the core clinical research hospitals program.

1. Introduction

Japan is an advanced country in the world in terms of basic medical research, but not as competitive as other medically developed countries in clinical research because it is costly and often requires a long period of time for development. In this sense, Japan is coming to a turning point and it is working toward achieving world-leading medical practices through the development of pharmaceuticals and medical equipment.

Against this background, the Japanese government passed a cabinet decision in 2013 on the country's new growth strategy, Japan Revitalization Strategy-JAPAN is BACK-, and established an innovative research and development program (Impulsing PAradigm Change through disruptive Technologies: [ImPACT] Program). Through this program, hospitals with globally competent clinical trial and research capabilities were to be designated as core clinical research hospitals. The program sets the following requirements that medical institutions which submit applications must meet in order to qualify as core clinical research hospitals.

1) The hospital secures all the necessary functions required for a core clinical research hospital under the initiative of hospital administrators and the hospital as a whole.
2) It is capable of preparing, planning and implementing clinical research that complies with the ICH-GCP[note 1)] regulations, with a focus on exit strategies.
3) It is capable of executing ethical evaluations that are appropriate and highly transparent from ethical and scientific perspectives as well as from the viewpoints of safety and credibility.

note 1) ICH-GCP: International Conference on Harmonisation-Good Clinical Practice. The protocol provides for bidirectional disclosure and exchange of clinical trial data among participating regions (Japan, the US and the EU) for pharmaceutical developments.

4) It ensures the credibility of data to meet the ICH-GCP standards.
5) It adequately manages intellectual property rights and technology transfer regarding seeds.[note 2)]
6) It is capable of providing education to the relevant bodies, and promoting research results to the nation and patients.

Between 2012 and 2013, a total of ten medical institutions were designated as core clinical research hospitals, five in each year. The selection criteria covers a wide range of measures and activities that must be in place, including information-and-communications-technology-enabled (ICT-enabled) administrative management; data utilization; and quality control in terms of personnel and organizations, facilities, the environment and other aspects of the hospital's operations.

This paper addresses the purpose of the core clinical research hospitals in Japan's pharmaceutical and medical equipment development, and the present circumstances in relation to the coordinated solution for medicine and pharmaceuticals which Fujitsu offers in the areas of clinical trial and research. It also describes the challenges to tackle in view of the future prospects of this solution.

2. ICT deployment at core clinical research hospitals

In this chapter, we describe in detail the facility that core clinical research hospitals require, with the focus on ICT deployment.

1) Clinical trial and research support system

The ICH-GCP provides for clinical trials in terms of implementation and management, trial procedures as well as ethical policies. A system must be developed to ensure the hospital complies with the regulations and guidelines issued by the ICH-GCP and other regulatory bodies. The hospital needs many features including, for example, a step-by-step administrative process management from application to assessment and approval of procedures required for drug development (**Figure 1**), and evidence/document management that covers records and reports.

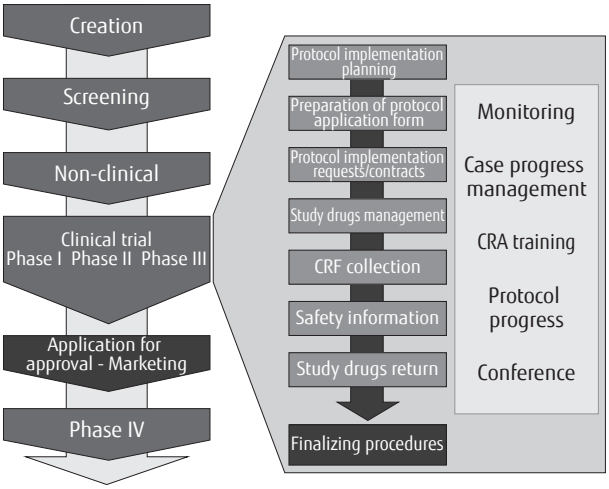


Figure 1
Administrative procedures of pharmaceuticals development.

2) Ensuring credibility of data

Case data such as case study reports, which serve as evidence in drug/medical equipment development, must meet various guidelines to ensure data authenticity (factuality) and reproducibility. Data of this kind has been stored in printed form previously, but more and more data is stored on an electronic basis through ICT programs such as Electronic Data Capture (EDC). Furthermore, there is an increasing demand to shift from a direct-input style to a coordinated system between clinical data systems (e.g., electronic medical records) and EDC (hereafter, EDC-coordination). This move would reduce the administrative burden of inputting a large amount of data, and as a result lower the risk of human error and improve the data accuracy. We will describe an initiative at Fujitsu in the next section "Effect of EDC-coordination" as a pioneering case.

3) Joint clinical trial/study conducted by a multiple number of hospitals

The system would offer great advantages in coordinating a number of hospitals through a network so that they can conduct joint clinical trial and study. ICT would help overcome the physical distances between participating hospitals in trial process management and centrally managing case data, particularly when many sites join in the development of the same drug or medical equipment. The benefits would increase as the number of participating institutions grows.

note 2) Seeds here refer to a company's technology and know-how that could potentially be commercialized. However, they are not provided directly to the customer, but are offered in the form of a product or service.

3. Roll-out of the coordinated solution for medicine and pharmaceuticals

This section describes Fujitsu's healthcare solution HOPE Cloud DDworks21 HC, a cloud-based service for core clinical research hospitals, applying its knowledge and experience gained through the development of solutions for the pharmaceutical industry (**Figure 2**).

1) GCP process administration feature

This feature offers support to physicians who aim to file applications for pharmaceuticals approval by facilitating an investigator-initiated clinical trial in compliance with the relevant regulations (Good Clinical Practice: GCP). Target tasks and their purposes are as follows:

- Integrative data management

Helps to manage the trial by protocol (theme for clinical studies) comprehensively in steps ranging from planning to submission of notification of completion of the clinical trial

- Protocol information management

Manages protocols for planning, team management and documents used for the protocol (version and data modification management).

- Trial sites management

Registers medical institutions and/or physicians in the system so that the user can easily select which hospital to use when commissioning clinical trials.

- Clinical trial notification management

Manages various notifications to be submitted to the Pharmaceuticals and Medical Devices Agency (PMDA) regarding clinical trials.

- Clinical trial procedure management

Manages various trial procedures such as contracts with practicing medical institutions and trial application documents for the Institutional Review Board (IRB), and verifies compliance with the relevant regulations.

- Study drugs management

Manages the study drugs inventory in various stages including stocking, releasing, dispensing, returning, destruction and shipping.

- Trial history management

Manages scheduled events and records during the clinical trial (conferences, orientations etc.) and roll call management.

- Support for Clinical Research Associate (CRA)

Provides support in preparing and managing monitoring reports. Features include case progress data output and data sharing.

2) Clinical study data collection (EDC management)

Manages electronic case reports and other data from the clinical studies, helping to improve efficiency

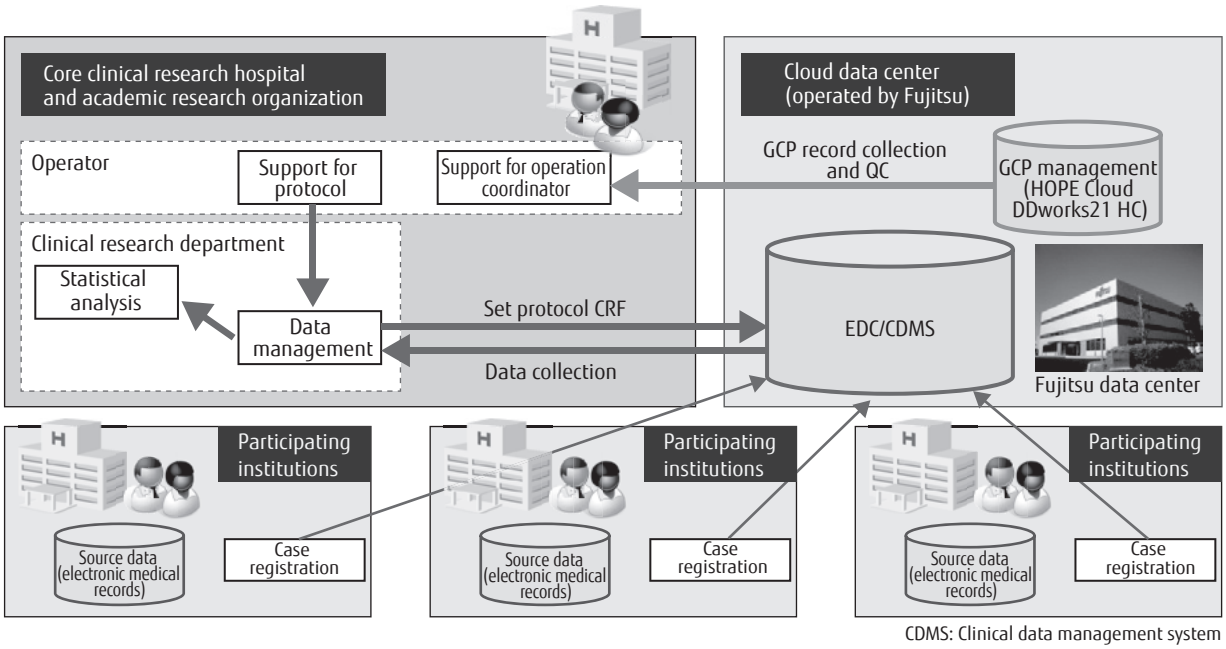


Figure 2
Multiple participation model of coordinated solution for medicine and pharmaceuticals.

in completing tasks.

- Case registration and assignment

  Issues registration numbers and assigns study drugs.
- Case study report registration

  Provides the user with support when entering data into the electronic case report form (eCRF).
- Electronic medical records data import

  Imports case data from electronic medical records.
- Queries

  Handles inquiries (data queries) to investigators and their responses.
- Source Data Verification (SDV)

  Provides support for CRAs when inputting data for the source data verification results (to verify the data credibility by comparing case reports and source data such as medical records).
- Data finalization

  Executes finalization of data related to trial subject visits (VISIT), cases, facilities and protocols.
- Electronic signature

  Adds electronic signatures to each VISIT and/or case.
- SAS dataset output

  Extracts finalized data to the SAS dataset, and submits it to statistical analyses.

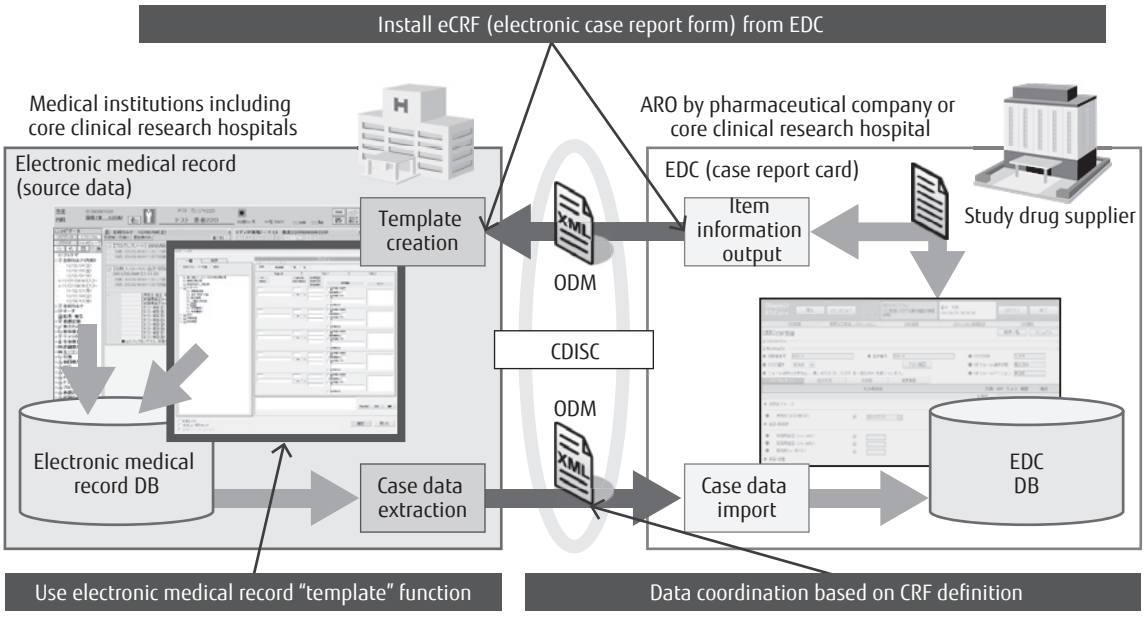
3) Tools dedicated to relaying information on GCP side effects and other adverse events

The unique system and features described above have been realized on a cloud platform. They will help core clinical research hospitals to complement the required functions and resolve challenges both in terms of trial (protocol) management and efficient data management, an area in which many participating institutions are involved. It will offer ITC infrastructure to expedite the development of drugs and medical equipment.

4. Effect of EDC-coordination

In this section, we describe the coordination between clinical data systems (e.g., electronic medical records) and pharmaceuticals (drug development) systems. This has been referred to in *(2) Ensuring credibility of data* in the above "ICT utilization at core clinical research hospitals" and ensuring EDC-coordination between systems is one of the most important aspects of future ICT utilization in medicine. **Figure 3** depicts the actual constellation of EDC-coordination.

1) A data format is agreed between the systems, based on the Original Design Manufacturing (ODM), for exchanging data. The electronic medical records are formatted using general-purpose



ARO: Academic research organization

Figure 3
System model for coordination between electronic medical records and EDC.

templates useful for medical data entry.

2) In actual operation, pieces of data are entered directly onto the template as defined for the electronic medical records.
3) Previously, pieces of data in the electronic medical records were manually copied to the pharmaceuticals systems. The format defined according to process (1) above will enable EDC-coordination.

The system as a whole has been designed while considering future development and expansion. Meanwhile, having further sophistication and wider deployment as a standard feature would lead to many medical institutions and pharmaceutical contract research organizations (CROs) adopting automated EDC entry, and electronic data will be more widely shared. This would help to considerably reduce development costs and lengthy development periods, and stimulate further progress in drug and medical equipment development in Japan.

5. System quality control in clinical trials

So far, we have mainly described the coordinated solution for medicine and pharmaceuticals. Clinical trials for drug/medical equipment development further requires the system to ensure data credibility through computerized system validation (CSV) (**Figure 4**) and other activities. Some points to note are as follows:

1) CSV should include procedures not only for the development and introduction phases, but also for the system operation, reconfiguration and destruction phases.
2) Clinical trial commissioners should remain accountable for the CSV policies and processes applicable to this EDC system and they should be capable of providing the necessary documents such as CSV reports if required, for the whole of the data retention period of the materials created by this system.
3) Medical institutions, vendors, CROs and pharmaceutical manufacturers may be held accountable for ensuring work quality.

For a coordinated solution for medicine and pharmaceuticals, Fujitsu is working on the development, introduction and maintenance of HOPE Cloud DDworks21 HC based on appropriate validation activities. In the future when EDC-coordination becomes a reality and it expands, the scope of CSV will be extensive and complex in a broad sense of the system scope within medical institutions including the clinical data system. Therefore, developing validation procedures for each core clinical research hospital and other facilities must be pursued very carefully.

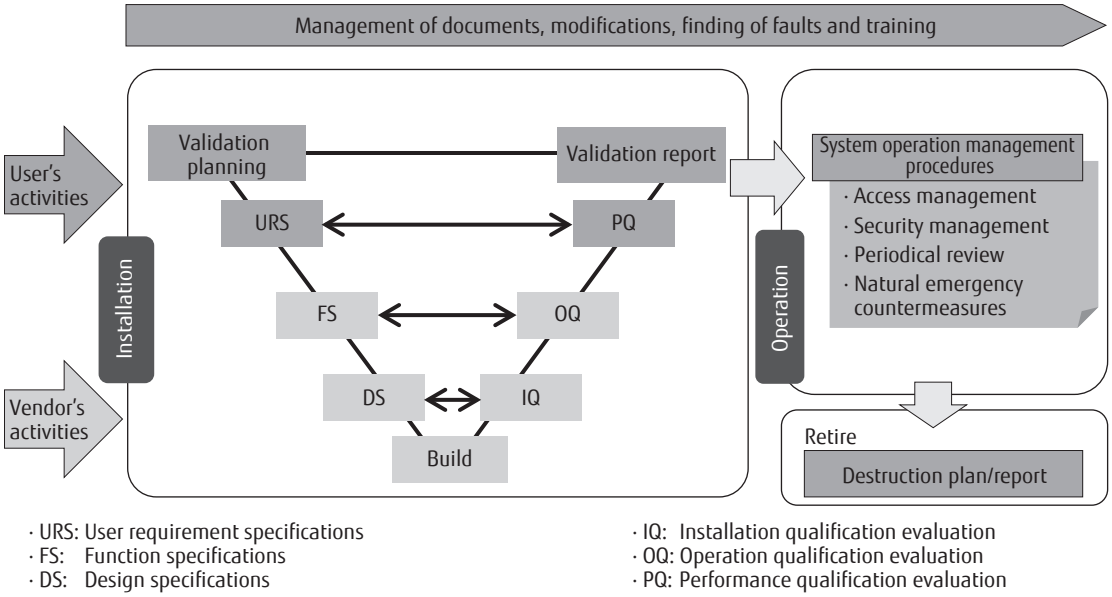


Figure 4
Illustration of concept of Computerized System Validation.

6. Future challenges

More and more hospitals and pharmaceutical companies will be turning to ICT in the foreseeable future. We will discuss our challenges for the future from the vendor's perspective.

1) Improve clinical information systems from the viewpoint of drug development

As was mentioned in "Effect of EDC-coordination" above, the need for liaising between medical and pharmaceutical institutions will potentially increase very quickly in the future. In terms of the development of drugs/medical equipment, the clinical information systems, which have so far been developed exclusively for medical consultations and treatments, need to have the existing features improved and need enhanced functions to be added. Modifications must take into account the need to make the clinical information system easy and efficient to use so that users can extract the necessary data from the enormous body of clinical data for the development of drugs and/or medical equipment. Also, the system must ensure that end users are always updated with critical information such as that regarding side effects and other adverse effects.

2) Sustained efforts in compliance with regulations/guidelines

Considering the increase in number of international collaborations in drug/medical equipment development, the ICT infrastructure for HOPE Cloud DDworks21 HC will need to comply not only with regulations of the ICH-GCP and Electronic Record/Electronic Signature (ER/ES), but also regulations of foreign countries when conducting clinical trials and studies. Therefore, there will be demands for services that presuppose continued quality assurance throughout the system's life cycle, including the aforementioned CSV activities.

3) Coordinate translational research of medical technology elements (medical seeds)

As seen in many translational research projects, the program to develop core clinical research hospitals and other state-led strategies place an emphasis on exit strategies to identify elements of medical technology at the level of basic research to turn into practicable applied technology. An example of an information infrastructure model of the future would be one that integrates ICT infrastructure into very important process management covering processes from the identification of medical seeds by academia to pharmaceuticals approval and post-market management.

4) Collaboration with state initiatives

The PMDA has announced that it will start accepting electronic data for submission attached to pharmaceuticals approval applications from 2016. At Fujitsu, we believe we must strive to work with state initiatives and policies, leveraging our technologies and know-how gained through providing clinical data systems for medical institutions and pharmaceuticals solutions, while at the same time developing application handling systems for regulatory agencies.

7. Conclusion

We have discussed the coordinated solution for medicine and pharmaceuticals offered by Fujitsu, in terms of its present statuses, challenges and future prospects, drawing on various social trends of today. ICT is an indispensable element for accelerating Japan's growth strategies and invigorating its industries and society. Fujitsu will continue to perform its role by continually providing better services through its technologies.

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Fujitsu Ltd.
Mr. Akahori currently engages in new business planning and development in healthcare fields.