

AstraZeneca Clinical Trial Transparency and External Sharing of Individual Patient-Level Data

Natalie Andrews, AstraZeneca, UK

ABSTRACT

AstraZeneca's policy on Clinical Trial Transparency is aligned with US and EU regulatory and legal requirements, European Medical Association Policy and EFPIA/PhRMA joint principles for responsible clinical data sharing. AstraZeneca's commitment is met by timely release of clinical study information providing details of AZ sponsored phases 1-4 interventional clinical studies (and qualifying non-interventional studies in patients).

One aspect of Clinical Trial Transparency is to provide, on request and subject to approval, de-identified Individual Patient-Level Data for clinical studies. AstraZeneca has implemented a process to ensure only requests which meet scientific rigor and safeguard patient privacy, commercially confidential information and intellectual property are upheld. Any data to be shared is then de-identified according to AstraZeneca Policy which goes above and beyond the US HIPAA regulations (considered as a minimum requirement). The data is then made available securely to the requestor for a timeframe that is dictated both in the approved use of the data and for a specific duration as defined within the Data Sharing Agreement put in place between AstraZeneca and the requestor.

INTRODUCTION

The poster outlines AstraZeneca's policy on Clinical Trial Transparency, the processes followed in the external sharing of patient-level data and the degree of de-identification applied to the data.

CLINICAL TRIAL TRANSPARENCY

AstraZeneca's policy on Clinical Trial Transparency is aligned with US and EU regulatory and legal requirements, European Medical Association Policy and EFPIA/PhRMA joint principles for responsible clinical data sharing. AstraZeneca's commitment is met by timely release of clinical study information providing details of (1) interventional (Phases 1-4 inclusive) clinical studies in healthy subjects and patients involving AstraZeneca products and (2) qualifying non-interventional studies in patients.

The Clinical Trial Transparency Task Force is a dedicated team within AstraZeneca whose strategic goal is to establish a single, unified and centralised office for meeting our Clinical Trial Transparency obligations and ensuring that we are compliance with external regulations and internal policies.

The focus of the task force is on four key areas:

- Patient Engagement
 - Sending Thank-you notes to patients for participation in trial
 - Sending ongoing study updates after a patient's last visit, but before last subject last visit
 - Sharing Lay Language summary of trial results with patients and post to EU portal
- Clinical Trial Posting
 - Information on registration and results of studies posted to:
 - AstraZenecaClinicaltrials.com
 - EudraCT (ClinicalTrialsRegister.eu)
 - ClinicalTrials.gov
- Redacted Documents
 - A redacted Clinical Report Package to be made available, to include:

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- Clinical Overview
 - Clinical Summary
 - Clinical Study Protocol
 - Sample Case Report Form
 - Statistical Analysis Plan
 - Clinical Study Report
- **De-identification of Individual Patient Level Data**
 - To be made available on request (subject to approval as per the formal review process outlined below)

EXTERNAL SHARING OF INDIVIDUAL PATIENT LEVEL DATA

Regarding external requests for access to Individual Patient Level Data, AstraZeneca has implemented a process to ensure that requests meet scientific rigour and safeguard patient privacy and commercially confidential information, and are responded to in a consistent manner.

Once a request has been submitted via the data request portal the following process begins:

- ✓ A triage review takes place to ensure that the request is complete and meets the requirements as outlined on the data sharing request portal before any action will commence by AstraZeneca
- ✓ AstraZeneca's Internal Due Diligence Review is undertaken to ensure that the data requested is in scope, and an information sharing assessment report is produced to confirm that there are no issues with patient privacy and the permission contained in the Informed Consent Form. In scope studies are defined as:
 - AstraZeneca-sponsored interventional Phase 1-4 patient studies
 - Studies initiated (defined as First Subject In (FSI)) since 2009
 - Studies that have been provided to health authorities to support approved indications in either US, EU or Japan and the approval process completed in all intended regions
 - *Compounds whose further development has been discontinued are also in scope providing they are AZ sponsored interventional Phase 1-4 patient studies that were initiated (FSI) since 2009*
- ✓ If a study is deemed in scope, an Independent Scientific Review Board will review the request to determine if the proposal has clearly defined research questions and scientific merit, and a decision is made as to whether the data can be shared with the researcher
- ✓ If a request does not meet the criteria outlined above, then it is treated on a case by case basis, and AstraZeneca will make a final determination as to whether the data will be shared
- ✓ If the data is approved for sharing, it is then de-identified according to strict standards to protect patient privacy (going above and beyond the US HIPAA requirements)
- ✓ If requested, AstraZeneca will make available a redacted version of the CSR depending on the needs of the research, other information sources, e.g. annotated case report forms, dataset descriptions, definitions of derived variables and pseudo analysis code
- ✓ Before accessing the data, researchers will be required to sign a Data Sharing Agreement in order to confirm appropriate use of the data once shared
- ✓ The data is loaded into a secure multi-sponsor environment which the researcher will have access to for a specified period of time

Once a comprehensive information sharing assessment has been done and approval for external re-use of individual patient level clinical trial data has been granted the data must first be de-identified to protect the privacy of all trial subjects. Any personally identifiable information must be removed from the information rendering it impossible to identify an individual without the use of extreme and inappropriate efforts.

Looking closer at the degree of programmatical de-identification applied to Individual Patient Level Data, the steps below provide an example of how an AstraZeneca study data may be de-identified for external use using our strict de-identification standards:

- Subject ID & any related variables are replaced with a random number or removed
- Centre ID is replaced with a random number or removed
- Geographical locations smaller than a state are removed
- Remove all patient related dates whilst preserving study timings
- Remove all verbatim text
- Replace individual ages with 5 year age bands

Assess further data protection risks and consider appropriate actions as needed, studies in rare diseases and small populations will require particular attention:

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- Consider deletion of a small random proportion of information records
- Ensure the company, products and studies are not identifiable
- Consider aggregating/removing individual data which is extreme or unique

AstraZeneca is currently working with an external provider to build a first-of-its-kind dedicated patient-level de-identification solution for use with SAS datasets used to conduct the original analyses. This will help reduce the time and effort required to de-identify clinical trial data as well as documenting all de-identification activities and ensuring consistency within the Company. Additional custom programming may be required on a study by study basis. The platform is being launched in September 2015 for use by a dedicated resource of programmers. In the interim a series of SAS macros are available to undertake the more routine elements of de-identification.

CONCLUSION

AstraZeneca is committed to ensuring the company stays in compliance with new regulatory requirements being established by European Medical Agency (EMA), and that the company delivers on the Responsible Data Sharing Principles as defined by the trade associations EFPIA/PhRMA.

The goal of the Clinical Trial Transparency Task Force, responsible for leading these efforts, is to unify, centralise and transform Clinical Trial Transparency across the AstraZeneca Group of Companies to a consistent state of readiness and create a sustainable and repeatable approach for responding to data requests from external parties and for providing information required by EFPIA/PhRMA: 'Joint Principles of Responsible Data Sharing'.

When considering specifically the external sharing of Individual Patient Level Data the implementation of streamlined robust internal processes, comprehensive information sharing assessment, strict data de-identification standards, plus the use of innovative technology is key to bringing the right information, to the right people, at the right time whilst protecting a patient's identity and maintaining confidentiality.

REFERENCES

Global Standard for Clinical Trial Transparency
Global Standard for Sharing Individual Patient Level Data
Functional Standard for Data Privacy Related to Clinical Information Sharing and Use
Functional Standard for Clinical Information Sharing

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Natalie Andrews
AstraZeneca
11G Mereside
Alderley Park
Macclesfield
SK10 4TG
Natalie.Andrews@AstraZeneca.com