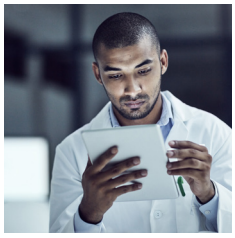
EFPIA-PHRMA PRINCIPLES FOR RESPONSIBLE CLINICAL TRIAL DATA SHARING

REPORT ON THE 2016 MEMBER COMPANY SURVEY




PREAMBLE

The European Federation of Pharmaceutical Industries and Associations (EFPIA) and the Pharmaceutical Research and Manufacturers of America (PhRMA) represent research-based biopharmaceutical companies. Our members discover, develop, manufacture, and market new medicines and vaccines to enable patients to live longer and healthier lives.

The development of new therapies to treat disease and improve quality of life is a long and complex process. A critical part of that process is clinical research, the study of a biopharmaceutical product in humans. Clinical trials generate incredible amounts of data that are used by sponsors to answer a specific set of questions; however, these data have the potential to be helpful in answering additional questions as well. To this end, our member companies make original datasets and other detailed clinical trial information available to qualified researchers, in an effort known as **data sharing**. Researchers then use these data in order to perform confirmatory analyses, but more often they use the data to explore answers to new questions in efforts to improve patient care and accelerate the development of new therapies.

The biopharmaceutical industry has long-established commitments to transparency throughout the lifecycle of a clinical trial including registration, results reporting, and data sharing. The biopharmaceutical industry has been at the forefront of initiatives to improve access to clinical trial data and has led the way in sharing patient-level data. Industry's commitments to data sharing are reflected in the joint EFPIA-PhRMA Principles for Responsible Clinical Trial Data Sharing. Under these Principles, biopharmaceutical companies voluntarily commit to enhancing data sharing with qualified researchers, working with regulators to adopt mechanisms for providing summary results to clinical trial participants, enhancing public access to the clinical study information, as well as reaffirm their commitment to consider all company-sponsored trials for publication and submit all phase 3 and other clinical trials of significant medical importance for publication.

The EFPIA-PhRMA Principles build on existing industry commitments to trial registration and routine disclosure of summary results (which are both now legislative and/or regulatory requirements in the major global markets), in addition to publication in scientific literature.

EXECUTIVE SUMMARY

BACKGROUND

The biopharmaceutical industry is committed to enhancing public health and advancing medical research through meaningful clinical trial data transparency. As part of the ongoing drive to improve transparency of clinical trial results, the biopharmaceutical industry developed a set of commitments to enable the responsible, routine sharing of clinical trial data and other detailed clinical trial information in a manner consistent with the need to safeguard patient privacy, respect the integrity of national regulatory systems, and maintain incentives for investment in biomedical research. These commitments were adopted in July 2013, as the EFPIA-PhRMA Principles for Responsible Clinical Trial Data Sharing (Principles), with implementation to begin on January 1, 2014. Under these Principles, biopharmaceutical companies voluntarily commit to enhancing data sharing with qualified researchers, working with regulators to adopt mechanisms for providing summary results to clinical trial participants, enhancing public access to the clinical study information, as well as reaffirm their commitment to consider all company-sponsored trials for publication and submit all phase 3 and other clinical trials of significant medical importance for publication.

METHODOLOGY

Between July and September 2016, PhRMA and EFPIA jointly administered a survey to (1) assess the degree to which member companies had implemented the commitments under the Principles, and (2) quantify the data sharing that occurred between the effective date of the Principles and the launch of the survey. The survey consisted of 30 questions and covered all five commitments outlined in the Principles. All member companies of at least one year's standing (of either EFPIA or PhRMA) at the time of the survey were invited to respond. The reported results reflect the membership of each association at the time the survey was completed.

RESULTS

All 44 member companies that met the inclusion criteria at the time of the survey responded yielding a 100% response rate. More than three-quarters of the member companies stated that they certify on a public website that they have systems and processes in place to implement the commitments made in the

Principles. 98% (43/44) of member companies confirmed that they share clinical trial information above and beyond existing legal and regulatory requirements.

84% (37/44) of member companies have a system or process in place for receiving requests for data of various types, and 64% (28/44) of companies had received at least one request since January 2014. The companies collectively reported 1,062 requests for data. Of those requests for which a decision had been made, 80% (750/935) were approved. The majority of requests for data, 64% (679/1062), were for patient-level data. Most companies (75%, 33/44) routinely post synopses of Clinical Study Reports (CSRs) soon after first registration of a new medicine, and 98% (43/44) have a strategy for publishing clinical trial results.

CONCLUSION

The majority of member companies have systems and processes in place to receive and evaluate requests for detailed data from qualified researchers. 84% of member companies have systems and processes in place to facilitate routine data sharing, and 80% of the requests that had been reviewed by the close of the survey were approved. The Principles support enhanced data sharing while safeguarding patient privacy, respecting the integrity of national regulatory systems, and maintaining incentives for investment in biomedical research by protecting commercially confidential information. Implementation of the Principles further improves transparency around clinical trial information, and ensures that when more detailed data are needed to advance medical research, there is a mechanism in place to provide the desired information.

REPORT

I. INTRODUCTION

The last decade or so has seen a great deal of improvement in the transparency of clinical trial results. At present, legal and regulatory requirements in the United States and European Union cover the routine registration and reporting of results for certain clinical trials. Routine sharing of patient-level data or full Clinical Study Reports (CSRs) goes beyond what is currently legally required.

The biopharmaceutical industry believes that enhanced data sharing is in the best interests of patients, clinicians, and medical research. In order to enable clinical researchers to access more detailed trial data, in July 2013, the joint Principles for Responsible Clinical Trial Data Sharing (the Principles[1]) were adopted by the industry associations EFPIA (European Federation of Pharmaceutical Industries and Associations) and PhRMA (Pharmaceutical Research and Manufacturers of America). These Principles were designed to support detailed data sharing on request, while addressing the key challenges of safeguarding patient privacy, respecting the integrity of national regulatory systems, and maintaining incentives for investment in biomedical research by protecting commercially confidential information.

The Principles, approved by the Boards of both industry associations, set out a number of commitments including the establishment of systems and processes to enable the implementation of these Principles. Subsequently, in 2016, a survey was carried out amongst members of the two industry associations to assess progress in the routine adoption of the Principles.

The objectives of the survey were to assess the degree to which the member companies have implemented the commitments outlined in the Principles to date and to quantify the data sharing that has occurred since the Principles became effective in January 2014 and up to September 2016, the end of the survey.

II. METHODOLOGY

The survey consisted of 30 questions, and was constructed to cover the five commitments outlined in the Principles under the following banners:

1. Enhancing data sharing with researchers
2. Enhancing public access to clinical study information

1 European Federation of Pharmaceutical Industries and Associations. (2013) Joint Principles for Responsible Clinical Trial Data Sharing. Available at: https://www.efpia.eu/media/25666/principles-for-responsible-clinical-trial-data-sharing.pdf

3. Sharing results with patients who participate in clinical trials
4. Certifying procedures for sharing clinical trial information
5. Reaffirming commitments to publish clinical trial results

Most of the survey questions and analyses concentrated on evaluating how the member companies have been able to set up systems and processes to enable enhanced data sharing with researchers and to quantify the amount of data shared.

The inclusion criteria for the survey were those companies that had been full members of either EFPIA or PhRMA (or an affiliate member of EFPIA) for at least one year at the time the survey was administered. All 44 member companies fulfilling the inclusion criteria at the time were surveyed. Only one response was sought from each company.

The following results should be read bearing in mind that the membership of EFPIA and PhRMA is not static, and that the results presented reflect the status of the implementation of the Principles and the number of requests received and decided upon at the time of the survey.

III. RESULTS

All of the 44 eligible companies surveyed responded yielding a 100% response rate.

The survey revealed that 98% (43/44) of EFPIA and PhRMA member companies share clinical trial information beyond legal and regulatory requirements in a variety of ways, including:

- Participation in an external data sharing platform,
- Publication of trial results in peer-reviewed journals,
- Presentations at scientific congresses,
- Posting trial results on sponsors' own websites, and / or
- Sharing data with qualified researchers.

COMMITMENT 1: ENHANCING DATA SHARING WITH RESEARCHERS

84% (37/44) of companies have systems in place for receiving requests for different types of data, with at least two-thirds having systems for receiving requests for each data type: patient-level data, study-level data, protocols, and full CSRs.

This commitment calls for sponsors to establish systems and processes to receive and process requests for clinical trial data. The survey revealed the extent to which companies have systems or processes in place for receiving requests for each data type described in the Principles: patient-level data, study-level data, protocols, and full CSRs.

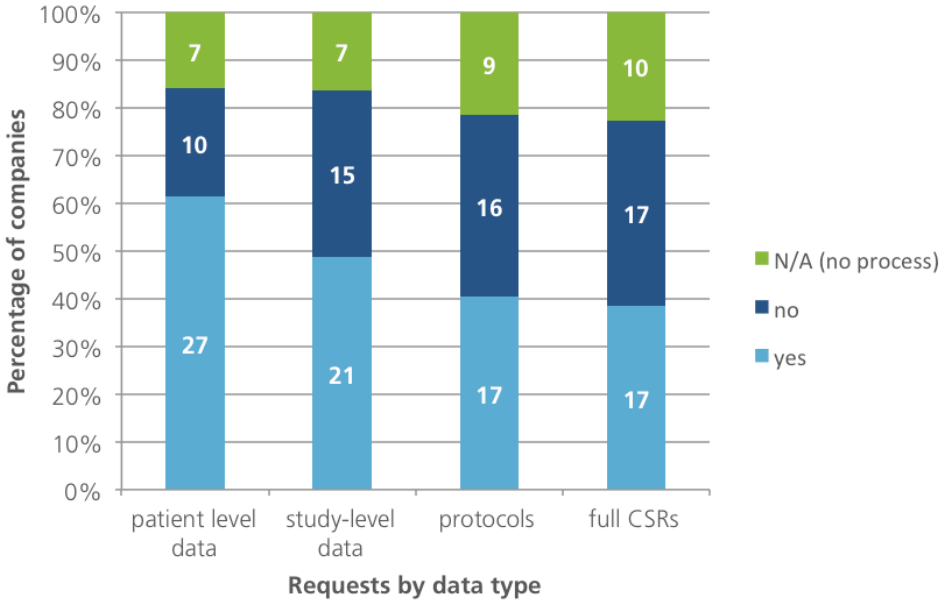
A substantial majority (84%) of our members now have systems or processes in place for receiving requests from qualified researchers for access to clinical trial data. Requests are accepted a number of ways, including through online in-take systems/web forms and email. Only 16% (7/44) did not have any system or process for receiving requests for data at the time of the survey.

82% of companies confirmed they have a system to receive and process requests for patient-level data, 80% for requests for study-level data, 73% for requests for protocols, and 70% for requests for full CSRs.

More than half of the member companies surveyed (64% or 28/44) received at least one request for trial data between the effective date of the Principles (January 1, 2014) and the administration of the survey (July to September 2016).

More than half of the companies surveyed received at least one request since January 1, 2014 (Fig. 1). 61% had received requests for patient-level data, 49% had received requests for study-level data, 40% had received requests for protocols, and 39% had received requests for full CSRs. 20% of member companies had not received requests for any type of data, but it is important to note that this was not limited to companies that did not have a system or process in place for receiving requests; there were companies with established systems that did not receive requests for data.

Figure 1. Percentage of companies that received requests by data type



A minority of companies (11%, 5/44) had received requests for the purpose of reanalyzing the data. Of these, only four companies had received requests for patient-level data; two companies for study-level data; one company for protocols; and one company for full CSRs. At the time of the survey only two companies reported that the sharing of data had led to publications.

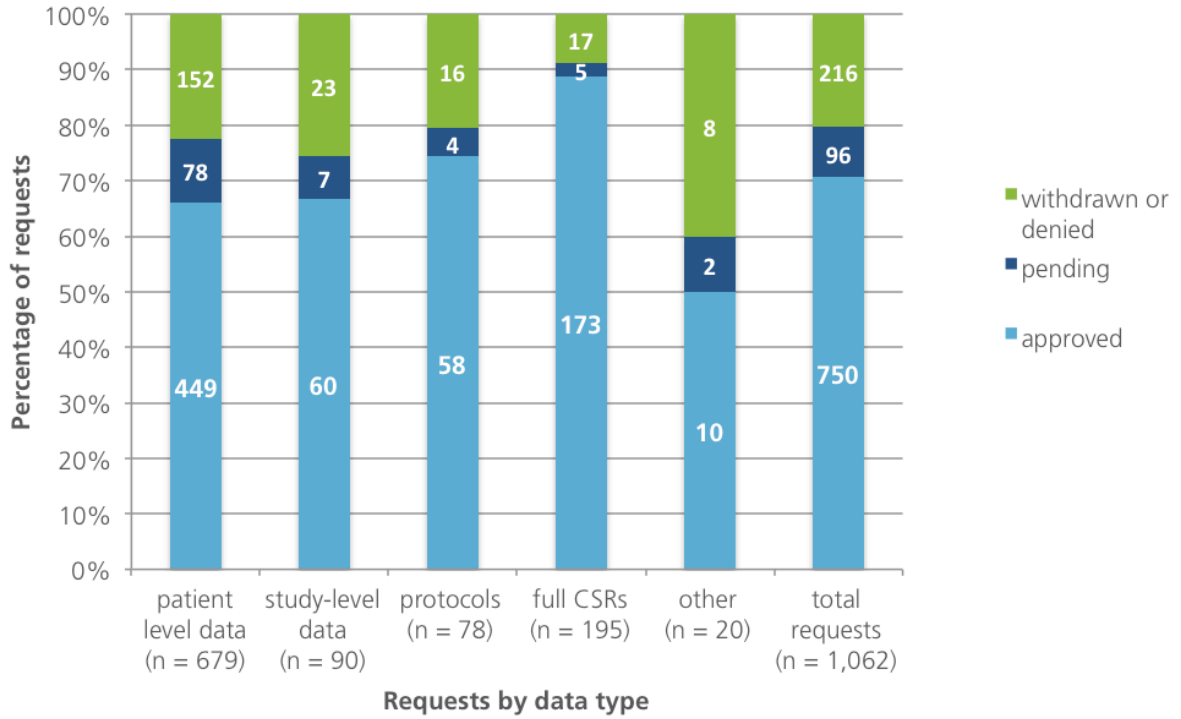
A majority of companies (61%, 27/44) stated that they had received requests for access to data in order to undertake novel analyses. Of these, 26 had received requests for patient-level data; 21 had received requests for study-level data; 17 for protocols; and 17 for full CSRs. Overall, at the time of the survey only 25% (11/44) of companies receiving these requests reported that researchers had published results from an analysis conducted with the shared data, although three additional companies were aware of manuscripts that had been submitted to journals.

> At the time of the survey, EFPIA and PhRMA member companies collectively documented more than 1,000 requests for clinical trial data since the Principles became effective on January 1, 2014. For all requests on which a decision had been made, 80% were approved.

Overall, the member companies reported receiving a total of 1,062 requests for data since the Principles became effective on January 1, 2014, of which 750 had been approved at the time of the survey, 9% (96/1062) were pending, 17% (185/1062) had been denied, and 3% (31/1062) had been withdrawn. A breakdown of total requests by data type is shown in Fig. 2.

Of those requests for which a decision had been made (i.e., excluding pending and withdrawn requests), 80% (750/935) were approved. Many of those denied were because the data requested pre-dated the effective date of the Principles. Requests were also denied for a variety of other reasons such as the informed consent for the trial did not allow for data sharing, researchers failed to submit a research proposal with their request or otherwise submitted incomplete applications, the requested data were undergoing review by a regulatory authority in support of marketing authorization, or the requested data were from a trial that was still ongoing at the time of the request. There were also cases where requests were denied because the data could not be sufficiently anonymized to safeguard patient privacy. Protecting the privacy of patients who participate in clinical trials is a critical obligation of biopharmaceutical companies that sponsor and conduct medical research and it is sometimes necessary to limit the availability of patient-level data for trials involving patients whose data are likely to be re-identified. For this reason, companies generally withhold patient-level information from disclosure when patient privacy could be jeopardized. The risk of "re-identification" is significantly higher when the number of patients is small, such as is typically the case for trials involving patients with rare diseases, which may include as few as 25 or fewer patients.

*Figure 2. Status of all received requests by data type at the time of the survey**



**Given the small number of withdrawn requests (n=31) and for visual simplicity of this figure, the number of withdrawn requests are combined with the number of denied requests.*

64% (679/1062) of all requests were for patient-level data, 8% (90/1062) for study-level data, 7% (78/1062) for protocols, and 18% (195/1062) for full CSRs. 2% (20/1062) of all requests were for other types of data (e.g., imaging scans). These numbers do not necessarily reflect that there is less interest in data types other than patient-level data. Certain company practices can account for the differences in the numbers shown; for example, some companies publicly post certain types of data so there is not a need to request that data. There are also cases where supporting data (e.g., protocols) may be provided automatically upon approval of a request for access to patient-level data, therefore researchers would not need to submit a separate request for the protocol.

COMMITMENT 2: ENHANCING PUBLIC ACCESS TO CLINICAL STUDY INFORMATION

Following the regulatory approval of a new medicine in the US and EU, three-quarters of the member companies (33/44) routinely post synopses of all relevant CSRs on a publicly available website. About half of the survey respondents post these summaries on their own websites. Few companies routinely post full CSRs on their own websites.

COMMITMENT 3: SHARING RESULTS WITH PATIENTS WHO PARTICIPATE IN CLINICAL TRIALS

Industry is working with regulatory authorities through its associations to define how results of clinical trials can be routinely communicated to the patients who participated in them. In addition, over 40% (18/44) of companies contribute to external initiatives, such as TransCelerate and the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard, in order to develop an approach to providing lay summaries. A small number of companies (n = 5) are driving their own advocacy in this space, and are working on initiatives with regulators to provide lay summaries to research participants.

COMMITMENT 4: CERTIFYING PROCEDURES FOR SHARING CLINICAL TRIAL INFORMATION

The majority of respondents, 77% (34/44) confirmed that they certify on a publicly available website that they have established policies and procedures to implement the data sharing commitments outlined in the Principles.

COMMITMENT 5: REAFFIRMING COMMITMENTS TO PUBLISH CLINICAL TRIAL RESULTS

The overwhelming majority (98%) of EFPIA and PhRMA member companies stated that they employ a publication strategy for sharing clinical trial results through articles published in peer-reviewed journals.

IV. CONCLUSIONS

The survey was administered to all full EFPIA and PhRMA member companies (as well as EFPIA's affiliate members) of at least one year's standing at the time of the survey, and achieved a 100% response rate. The results are therefore fully representative of the member companies at the time the survey was conducted.

The survey results show that an overwhelming majority of companies have implemented the Principles, confirming our member companies' support of the commitments outlined therein. The sharing of patient-level data or full CSRs is not a legal requirement; therefore, implementation of the Principles in itself confirms that disclosure goes beyond legal requirements.

In implementing the commitments outlined in the EFPIA-PhRMA Principles, the overwhelming majority of member companies confirm their commitment to sharing detailed clinical trial data, which is in the best interests of patients, clinicians, and further medical research. At least 84% of these companies now have formal processes in place to facilitate routine data sharing, and with 80% of requests for data having been approved, the survey shows that considerable data sharing is now taking place.

The EFPIA-PhRMA Principles for Responsible Clinical Trial Data Sharing support enhanced data sharing while safeguarding patient privacy, respecting the integrity of national regulatory systems, and maintaining incentives for investment in biomedical research. The results of this survey confirm the biopharmaceutical industry's commitment to transparency around clinical trial information, building on prior commitments to trial registration, routine disclosure of summary results, and publication[2,3], and ensure that when more detailed data are needed to advance medical research, there is a process for providing the desired information.

The biopharmaceutical industry believes that disclosure of clinical trial results and responsible sharing of clinical trial data is in the best interests of patients, clinicians, medical research, and the biopharmaceutical industry. EFPIA and PhRMA member companies have made significant progress in developing processes for clinical trial data access schemes and translating principles into practice.

2 IFPMA Joint Position on the Publication of Clinical Trial Results. 10 June 2010. Available at: https://www.ifpma.org/wp-content/uploads/2010/11/Joint-Position-on-Publication-of-CT-Results-in-Literature-Revised-Oct2017vF.pdf

3 IFPMA Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases. Updated 10 November 2009. Available at: https://www.ifpma.org/wp-content/uploads/2010/11/Joint-Position-on-Disclosure-of-CT-Info-via-CT-Registries-Revised-Oct2017-vF.pdf

GLOSSARY

CLINICAL STUDY REPORT

A clinical study report (CSR) on a clinical trial is a very long and detailed document giving much detail about the methods and results of a trial. A CSR is a scientific document addressing efficacy and safety, not a sales or marketing tool; its content is similar to that of a peer-reviewed academic paper.

PATIENT-LEVEL DATA

Information on individual patients collected during a clinical study, including: demographic data, lab results, baseline characteristics, drug concentration, biomarker and pharmacogenetic data, and adverse events experienced.

PROTOCOL

Clinical trial design information and **protocols** direct investigators how to run a particular trial. Protocols give instructions to the investigators on, for example, what drug to give and when, what trial measurements to take and when and how to record them, and how to treat and record adverse events.

SPONSOR

A sponsor can be defined as "a person oversees the clinical study and is responsible for analyzing the study data". The sponsor may be an individual or a pharmaceutical company.

STUDY-LEVEL DATA

Study-level data consist of patient-level data that have been amalgamated, compiled and tabulated, manipulated, stratified, or otherwise organized into study-level data sets, to be used in interpreting the outcome of a clinical study. Study-level data present clinical trial data in an objective manner, without subjective analysis or interpretation, usually in tabular, graphic, or statistical form showing, for example, averaged, stratified, or patterned presentations of study data gathered. Examples would include a table that presents cross-patient data on baseline patient characteristics (demographic and disease-related), patient disposition (i.e., numbers/percentages of patients who completed or discontinued the trial), endpoints (primary, secondary, and other), study drug exposure, adverse events, vital signs, and laboratory and other safety measures provided for the overall study population, and by subgroups.

SYNOPSES

Synopses are summaries of more extensive clinical study reports (CSRs).