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Patient Level Data Sharing (PLDS) initiatives in Pharmaceutical Companies

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ABSTRACT

Transparency, in sharing patient-level data for scientific research, is an increasingly important topic for the pharmaceutical industry and other organizations that sponsor and conduct clinical trials as well as generally in the interest of study participants.

INTRODUCTION

Patient Level Data Sharing (PLDS) is an initiative started a few years ago to provide access to anonymized documents/data to external researchers.

This paper will lead you from the start of the initiative up until now and will question where this may lead within pharmaceutical companies, who besides their own internal requirements, now also face a growing number of external requirements which are pushing for near full transparency.

We will specifically explore what internal requirements pharmaceutical companies may decide to apply to go even beyond the external requirements to proactively adapt to future requirements by standardizing the sharing processes and data.

CURRENT PLDS PRACTICES OF MAJOR PHARMACEUTICAL COMPANIES

May 2013: GlaxoSmithKline made available to investigators the patient-level data and study documents from more than 200 trials that had started since January 1st, 2007 and continued with all their interventional trials since the formation of GlaxoSmithKline in 2000 to end up in access to data from more than 1500 trials at that time.

January 2014: due to a growing number of requests for availability of patient-level data for scientific research, several large pharmaceutical companies have established a website (https://www.clinicalstudydatarequest.com) accessible to external researchers.

ClinicalStudyDataRequest.com (CSDR) is a consortium of clinical study data providers. It is a leader in the data sharing community inspired to drive scientific innovation and improve medical care by facilitating access to patient-level data from clinical studies. The retrospective/prospective studies are listed on this website. The site also provides information on study sponsor's criteria for listing studies and other relevant sponsor specific information.

Researchers can use this site to request access to anonymized patient level data and supporting documents from clinical studies to conduct further research. SHARE (Sharing of Anonymized and Redacted Elements) requests are being followed-up until they are resolved.

Pro-active redaction of documents and anonymization of data for prospective studies is performed within the pharmaceutical companies. Retrospective documents are also being redacted and external requirements are being implemented.

In March 2015, the Wellcome Trust took over running the independent review panel for CSDR. At that time, data from 3049 trials were available through the website, from Astellas, Bayer, Boehringer Ingelheim, Daiichi Sankyo, Eisai, GlaxoSmithKline, Lilly, Novartis, Roche, Sanofi, Takeda, UCB, and ViiV Healthcare.

The panel had 30 working days to complete their reviews and companies have 30 days to submit PLDS to requester once accepted. Since the beginning of the initiative, less than 200 requests were submitted and access was granted for most of the submitted proposals.

Access to clinical trial data provides opportunities to conduct further research that can help advance medical science or improve patient care. This helps ensure the data provided by research participants are optimally used for the creation of knowledge and understanding.

Globally, the data sharing principle is moving around including different ideas and models. The one described above is called the gatekeeper model. Other models exist, for example Project Data Sphere (PDS) which is more of a sharing platform.

CURRENT REQUIREMENTS LINKED TO CLINICAL TRIAL DATA

	Interventional human subject research		Non-interventional studies and studies using data or biological samples from previous studies	
	Studies that evaluate products	Studies that do not evaluate products	Studies that evaluate products	Studies that do not evaluate products
Full Protocol	At the time of results summary posting[a]			-
Statistical Analysis Plan	At the time of results summary posting[a]			-
Regulatory package	Within 60 days of decision for marketing authorisation[b]			-
Clinical study report (CSR)	This is not yet subject to external requirements- companies develop their own internal policies			
Patient-Level-Data-Sharing (PLDS)				

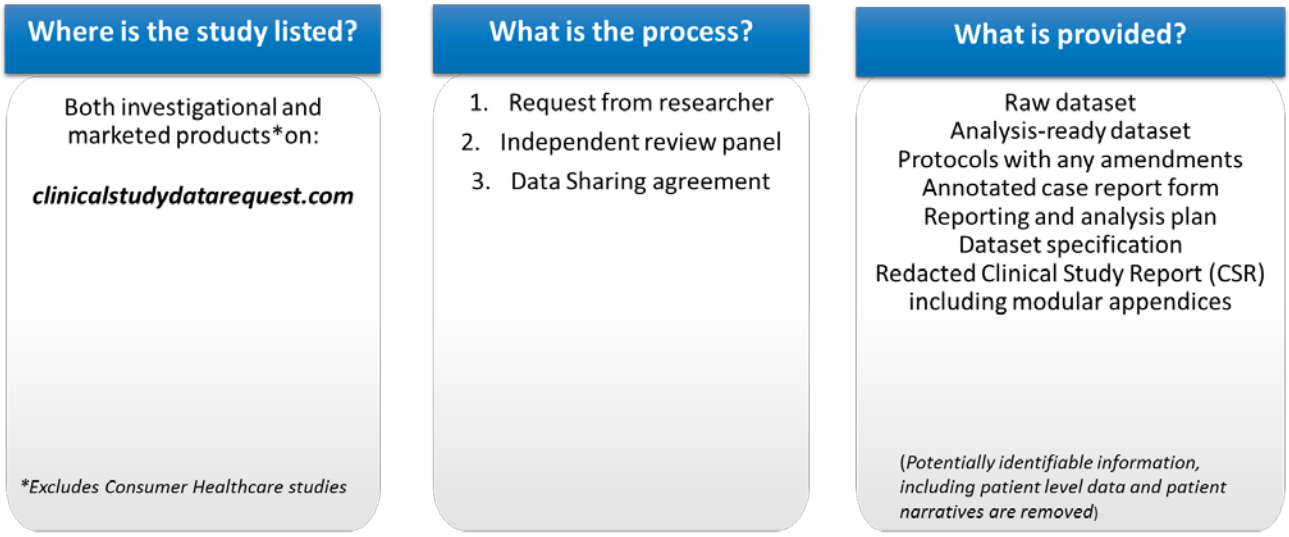
PROCESS OF SHARING PLDS WITH EXTERNAL RESEARCHERS

1. Researchers can select and submit research proposals and request anonymized data from clinical studies listed on the CSDR website. Researchers can also submit enquires to some study sponsors to ask about the availability of data from studies that are not listed on this site. It is also possible to request or access study documents without patient-level data. Information on sponsor's criteria for listing clinical studies, accessing study documents, and other relevant sponsor specific information is provided in the Study sponsors section.

2. Research proposals are reviewed by an Independent Review Panel. The study sponsors are not involved in the decisions made by the panel.

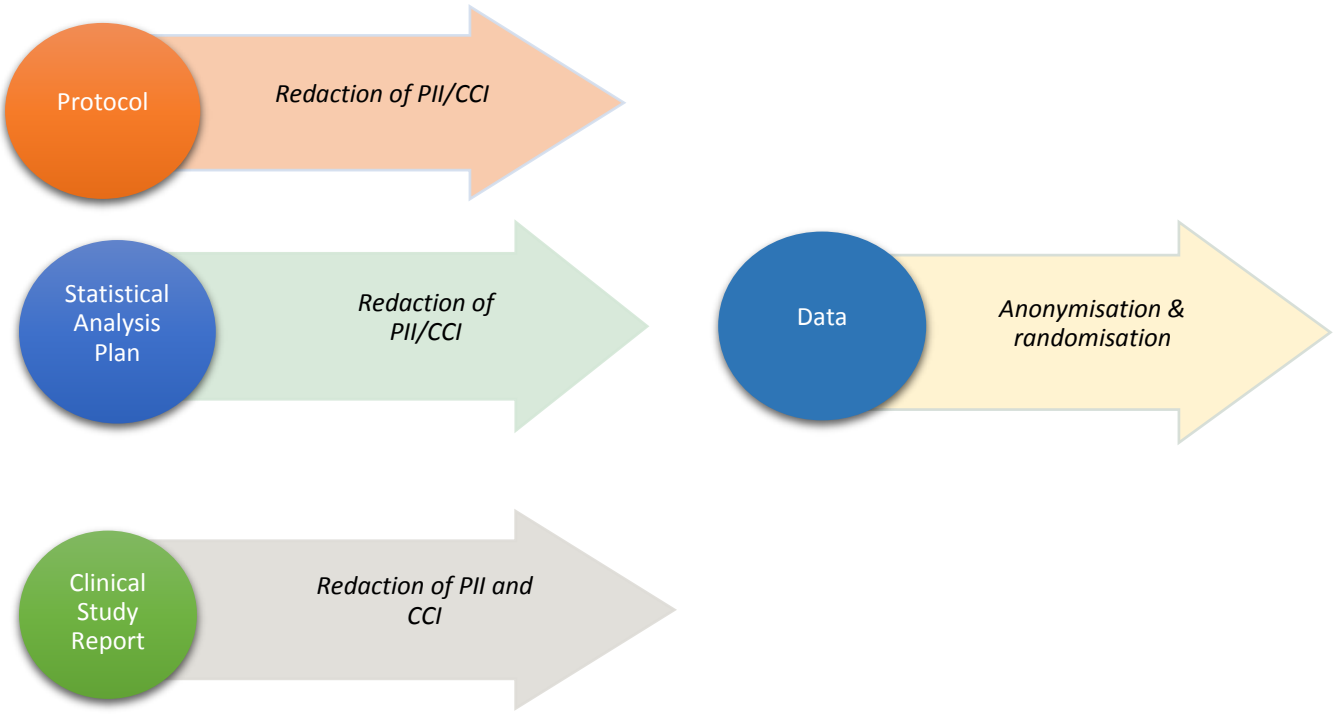
3. Following approval and after the relevant study sponsor or sponsors receive a signed Data Sharing Agreement, access to the data needed for the research is provided on a password protected website.

4. What data is provided: Raw dataset, Analysis-ready dataset, Protocols with any amendments, Annotated case report form, Reporting and analysis plan, Dataset specification, Redacted Clinical Study Report (CSR) including modular appendices (potentially identifiable information, including patient level data and patient narratives are removed).



THE REDACTION PROCESS

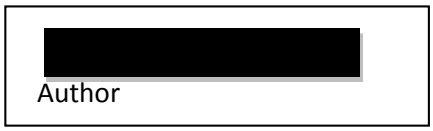
To redact is a process of preparing a document for being public by removing or blacking out personal (or possibly actionable) information. Redaction principles are defined by each company based on external policies but adapted depending on internal one.



CCI: Commercially Confidential Information
PII: Personally identifiable information

Removal of PII/CCI involves redacting (masking from view with a black bar) specific content and removing certain sections of the CSR with an explanation of what has been removed and why.

For example:



Examples:
PII: investigator CV, subject ID…
CCI: doses/composition of products…

DATA ANONYMISATION PRINCIPLES

Companies should ensure that data to be shared for this purpose has been de-identified and anonymized so that Personally Identifiable Information (PII) has been removed and that the link (key code) between individual subject data and the PII has been destroyed and cannot be recreated.

In order to meet legal and regulatory requirements for anonymization the anonymized datasets shall be stored in a central holding repository to ensure that they are stored separately from the original coded datasets.

De-Identification: data are considered de-identified if the PII elements are coded or removed in such a way that it would not be possible (even if difficult) to re-create the PII without a code or key. The code, key or other means of record identification is not derived from or related to the PII about the individual, and is not otherwise capable of being translated so as to identify the individual.

Anonymization: data are fully anonymised if the data have been de-identified and then the link (key code) between the individual and the PII has been destroyed. Anonymous means data will not have a link between the data and the subject identity.

FUTURE REQUIREMENTS LINKED TO SHARING PATIENT-LEVEL DATA

At this point in time the companies are following their internal requirements regarding Patient level data sharing and therefore can go beyond with internal guidance to proactively prepare for next steps.

- Some scientific journals will require authors to agree to share the data underlying the studies they publish
- According to the EMA upcoming requirement effective as of October 2018 it will be obligatory to make all clinical trial-related information generated during the life cycle of a clinical trial on a future EU portal for the following clinical trials available: Clinical trials conducted in the EU and pediatric trials conducted outside the EU that are part of pediatric investigation plans. This will also be applicable for clinical trials included in a marketing authorization application in EU (EU CTR, Q4 2018) within 30 days of decision on marketing authorization.
- According to the FDA Final Rule valid from 18 Jan 2017, the scope of the studies whose protocol and results summary should be shared has been expanded (Statistical analysis plan and protocol to be shared at the time of results posting hence 12 month after end of study)

REFLECTION ON HOW THE PROCESS CAN BE FACILITATED

Taking into consideration all the obligatory external requirements that will be applicable in the near future, standardization of templates and databases comes to mind as the most convenient way to empower and expedite the process of patient level data sharing.

Standardized templates and database would allow external researchers to compare results/conclusions from different trials. They would also help them to develop databases that can be used for future trials.
Standardized templates and database would allow general comparison from different trials on the same kind of products and facilitate the process.

Currently, data sharing and use of data is subject to discussion because of the format; this will have to be discussed and changed to ensure “true data sharing”.
Sharing patient level data seems ethically important and scientifically justified and has the potential to increase public understanding and interest and therefore support for clinical research. It is therefore very important to find ways to improve the use and output of data-sharing projects before the clinical research community invests the substantial effort and resources required to broaden the effort to include academic and other non-commercial investigators.

CONCLUSION

We can see that the transparency in clinical trials has one constant trend and this is expansion. New requirements are being created on an ongoing basis and the final goal is to be able to be fully transparent will all study-related data.

At this point we are witnessing the stepwise evolution of large pharmaceutical companies adapting to external requirements. The current requirements imposed on the pharmaceutical industry have been explored and the outcome of this research is standardization as a key element.

The data-sharing community is undergoing rapid development, with several potential models and approaches. External environment is encouraging multiple models to co-exist, either as a single platform with tiered access or as discrete platforms with the potential for cross-communication that includes truly open platforms. As the scientific community sees the benefits of sharing trial data, more will be shared.

REFERENCES

[a] FDA Final Rule 801 on Clinical Trials Registration and Results Information Submission effective 18 Jan 2017

[b] EMA POL0070 , effective date 1 Jan 2015

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