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Comment

For Sharing Individual Participant/Patient Data (IPD) from Clinical Trials

With recent trends

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In the two years that have passed since the publication of a CTDS report entitled "Sharing Individual Participant/Patient Data from Clinical Trials: CTDS (Clinical Trial Data Sharing)" [1] by the Data Science Expert Committee (DS-committee) of the Japan Pharmaceutical Manufacturers Association's Drug Evaluation Committee in June 2017, major changes have occurred in the circumstances surrounding CTDS. In Japan, changes such as more pharmaceutical companies engaged in CTDS over the past two years have been observed. This article introduces the changes that have occurred in the last 2 years and summarizes the points to be addressed when implementing CTDS. We hope that this will help those involved in CTDS, particularly those who are considering or have just begun implementing CTDS, and researchers considering using CTDS for their own research.

What is CTDS again?

Efforts to share Individual Participant/Patient Data (IPD) obtained from clinical trials with researchers (Clinical Trial Data Sharing: CTDS) began in earnest, mainly in Europe and the United States, in response to the publication of the Principles for Responsible Clinical Trial Data Sharing by the European Federation of Pharmaceutical Industries and Associations (EFPIA)/the Pharmaceutical Research and Manufacturers of America (PhRMA) [2] in July 2013. The main benefits and risks of CTDS are as follows.

Benefit

Improvement of medical care and public health

- New findings not obtained in the primary analysis planned and conducted in clinical trials may be obtained in the secondary analyses
  - Improvements in existing therapies (e.g., identification of common side effects in specific subgroups) and elucidation of disease mechanisms
  - Based on new findings from secondary analyses, more efficient study designs may be investigated, leading to improvements in the probability of successful clinical development, and consequently reduce the cost of drug development
- Avoiding unnecessary repeats of clinical trials and minimizing unnecessary exposure of subjects to the drug

Ensuring transparency in clinical trials

- Disclosure of clinical trial results, as well as sharing of IPD, will gain public understanding and confidence in clinical trials.
- Clinical trial results are publicly substantiated when evaluated by third parties in a secondary analysis using the IPD

Benefits to the pharmaceutical business

- Improving health care and public health and ensuring transparency in clinical trials through CTDS will have positive impact on company assessment and confidence
- Efforts to share and utilize data with each other across the industry-academia framework can promote the efficiency of drug development

[1] http://www.jpma.or.jp/medicine/shinyaku/tiken/allotment/pdf/ctds.pdf
[2] https://www.efpia.eu/media/25189/principles-for-responsible-clinical-trial-data-sharing.pdf

Risk

Conduct of secondary analyses that are medically or statistically invalid

- If an invalid secondary analysis publishes results against a useful treatment, it may have a substantial impact on the judgment of the physicians or patients even though the secondary analysis result is without credibility
- Personnel performing secondary analyses may have poorer understanding of the data structure and handling than primary analysts and may misinterpret the analysis based on misconceptions
- Intentionally invalid secondary analyses
  - Exaggerating risk based on invalid analysis could be a means of attack against data providers
  - Interactions between secondary analysts and primary analysts involved in the original clinical trial may be used to acquire intellectual property and commercial information

Violation of clinical trial participants' privacy or personal information-related regulations

- Data subjects may be identified from shared data, resulting in violation of clinical trial participants' privacy.
- Rigorous data anonymization/de-identification[3] in order to ensure privacy protection may lead to increased effort and costs for data anonymization/de-identification, as well as reducing the utility of the data (the amount of information)
- Tightening regulations and growing public awareness regarding personal information protection. In case where the EU General Data Protection Regulation (GDPR)[4] is applicable, sanctions may be imposed if the data processing is deemed to violate the GDPR. In addition, if the data is handled inappropriately, not only may the social credibility of the company concerned be damaged but could also lead to other negative effects such as fewer people willing to participate in subsequent clinical trials.

Decreased incentives for conducting clinical trials

- Should CTDS prove to be too profitable, the incentives to invest clinical trials which take much time and resources are undermined. This may lead to a decrease in new clinical trials resulting in the depletion of shared clinical trial data, leading to a decrease in the usefulness of CTDS.

Global Trends in CTDS

In June 2017, the International Committee of Medical Journal Editors (ICMJE) released an editorial about the conditions of consideration for publication of a clinical trial report in their member journals: “Data Sharing Statements for Clinical Trials: A Requirement of the ICMJE” [5]. This editorial mandates that as of 1 July 2018 manuscripts submitted to ICMJE journals that report the results of clinical trials must contain a data sharing statements, and Clinical trials that begin enrolling participants on or after 1 January 2019 must include a data sharing plan in the trial's registration. Pharmaceutical companies seem to be dealing with these conditions. For example, the number of studies with "Plan to Share IPD” in ClinicalTrials.gov[6] is increasing. In addition, the “IFPMA Principles for Responsible Clinical Trial Data Sharing” [7] has been released by International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) and commitment to CTDS (sharing IPD from clinical trials) under the Principles of Responsible Clinical Trial Data Sharing are now the challenges to be addressed not only by the EFPIA/PhRMA but also by the Japan Pharmaceutical Manufacturers Association and other global pharmaceutical organizations affiliated with IFPMA, which has also contributed to promote CTDS.

In 2014, the EMA finalized a Policy 0070[8] on publication of clinical data. Policy 0070 is implemented in two phases. The first phase is already undertaken in the Policy on publication of Clinical reports[9]. The necessity, conditions, etc. of making IPD available in the second phase have been discussed within the EMA. In 2016, External Guidance on the first phase of Policy 0070 was subsequently

[3] The data anonymization/de-identification process varies widely, including whether or not the processed data corresponds to personal information. In this paper, the anonymization/de-identification process is used in the meaning of the process to make it difficult to identify the person in order to reduce the risk of identifying the person linked to the data.

[4] https://eur-lex.europa.eu/eli/reg/2016/679/oj

[5] http://www.icmje.org/news-and-editorials/data_sharing_june_2017.pdf

[6] https://clinicaltrials.gov/(Link)

[7] https://www.ifpma.org/wp-content/uploads/2010/11/IFPMA-Principles_Data-Sharing-FINAL-w-QA-vF.pdf

[8] https://www.ema.europa.eu/en/documents/other/european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use_en.pdf

[9] In Policy 0070, the Clinical report means the Clinical Overview (module 2.5), Clinical Summaries (module 2.7) and Clinical Study Reports (module 5) in the Common Technical Document for application dossier for the registration of medicines

published as a technical supplement, including anonymization methods of clinical report. In addition, workshops[10] have been held since 2017 to discuss CTDS issues, legal regulations, and methods of anonymization. As of May 2019, however, Policy 0070 activities had stopped in order to respond to Brexit[11][12], and the scope, procedures, and date of coming into effect of the second phase have not been clarified.

Although the FDA does not mention disclosure of IPD, the Final Rule of Food and Drug Administration Amendments Act (FDAAA) 801[13] has made protocol and statistical analysis plan publicly available at ClinicalTrials.gov since 2017. In January 2018, it was announced a new pilot program on disclosing portions of clinical study reports (CSRs) from nine-recently approved new drug applications[14]. In this pilot program, the FDA will redact information such as confidential commercial information and personal privacy information, but full patient adverse event narratives and complete line listings of patient information are outside the scope[15]. Once this clinical trial transparency pilot program is complete, the FDA will consider promoting transparency in the future based on feedback from the public. The FDA draft guidance on meta-analysis evaluating the safety of human drugs and biological products published in November 2018 showed that the use of subject-level meta-analyses improve the quality of meta-analyses and allow for a broader range of analysis methods, which may increase the number of researchers considering subject-level meta-analysis.[16]

Health Canada finalized Guidance document on Public Release of Clinical Information in March 2019[17]. This guidance is intended to disclose clinical information contained in CTD modules 2.5 (Clinical Overviews), 2.7 (Clinical Summaries), 5.3 (Clinical Study Reports), Protocol and Protocol Amendments, and Sample Case Report Forms and Statistical Analysis Plan. One drug information has been published as of May2019[18]. However, individual patient records will not be publicly released proactively.

In Australia, a clinical trial registry site, the Australian New Zealand Clinical Trial Registry (ANZCTR) [19] has been launched and any trials can be registered regardless of where the trial is conducted. When Australian and/or New Zealand sites are registered on ClinicalTrials.gov, those clinical trials are displayed on the ANZCTR automatically and additional information specific to ANZCTR can be entered. Population Health Research Network (PHRN) [20] mainly funded by the Australian Government, provides services that link existing information from different sources such as health and health related data collections to provide data to researchers approved research with consideration of minimizing the risks to individual patient privacy.

Regarding CTDS activities conducted by organizations other than the regulatory authorities, we will introduce those undertaken by TransCelerate BioPharma Inc[21] and PhUSE[22].

TransCelerate BioPharma Inc published the paper, “De-identification and Anonymization of IPD in Clinical Studies – A Model Approach V2.0[23]” at the end of 2016 which describes methods of de-identification and anonymization applicable to IPD when sharing data. V2.0 takes the EU’s GDPR and Policy 0070 into consideration, as well as emphasizes the need for assessment of residual re-identification risks as compared to V1.0, which focused on the U.S. HIPAA Privacy Rule[24]. The Placebo and Standard of Care (PSoC)

[10] https://www.ema.europa.eu/en/events/data-anonymisation-workshop
[11] https://www.ema.europa.eu/en/documents/other/european-medicines-agency-brexit-preparedness-business-continuity-plan_en.pdf
[12] https://www.ema.europa.eu/en/news/update-emas-brexit-preparedness
[13] https://clinicaltrials.gov/ct2/manage-recs/fdaaa
[14] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm592566.htm
[15] https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm606305.htm
[16] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM625241.pdf
[17] https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/profile-public-release-clinical-information-guidance.html
[18] https://clinical-information.canada.ca/search/ci-rc
[19] http://anzctr.org.au/Default.aspx
[20] https://www.phrn.org.au/(Link)
[21] https://www.transceleratebiopharmainc.com/(Link)
[22] https://www.phuse.eu/(Link)
[23] http://www.transceleratebiopharmainc.com/wp-content/uploads/2015/04/TransCelerate-De-identification-and-Anonymization-of-Individual-Patient-Data-in-Clinical-Studies-V2.0.pdf
[24] https://www.hhs.gov/hipaa/for-professionals/index.html

Initiative[25] has also been launched and attempts have been made to share the placebo and standard of care control arms of clinical trials among the member companies. In July 2018, TransCelerate BioPharma Inc., in collaboration with BioCelerate[26], a member of TransCelerate BioPharma Inc, released a repository which, as of the end of 2018, has 119 trials and more than 82500 participants' data. This is expected to improve the design of clinical trials, accelerate the conduct of clinical trials, and promote further understanding of diseases, and the historical usage of PSoC data as a control arm substitution is also being considered. Member companies have already begun using this data.

The "De-Identification Standard for CDISC SDTM 3.2 v1.01[27]", released by PhUSE in May 2015, is still widely used as a de-identification standard. An updated version of "Appendix 1: Date Offsetting" was released on May 19, 2017[28] which emphasized the importance of making offset dates partial again during the final step when the algorithm to offset dates[29] is applied to a partial date[30]. This is because the applied difference (offset delta) is likely to be inferred from the offset imputed date. A description of the Offset of dates for ADaM has also been added. Howevwe, ADaM's De-Identification Standard has not yet been released as of May 17, 2019.

The current status of ClinicalStudyDataRequest.com (CSDR) [31] and Vivli[32], which multiple organizations and companies join, are presented as a trend of CTDS platforms. However, this does not mean the Japan Pharmaceutical Manufacturers Association recommends any particular CTDS platforms.

CSDR, which 19 organizations and companies including several Japanese pharmaceutical companies join as of May 17, 2019, is one of leading CTDS platforms. Once a data sharing agreement has been reached between the researcher who wants to use the data and the data provider, the researcher can use the de-identified data of the relevant study free of charge in an access-controlled, secure analytical environment. The CSDR has been in operation for approximately 6 years, and the number of trials listed in the list for sharing has reached 3344 (as of May 17, 2019). The number of research plans submitted by March 31, 2019 was 494, of which more than 80 are research plans using clinical trial data from multiple companies[33]. As of 31 March 2019, 42 research results have been published.

Vivli, an independent nonprofit organization established by Multi-Regional Clinical Trials Center (MRCT center) of Brigham and Women's Hospital and Harvard University, launched its own data-sharing platforms in July 2018. In addition to pharmaceutical companies, the Vivli is also working with existing data-sharing platforms, such as Project Data Sphere[34] and ImmPort[35], and as of May 2019, 19 organizations and companies have become the Vivli's members. Member pharmaceutical companies include Japanese pharmaceutical companies. More than 3,900 trials with approximately 1.9 million participants from 105 countries can be shared on Vivli platform. One of Vivli's CTDS platform's characteristics is its flexible research environment. For example, data users can upload external data they want to use for their study to Vivli's CTDS platform and analyze them with data shared within the Vivli. Another feature is that data users pay the cost. Costs depend on the specifics of the research environment used, but there are considerations for the data user. For example, the standard environment can be used free of charge for up to 365 days. This is an incentive for data users to conduct research using shared data in a timely manner. Vivli is vigorously conducting webinars and educational events, actively communicating with medical journals (organizations) such as AllTrials[36] and ICMJE, and with various organizations such as the Cochrane[37], and acting as neutral broker between data providers, data users, and the wider data-sharing community.

[25]https://www.transceleratebiopharmainc.com/initiatives/placebo-standard-of-care/(Link)
[26]https://www.transceleratebiopharmainc.com/biocelerate/(Link)
[27]https://www.phuse.eu/data-transparency-download
[28]https://www.phuse.eu/documents//working-groups/dt/phuse-deid-standard-sdtm-32-appendix-1-date-offsetting-v200-19889.pdf(Link)
[29] Data processing, in which the delta computed based on a specific anchor date for a given patient is subtracted from all collected source, is called date offsetting in the PhUSE data de-identification standard
[30] Partial date means only partial date information such as year (e.g. 2019) or month (e.g. May 2019)
[31]https://clinicalstudydatarequest.com/(Link)
[32]https://vivli.org/(Link)
[33]https://clinicalstudydatarequest.com/Metrics.aspx
[34]https://projectdatasphere.org/projectdatasphere/html/home
[35]https://www.immport.org/home
[36]http://www.alltrials.net/(Link)
[37]https://www.cochrane.org/news/vivli-use-cochrane-vocabulary-power-vivlis-search

Domestic Conditions Surrounding CTDS in Japan

As for changes in the domestic situation, the IPD sharing statement added to the registration items in accordance with the "Registration of the Conduct of Clinical Trials (Notification dated March 26, 2018)" [38] issued by the Ministry of Health, Labor and Welfare. As a result of this movement, for example, in JapicCTI[39], the fields "plan to share IPD" and "plan description" have been added. Therefore, when conducting clinical trials, the pharmaceutical company must state the plan to share IPD. Enter "Yes" if IPD sharing is planned, or "No" if it is not planned, or "Undecided" if it is not decided yet. This comes from 24 items in the WHO Trial Registration Data Set at the International Clinical Trials Registry Platform (ICTRP) [40][41].

On the other hand, CTDS activities require the establishment of systems and environments for data-sharing, such as affiliation with existing CTDS platforms. Recent growth in the number of member companies on CTDS platforms indicates that CTDS is spreading throughout the industry in Japan. Among Japanese domestic pharmaceutical companies, the number of affiliated companies has increased compared with the previous publication of our CTDS report.

The CTDS is being promoted in Academia, and the Japanese Society of Neuropsychopharmacology[42] has launched a Preparatory Committee for the establishment of a "Psychiatric and Neuropsychiatric Data Sharing Promotion Association" which consists of some pharmaceutical companies who agreed to the activities, as an effort to promote data sharing in the psychiatry and neurology field[43].

Laws and regulations related to CTDS

There are many laws and regulations related to CTDS in Japan and overseas, and the regulations that should be followed must be examined according to the scope of data to be shared, the location of data to be shared, and the methods of sharing data. In addition, we should pay attention that the rules, conditions and terminology used vary among regulations. As an example, Table 1 shows comparison in definition of some of representative terms among relevant regulations in Japan, the United States, and Europe. In the table, some similar terms are condensed into same column for simplicity and the regulation which has a missing of definition is still included in the raw for comprehensiveness. Please be aware that the original long texts in each regulation have been summarized and then temporarily translated. Please confirm the original texts of each regulation for details.

[38] https://www.pmda.go.jp/files/000223575.pdf
[39] https://www.clinicaltrials.jp/cti-user/common/Top.jsp
[40] https://www.who.int/ictrp/en/(Link)
[41] https://www.who.int/ictrp/network/trds/en/(Link)
[42] http://www.asas.or.jp/jsnp/(Link)
[43] http://asas.or.jp/jsnp/csrinfo/02.html

Table 1. Terminologies of regulations related to CTDS in Japan, the United States, and Europe

Regulation \ Terminology		Personal information, Personal data	Anonymized, anonymously processed or de-identified information/data
Japan	**Act on the Protection of Personal Information**[44]	A living individual that (1) can identify a specific individual (name, address, etc.), and (2) contains individual identification codes*	"Anonymous Processed Information" is the information relating to an individual produced by deleting or replacing all or a part of descriptions (including individual identification code*) that can identify a specific individual, and which makes it impossible to restore the personal information. If there is a possibility that the original personal information can be restored even after processing stated above, proper additional measures (generalization, noise addition, etc.) should be taken, taking into account the characteristic of the personal information database.
	Next Generation Medical Infrastructure Act[45]	"Medical information" includes information relating to a deceased individual, and "personal information" means information relating to a living individual.	"Anonymously Processed Medical Information" is the medical information relating to an individual produced by deleting or replacing all or a part of descriptions (including individual identification code*) that can identify a specific individual, and which makes it impossible to restore the personal medical information., and is prepared only by a certified business entity. If there is a possibility that the original personal medical information can be restored even after processing stated above, proper additional measures (generalization, noise addition, etc.) should be taken, taking into account the characteristic of the personal medical information database.
	Ethical Guidelines for Medical and Health Research Involving Human Subjects[46]	The definition of personal information is the same as that of Act on the Protection of Personal Information, but "Personal Information, etc." means information including the personal information as well as information about a deceased individual.	"Anonymized information" refers to the removal or replacement of all or part of an identifiable description (including personal identification code *) of a specific individual, including the deceased, and includes both identifiable information, which can be restoring the personal information by using a corresponding chart, etc., and unidentifiable information.
US	**Common Rule**[47]	Private information includes information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).	(unknown)
	HIPAA Privacy Rule	"Individually identifiable health information" means health information with respect to which there is a reasonable basis to believe the information can be used to identify the individual	De-identified health information neither identifies nor provides a reasonable basis to identify an individual.
European	**GDPR**[48]	personal data means any information relating to an identified or identifiable natural person who can be identified, directly or indirectly (excluding deceased persons)	Anonymous information, namely information which does not relate to an identified or identifiable natural person or to personal data rendered anonymous in such a manner that the data subject is not or no longer identifiable. Not subject to GDPR. (Pseudonymised data** is subject to GDPR.)
	EMA Policy0070	personal data means any information relating to an identified or identifiable natural person who can be identified, directly or indirectly	(From External guidance) “Anonymised/de-identified data” is the data in a form that does not identify individuals and where identification through its combination with other data is not likely to take place.

* In the Act on the Protection of Personal Information, "Individual Identification Code" means electronic letters, numbers, and codes that can identify a specific individual from the relevant information alone, such as a bodily partial feature of the specific individual (fingerprints, veins, etc.) and numbers uniquely assigned to an individual (passport number, My Number (an individual number in Japan), etc.)

[44] https://www.ppc.go.jp/personalinfo/legal/(Link)
[45] http://www.kantei.go.jp/jp/singi/kenkouiryou/jisedai_kiban/houritsu.html
[46] https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/hokabunya/kenkyujigyou/i-kenkyu/index.html
[47] https://www.gpo.gov/fdsys/pkg/FR-2017-01-19/pdf/2017-01058.pdf
[48] https://www.ppc.go.jp/enforcement/cooperation/cooperation/GDPR/(Link)

** In the GDPR, "pseudonymization" means the processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information kept separately.

For the implementation of framework for CTDS

When a pharmaceutical company actually introduces a CTDS system, it is generally the data science department that is primarily responsible for the practice of de-identification of data, but various other departments must work together to prepare and operate.

When introducing CTDS, it would be better to decide the control department in order to explain it to upper management in the company and to secure budgets. Whereas some companies build new organizations with their main responsibility for CTDS management, others have existing departments assigned to CTDS management. In order to share data with researchers, it is also the role of the control department to determine CTDS platforms: whether to create a new independent CTDS platform owned by the company, whether to participate in an existing CTDS consortium, etc., and to manage the progress of the work in each department toward CTDS implementation.

Because of the diverse range of areas to be considered, it is necessary to involve not only the data science department but also the medical writing department (the department in charge of preparing clinical study reports), the clinical control department (the department in charge of submitting clinical trial notifications and monitoring the development of products), the legal affairs department, the medical affairs department (the department in charge of publication), the regulatory affairs department, and the IT department. Involvement of public relations department is also required for the establishment of company policies that define the scope of study to be shared, as well as information disclosure on the company website, and involvement of the department in charge of CSR (Corporate Social Responsibility) may be required considering the nature of the CTDS's activities.
In the preparation stage, the data science department must prepare procedures that specify rules for de-identification of data, and prepare and review procedures that specify redact rules for clinical study reports, statistical analysis plans, etc. After the CTDS operation is started, it is the main role for the data science department to de-identify the data based on the procedure in response to the request from the researcher and to share it with the researcher, and to produce a report documenting the process and results of data de-identification to keep the records.

Various efforts and deliverables are needed to ensure that the company can receive requests from the researchers routinely. It is quite likely that it will take years from the commencement of discussion for CTDS implementation until the company gets to start data sharing with researchers. Even after starting data sharing with researchers, not only direct jobs such as de-identification of data, redaction of documents, but also keeping up on the laws and regulations related to CTDS activity, as well as maintenance of the standard procedures and decision-making in the event of situations that fall outside the scope of standard procedures are essential. Therefore, human and financial resources dedicated to CTDS activity are required in each department to continue operation.

Table 2 summarizes the relationships between the main tasks required for preparation and operation of CTDS activity and the organizations that may require to be involved. Please note that this is an example and that the optimal roles and responsibilities may differ depending on the organization and segregation of duties of each company.

Table 2: Examples of Roles and Responsibilities of Relevant Departments

Activity	Contents of work, Major Deliverables	Department								
		Control	DS	MW	Clinical Control	Legal	MA	RA	IT	PA, CSR
Preparation										
Establish the internal systems	Explanation to upper management in the company	◎	○	○			○	○		○
	Decision-making body and administrative office	◎								
	Determining CTDS platform	◎	○	○					○	
	Securing budgets	◎								
CTDS platform	Platform contract	◎				○				

Activity	Contents of work, Major Deliverables	Department								
		Control	DS	MW	Clinical Control	Legal	MA	RA	IT	PA, CSR
preparation	Preparation of CSV documents	○	◎	○					◎	
Establishment of Company policy	Establishment of data sharing policy	○			◎	○		○		○
	Posting the policy on the company website	○							○	◎
Maintenance of ICF	ICF template that describes the potential future secondary use of data			○	◎					
Study information management	Creation of the list of studies for data sharing [c]	○			◎					
Publication	Preparation of fixed phrase of Data Sharing Statement for papers	○					◎			
	Preparation of fixed phrase of data sharing plans for study registry				◎		○			
Data de-identification	Create data de-identification procedure	○	◎	○						
Redaction [b] of documents [a]	Create a procedure for redaction of documents	○	○	◎						
Operation										
Data Sharing Agreement (DSA) with researchers	Prepare template for DSA and make DSA with researchers	○	○	○		◎	○	○		
Data de-identification	Report on data de-identification work	○	◎	○						
	de-identified data (SDTM/ADaM)		◎							
Redaction of documents	Reports of Redaction work	○	○	◎						
	Redacted Documents		○	◎						
Routine tasks	Periodic Reporting to Upper Management	◎								
	Update of the list of studies for data sharing				◎					
	Periodic review of CSV	○	◎	○					◎	
	Keeping up on regulations	○			○	○		◎		○

◎:Department with primary responsibility ○: Support department

DS: Data Science
MW: Medical Writing
MA: Medical Affairs
RA: Regulatory Affairs
PA: Public Affairs
CSR: Corporate Social Responsibility
CSV: Computerized System Validation
ICF: Informed Consent Form

a) Documents such as clinical study reports, clinical study protocol, and statistical analysis plans
b) Redaction means masking of a document
c) List of studies of which IPD can be shared with researches. The studies are identified based on company policies that define the scope of the trials to be shared.

Conclusions

CTDS is now progressing beyond the framework of data sharing from pharmaceutical companies to researchers to the utilization of more data, as represented by TransCelerate's PSoC initiatives and data sharing promotion activities in the psychiatric and neurological fields. To promote drug development and maximize the benefits for all people through further improvement of health care and public health, it is important to reduce the risk such as medically and statistically invalid secondary analyses and the violation of clinical trial

participants privacy. For the risk reduction measures, controlled-access and secure CTDS platforms that only the authorized researchers can access anonymized/de-identified data from the relevant trials are used. The number of Japanese companies that are members of these controlled-access CTDS platforms is increasing. Furthermore, the risk reduction by the process such as the conclusion of a legally binding data sharing agreement is implemented.

Regulatory authorities in different countries have taken various actions related to CTDS. Since March 2018, posting IPD sharing statement/plan at the time of clinical trial registration has been required in Japan. Now we have to consider sharing the participant-level data from the planning phase of a clinical trial. When a pharmaceutical company implement a CTDS framework, it is essential for related departments to work together to establish policies and procedures, establish a new CTDS platform that is data-sharing environment, or join existing platforms, and continue to operate on a daily basis to respond to data-sharing requests. There are many laws and regulations related to CTDS, and it is also necessary to keep up on them periodically.
In order to organize these necessary measures/actions for CTDS and maximize the benefits of data utilization, the DS-Committee of the Japan Pharmaceutical Manufacturers Association will continue to provide technical support, mainly in the process of data de-identification for CTDS.

※URLs in footnote accessed 17 May 2019