Commitments by the biopharmaceutical industry to clinical trials transparency: the evolving environment

Slavka Baronikova, publication lead,[1] Jim Purvis, medical writer,[2] Eric Southam, communication director,[2] Julie Beeso, global quality director,[2] Christopher C Winchester, chief executive officer,[2] Antonia Panayi, medical evidence generation head[1]

[1]Shire International GmbH, Global Medical Affairs, Medical Shared Services, Zug, Switzerland

[2]Oxford PharmaGenesis, Oxford, UK

Correspondence to:

S Baronikova, Shire International GmbH, Global Medical Affairs, Medical Shared Services, Zug, Switzerland, sbaronikova-c@shire.com

E-mail:

Jim Purvis, jim.purvis@pharmagenesis.com

Eric Southam, eric.southam@pharmagenesis.com

Julie Beeso, julie.beeso@pharmagenesis.com

Christopher Winchester, chris.winchester@pharmagenesis.com

Antonia Panayi, apanayi@shire.com

Abstract

Introduction

All sponsors of clinical research have ethical obligations to register protocols and report the results of their studies in a timely and transparent manner; and for applicable trials, they must also comply with the legal requirements imposed by regulators.

Objective

To evaluate the extent to which biopharmaceutical companies that are members of the European Federation of Pharmaceutical Industries and Associations (EFPIA) and/or the Pharmaceutical Research and Manufacturers of America (PhRMA) have made public their commitments to clinical trials disclosure, in comparison with non-members, and to assess the extent to which they are disclosing clinical trial data, in comparison with non-members and non-industry funders.

Methods

Websites of the top 50 biopharmaceutical companies ("top 50 companies") as ranked by 2015 global sales were searched for statements relating to clinical trial data disclosure. The disclosure of data to April 2017 by biopharmaceutical industry and non-industry sponsors with at least 30 interventional phase II-IV clinical trials registered on ClinicalTrials.gov and completed during 2006-2015 was assessed using the independent online tool TrialsTracker. Biopharmaceutical industry sponsors were stratified by sales and EFPIA/PhRMA membership.

Results

Among the top 50 companies, 30 were EFPIA/PhRMA members and were pharmaceutical/biotechnology companies; the 20 non-members were biopharmaceutical/biotechnology, generics/biosimilars, medical devices, intravenous products, plasma products, and nutraceuticals companies. A general statement committing to disclosure of clinical trial data was found on 26 of the top 50 company websites (52%): all 26 were EFPIA/PhRMA members. Disclosure statements were easily accessible (within four clicks) for 19 EFPIA/PhRMA members. A statement referring to the adoption of EFPIA/PhRMA disclosure principles was found on 20/30 (67%) member websites. Of 29 377 trials listed in TrialsTracker, 9511 were sponsored by 69 biopharmaceutical industry companies (mean 138 trials per company) and 19 866 were sponsored by 254 non-industry institutions (mean 78 trials per institution). The mean disclosure rate for these trials was 55%, with rates higher for industry (74%) than for non-industry sponsors (46%). For the 30 companies in TrialsTracker that were among the top 50 companies, the mean disclosure

rate was 76%. Within this group of 30 companies, 25 were EFPIA/PhRMA members, the mean disclosure rate for 25 EFPIA/PhRMA members and 5 non-members was 77% and 67%, respectively.

Conclusions

Our research shows that the majority of the top 50 biopharmaceutical companies have made public commitments to the disclosure of clinical trial data. For most EFPIA/PhRMA members, such commitments are easily accessible. Biopharmaceutical industry sponsors have responded to the ethical and legal demands of clinical trial disclosure to a greater extent than non-industry sponsors.

Key words

Clinical trials, transparency, disclosure, reporting

What is already known on this topic

Clinical trial sponsors are ethically bound to register every trial and report the results in a timely fashion

Not all clinical trials are reported via public registries and/or primary manuscripts

By joining the European Federation of Pharmaceutical Industries and Associations (EFPIA) and/or the Pharmaceutical Research and Manufacturers of America (PhRMA), biopharmaceutical companies make a commitment to reporting clinical trial data

What this study adds

Publicly stated commitment to transparency in clinical trial disclosure is more common among biopharmaceutical companies that are members of EFPIA and/or PhRMA than among non-members

Three quarters of studies sponsored by the biopharmaceutical industry were reported on ClinicalTrials.gov.

Most undisclosed clinical trials are sponsored by non-industry funders such as government agencies, research charities, and universities rather than by the biopharmaceutical industry.

Introduction

A perceived lack of transparency, including under-reporting of results, undermines the confidence of healthcare professionals and patients in conclusions based on clinical trials.[1] All clinical trial sponsors, be they biopharmaceutical companies or non-industry bodies such as government agencies, universities, and research charities have ethical obligations to register and disclose trials.[2 3] In the USA, EU (Table 1) and other countries, it is required that certain types of clinical trial are registered and their results posted on dedicated registries (e.g. EudraCT, the EU electronic Register of Post-Authorisation Studies and ClinicalTrials.gov).[4-11] Other bodies, such as the World Health Organization (WHO) and the International Committee of Medical Journal Editors (ICMJE), have issued transparency standards and recommendations,[2 12-14] and some biopharmaceutical companies have websites dedicated to their own trial results.[15 16] This makes the clinical trial data transparency environment highly complex and diverse.

Within the biopharmaceutical industry, which is responsible for approximately one-third of all clinical trials,[17 18] two large associations, the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the Pharmaceutical Research and Manufacturers of America (PhRMA), have developed joint “Principles for responsible clinical trial data sharing”.[19] These joint principles, which became effective on 1 January 2014, make the following five commitments:

1. to enhance data sharing with researchers
2. to enhance public access to clinical study information
3. to share results with patients who participate in clinical trials
4. to certify procedures for disclosing clinical trial information
5. to reaffirm commitments to publish clinical trial results.

In the present study, we set out to evaluate the extent to which EFPIA/PhRMA members and non-members among the leading biopharmaceutical companies have committed to responsible clinical trial data disclosure. We also evaluated the reporting of results from clinical trials sponsored by biopharmaceutical companies compared with other sponsors.

Methods

Commitment to disclosure of clinical trial data

The global public websites of each EFPIA and/or PhRMA ("EFPIA/PhRMA") member and non-member company in the top 50 companies by 2015 worldwide prescription sales ("top 50 companies")[20] were searched by one researcher (JP) for direct links to pages containing: (i) a general statement of commitment to disclosing clinical trial data; (ii) a general statement of commitment to disclosing clinical trial data referencing EFPIA/PhRMA joint principles; and (iii) specific statements detailing commitments to upholding the five individual EFPIA/PhRMA joint principles for responsible disclosure of clinical trial data. If no direct links to such pages were found, the website's free-text search function was used to search for statements relating to clinical trial data disclosure and implementation of the EFPIA/PhRMA disclosure principles using the key words "EFPIA" or "PhRMA", "data sharing", "clinical trials", and "transparency". EFPIA /PhRMA membership was determined from the websites of these two organizations (www.efpia.eu/about-us/membership and http://www.phrma.org/about/members).

Ease of access to relevant information was assessed, with good access rated as requiring no more than four clicks from the homepage of the company website[21] or a clear, direct link, and poor access rated as needing more than four clicks or requiring navigation to satellite websites (e.g. blogs).

Clinical trial results reporting

TrialsTracker is an independent, semi-automated, web-based tool that has been developed in an effort to incentivize sponsors of clinical trials to improve disclosure rates by highlighting the disclosure performance of individual sponsors (trials without results disclosed as a proportion of trials registered).[22] For clinical trial sponsors to be included in TrialsTracker, they must have more than 30 phase II-IV clinical trials registered on ClinicalTrials.gov that were recorded as completed after 1 January 2006 and at least 24 months before the most recent TrialsTracker update. Because the most recent update to the database was in April 2017, the latest studies to be included in this analysis were completed in April 2015.

Data detailing the number of trials registered on ClinicalTrials.gov by clinical trial sponsor, and the corresponding number of those trials without results reported for each year from 2006 to 2015, were downloaded as a comma-separated values (CSV) file from the TrialsTracker website (https://trialstracker.ebmdatalab.net). TrialsTracker identifies sponsors as industry ("biopharmaceutical companies"; e.g. pharmaceutical/biotechnology, generics/biosimilars, medical devices, plasma products, and nutraceuticals, classified using information on the company websites that was found during the research for our study) or

non-industry (classified as National Institutes of Health, US Federal, or other in TrialsTracker) institutions. For each industry and non-industry sponsor, the number of disclosed trials and the percentage of eligible studies with disclosed results were calculated in Microsoft Excel 2016.

An analysis of disclosure rates was performed on subsets of the industry sponsors within TrialsTracker based on sales revenue (the top 50 companies)[20] and membership of EFPIA/PhRMA. An arbitrary disclosure rate threshold of 80% was applied to sponsor subgroups.

Exploratory analysis of results posted on websites other than ClinicalTrials.gov

In an exploratory analysis of clinical trial results found in locations other than ClinicalTrials.gov or in linked publications in PubMed were sought for three blindly selected studies each for four of the top 50 companies. ClinicalTrials.gov was searched by National Clinical Trial (NCT) identifier in order to establish the presence or absence of posted results and/or links to publications on PubMed. We made a separate search of PubMed, Google Scholar, and Google using the NCT identifier, and of EudraCT and the company's website based on NCT identifier and study title.

Data analysis

Disclosure rates for all industry sponsors, the top 50 companies, and EFPIA/PhRMA members in the top 50 companies were compared with non-industry sponsors.

Results

Commitment to disclosure of clinical trial data

EFPIA/PhRMA membership

Of the top 50 companies, six were EFPIA members only, two were PhRMA members only, 22 were both EFPIA and PhRMA members, and 20 were not EFPIA or PhRMA members. Of the 25 largest companies, 23 were EFPIA/PhRMA members compared with 7 of the next 25 companies. A breakdown of EFPIA/PhRMA membership among the top 50 biopharmaceutical companies is shown in figure 1.

All 30 EFPIA/PhRMA members in the top 50 companies were pharmaceutical/biotechnology companies, whereas the 20 non-members comprised pharmaceutical/biotechnology (n=8), generics/biosimilars (n=6), medical devices (n=1), both generics and medical devices (n=2), intravenous products and medical devices (n=1), plasma products (n=1), and nutraceuticals (n=1) companies. Of the two EFPIA/PhRMA non-members in the top 25 companies, one was a biotechnology company and the other was a generics company.

Access to a general disclosure statement

A general statement committing to disclosure of clinical trial information was found on 26 of the top 50 company websites (52%), all of which were EFPIA/PhRMA members (table 2). In 19 cases (38% of the top 50 companies; 63% of EFPIA/PhRMA members) the statement was found within four clicks of entering the website and in seven cases, access was rated as poor or non-existent. An analysis of the proportion of EFPIA/PhRMA members versus non-members in the top 50 companies with statements committing to responsible data transparency is shown in Supplementary material, table S2.

Specific EFPIA/PhRMA principles

An overview statement referring to the adoption of EFPIA/PhRMA principles was found on 20/30 (67%) websites of member organizations. Reference to all five joint principles was found for 16/30 (53%) members. Of non-member companies, only one made a specific disclosure statement (to enhance public access to clinical study information by making synopses of clinical study reports publicly available) (table 2). The most frequently communicated commitments were to share clinical trial data with researchers (83% of EFPIA/PhRMA members; 50% of the top 50 companies) and to publish clinical trial data (80% of members; 48% of the top 50 companies).

Clinical trial results reporting

Disclosure of clinical trial results by biopharmaceutical industry and non-industry sponsors

Of 29 377 trials listed in TrialsTracker, 9511 (32%) were sponsored by 69 biopharmaceutical companies (a mean of 138 trials per company) and 19 866 (68%) were sponsored by 254 non-industry institutions (a mean of 78 trials per institution) (figure 2). Of all undisclosed trials, 81% were sponsored by non-industry institutions and 19% were sponsored by industry. The mean disclosure rate for all trials was 55%, with rates higher for industry (74%) than for non-industry sponsors (46%) (figure 3; Supplementary material, table S1).

The overall disclosure rate for all clinical trials increased dramatically during 2007 and 2008 before declining thereafter. The maximum mean disclosure rate for all clinical trials was observed in 2008 (66%); for industry and non-industry sponsored trials, the maximum mean disclosure rate was in 2012 (83%) and 2009 (56%), respectively (figure 3). Disclosure rates for non-industry sponsors followed a trend similar to those for all sponsors, whereas those for industry sponsors were maintained at approximately 80% until 2014 (figure 3).

Variability between sponsor type in disclosure rate was high (figure 4A). The highest disclosure rate achieved by a non-industry sponsor was 84%, whereas two biopharmaceutical industry sponsors achieved 100% disclosure. An arbitrary disclosure rate

threshold of 80% was reached by fewer than 1% of non-industry sponsors compared with 39% of industry sponsors. Of the 69 biopharmaceutical industry sponsors with results in TrialsTracker, the 80% threshold was met by 56% of EFPIA/PhRMA members in the top 50 companies, 20% of EFPIA/PhRMA non-members in the top 50 companies, and 31% of biopharmaceutical industry sponsors that were not members of EFPIA/PhRMA.

The proportions of companies in the top 50 with statements committing to responsible data transparency that are EFPIA/PhRMA members and those that are non-members, are described in Supplementary material.

Disclosure of trial results by EFPIA/PhRMA members

Of the top 50 companies, a mean of 76% of trials were disclosed by the 30 EFPIA/PhRMA members and non-members with data reported in TrialsTracker (all of which were pharmaceutical/biotechnology companies). The mean disclosure rate for EFPIA/PhRMA members and non-members was 77% (25 companies) and 67% (5 companies), respectively. The arbitrary disclosure rate threshold of 80% was achieved by 14/25 (56%) members and 1/5 (20%) non-member companies (figure 4B).

Discussion

This analysis of the disclosure environment of clinical trial sponsors began with a review of the publicly stated disclosure policies of the top 50 biopharmaceutical companies. Of these, 26 companies (52%; all of which were members of one or both of the two leading international industry bodies, EFPIA and PhRMA) had disclosure policies available on their websites. Most (87%) EFPIA/PhRMA members communicated that they had a commitment to disclose clinical trials results and two thirds (67%) specifically referred to the EFPIA/PhRMA joint principles; approximately half (53%) described those principles in detail. While only EFPIA members are bound by these commitments, we found in our subsequent analysis that members of EFPIA/PhRMA had a higher rate of reporting clinical trial data than non-members.

To be useful, information on websites should be easy to find and have a logical flow. The 'three-click rule',[21] once a standard for web designers, is no longer regarded as the benchmark for website utility,[23] so we used four clicks as the cut-off for defining information as easy to find. Inherent in the principle of publicly committing to responsible data disclosure should be that the statements are easily accessible; however, this was true for only 63% of the EFPIA/PhRMA membership group.

The present research, which collates disclosure information on a large number of trials and sponsors worldwide over a 10-year period using data from TrialsTracker,[22] shows that

disclosure of clinical trial data remains suboptimal, with data for only just over half of phase II-IV trials registered on ClinicalTrials.gov and completed in the period 2006-2015 being disclosed by the end of April 2017. Over this period, biopharmaceutical industry sponsors performed better than non-industry sponsors with results disclosed by three-quarters of the former compared with less than half of the latter. Of undisclosed trials, just over 80% were originally funded by governmental, charitable, or academic institutions, compared with just under 20% by industry, even though approximately one-third of all trials in our data set were industry funded. Disclosure rates for both types of funder increased dramatically between 2007 and 2008, coinciding with mandatory reporting as required by the Food and Drug Administration Amendments Act 801 (FDAAA 801). For industry sponsors, disclosure rates were maintained for the next 6 years before declining slightly in 2015. This decline may reflect delays in the publication process, which typically takes about 2 years from study completion. With the implementation of the "Final Rule" in January 2018, there should no longer be delays in the posting of results from applicable clinical trials.[24-26] In contrast, disclosure rates for non-industry studies declined steadily after 2009 possibly reflecting the lack of policing of FDAAA 801.

The proportion of trials identified in the present study as sponsored by the biopharmaceutical industry (approximately one-third of all trials) was similar to that reported previously.[17 26] Whereas the disclosure rate for industry-sponsored studies was similar to that previously observed using TrialsTracker,[22] it is lower than rates reported for newly approved drugs in the USA and Europe,[27 28] and lower than or similar to rates of publication that have been reported by single sponsors.[24 25] Similarly, for non-industry studies, the disclosure rate was similar to that previously seen with TrialsTracker,[22] and lower than or similar to those reported for academic medical centres in the USA and the UK.[29 30]

Our assessment of biopharmaceutical company disclosure policies showed results similar to those of a recent EFPIA/PhRMA survey in which 77% of the 44 EFPIA/PhRMA members confirmed that they state on a publicly available website that they adhere to the joint principles.[31] In a recent survey of the internal disclosure policies of 25 top biopharmaceutical companies, 96% reported that they had a policy committing to the sharing of summary results in academic articles or on a clinical trials registry.[32] The fact that we found such commitments on the websites of only just over half of the top 50 companies in the present study suggests that many companies are missing the opportunity to share their disclosure policies.

In contrast to the results for EFPIA/PhRMA members, but in line with those for non-member companies, a preliminary review of commitments to data transparency that was conducted for 10 non-industry sponsors by total number of clinical trials completed in the period 2006-

2015 demonstrated that only one made reference to disclosure of clinical trial data (Supplementary material, table S3). The requirement for EFPIA/PhRMA members to commit to data disclosure publicly is reflecting clear differences between members and non-members/non-industry sponsors.

Because we used data from TrialsTracker, which searches for clinical trials on ClinicalTrials.gov using only NCT numbers, we made an exploratory search of alternative sources of clinical trial data for 12 clinical trials sponsored by four of the top 50 biopharmaceutical companies. Some results missing from ClinicalTrials.gov were found on EudraCT and company websites, suggesting that TrialsTracker was underestimating the number of trials with published results. The inclusion of the study, NCT, and EudraCT numbers in the abstract of publications linked to clinical trials would help to improve transparency in the disclosure of clinical trial data.[7]

The problem of incomplete and inconsistent clinical trial disclosure still remains, despite public awareness campaigns and the introduction of various policies, legislation, and even fines. There is also a human side that must be considered: patients participate in trials in the hope that they will help further the understanding of their condition and its treatment options. Not disclosing the results of trials may be viewed by trial participants as a betrayal of the trust they have placed in the trial sponsor. Company-sponsored trials have been the focus of many of these activities because of perceived commercial influence.[22] However, the present data demonstrate that trials sponsored by the biopharmaceutical industry are disclosed far more often than non-industry funded studies. The results of our analysis are backed up by a recent study which reported that industry funders disclosed the results a higher proportion of their trials than non-industry funders.[33] This may reflect the considerable resources that commercial organizations have devoted to clinical trial disclosure. They also suggest that the focus of future efforts to improve trial disclosure should shift to harmonization of clinical trial data transparency principles. This should be achieved by active discussion between, and endorsement by, all stakeholders including clinical trials sponsors, regulatory, and other public bodies (e.g. WHO, ICMJE, EU Council), as well as those campaigning for increased transparency of clinical trial information. Simplification of transparency rules and regulations, the implementation of a single identifier that can be used across all registries and results databases, and imposing the scrutiny of compliance should extend across all aspects of clinical trials and those who sponsor them.

Currently, transparency around clinical trial disclosure is very complex and is hindered by the absence of harmonized rules and a globally applicable platform that encompasses all registration and reporting of clinical trials for all sponsors. Such harmonization and

simplification would require agreement on the definition of transparency and clinical trials disclosure, and the process of how this should be managed in practice.

We believe that well-defined EFPIA/PhRMA joint principles could be used as a basis for the development of harmonized transparency and disclosure principles, and meanwhile should be established as an example of best practice in order to encourage consensus.

Strengths and limitations

Our study was based on an evaluation of a large number of phase II-IV clinical trials from industry and non-industry sponsors over a 10-year period; however, several caveats should be considered when interpreting the results. First, we may not be able to generalize our findings to all sponsors and clinical trials because our analysis included sponsors of only 30 or more trials. (CCW has previously calculated that sponsors of 30 studies or fewer are responsible for approximately half of registered trials).[34] Secondly, only two types of disclosure were included: publication and posting of results on ClinicalTrials.gov. Because publications were identified through automated searches of PubMed for NCT numbers, identification and discoverability were limited to trials published with NCT numbers included in the secondary source ID field of PubMed, title or abstract.[35 36] Results disclosed elsewhere (e.g. institutional websites), or published without reference to the NCT number, could lead to the understating of disclosure rates. Thirdly, our study looked only at disclosure of registered studies and not all studies are registered; indeed, unregistered studies appear less likely to be published than registered studies.[37] Finally, our analysis of publicly available disclosure policies used key word searches focused on disclosure and so it is possible that specific publication policies were missed. Nevertheless, our findings do suggest that statements related to disclosure of results are difficult to find in many cases.

Conclusions

More than half of the top 50 biopharmaceutical companies had a readily available statement on their public website expressing commitment to the principles of data disclosure. More EFPIA/PhRMA members than non-members made a public commitment to disclosing clinical trial data, with half describing clearly the five EFPIA/PhRMA joint principles that, as member companies, they have committed to adopting.

The disclosure rate of 74% for industry sponsors is better than that of non-industry sponsors, which, on average, have disclosed the results of fewer than half of trials over the same period. The disclosure rate for all sponsors increased sharply between 2006 and 2008. Since then, the disclosure rate for non-industry sponsors has declined, but industry sponsors have maintained the improved rates of disclosure.

Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: SB is a consultant to Shire International GmbH; JP, ES, JB, and CCW are employees of Oxford PharmaGenesis, Oxford, UK; CCW owns shares in Oxford PharmaGenesis Holdings Ltd; AP is an employee of Shire International GmbH.

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Data sharing

The data presented in this article are updated from the following presentations:

Baronikova S, Purvis J, Beeso J, Southam E, Winchester C, Panayi A. Commitments to data sharing by pharmaceutical companies: the evolving environment. Presented at the 2017 European Meeting of the International Society for Medical Publication Professionals (ISMPP), London, UK, 17-18 January 2017 [poster presentation].

Baronikova S, Purvis J, Beeso J, Southam E, Winchester C, Panayi A. Commitments to data sharing by pharmaceutical companies: the evolving environment. Presented at the 2017 Annual Meeting of ISMPP, National Harbor, MD, USA, 1-3 May 2017. *Curr Med Res Opin* 2017;33(Suppl 1):7 [oral presentation].

Baronikova S, Purvis J, Beeso J, Southam E, Winchester C, Panayi A. Disclosure of results of clinical trials sponsored by pharmaceutical companies. Presented at the 2017 Meeting of the International Peer Review Congress (PRC), Chicago, IL, USA, 10-12 September 2017 [poster presentation].

Baronikova S, Purvis J, Winchester C, Southam C, Beeso J, Panayi A. Disclosure of results of clinical trials sponsored by pharmaceutical companies. Presented at the 2018 European Meeting of ISMPP, London, UK, 23-24 January 2018 [poster presentation].

This research has also been accepted for presentation at Evidence Live 2018, Oxford, UK, 18-19 June 2018.

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Table 1 Key elements of the "Final Rule", EMA clinical data publication policy 0070, and EMA clinical trial regulation EU no. 536/2014[7]

	FDAAA 801 the "Final Rule"[4]	EMA clinical data publication policy 0070[5]	EMA clinical trial regulation EU no. 536/2014[6]
Medicinal products covered	FDA-regulated products, which have not yet been approved, licensed, or cleared by the FDA	Centrally authorized products only	Investigational medicinal products regardless of whether they have a marketing authorization
Clinical studies covered	Includes all clinical trials for products as listed above	Clinical studies submitted to the agency as a MAA, Article 58, line extension, or new indication, regardless of where the study was conducted	Clinical trials conducted in the EU and paediatric trials conducted outside of the EU that are part of paediatric investigation plans
Documents published	Additional registration, summary results, full protocol, and SAP, and including more frequent updates to posted data	Clinical data overview (clinical overview, clinical summaries, and CSRs) and the anonymization report	All clinical trial-related information generated during the life cycle of a clinical trial (e.g. protocol, assessment of and decision on trial conduct, summary of trial results including a lay summary, study reports, inspections)
Publications channel	ClinicalTrials.gov	https://clinicaldata.ema.europa.eu	Future EU portal and database (https://eudract.ema.europa.eu until that time)
Effective date	18 January 2017	1 January 2015 (MAA or Article 58) or 1 July 2015 (line extension or new indication)	October 2018
Posted from	18 April 2018	October 2016	2019

CSR=clinical study report; EMA=European Medicines Agency; FDA=Food and Drug Administration; FDAAA=Food and Drug Administration Amendments Act; MAA=marketing authorization application; SAP=statistical analysis plan.

Table 2 Number of EFPIA and PhRMA member and non-member companies in the top 50 biopharmaceutical companies as ranked by 2015 worldwide prescription sales and their public commitment to disclosing clinical trial data

Top 50 companies: membership of EFPIA and/or PhRMA	General data sharing statement	EFPIA/PhRMA principles	Five EFPIA/PhRMA joint principles of responsible clinical data sharing					
			Commitment to sharing clinical trial data with researchers	Public availability of CSR synopsis as a minimum	Availability of results for trial participants	Public certification of adoption of EFPIA/PhRMA commitments	Commitment to publish clinical trial data (phase III minimum)	All five principles
Member (n=30)	26 (86.7%)	20 (66.7%)	25 (83.3%)	22 (73.3%)	18 (60.0%)	21 (70.0%)	24 (80.0%)	16 (53.3%)
Non-member (n=20)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total (n=50)	26 (52.0%)	20 (40.0%)	25 (50.0%)	23 (46.0%)	18 (36.0%)	21 (42.0%)	24 (48.0%)	16 (32.0%)

CSR=clinical study report; EFPIA=European Federation of Pharmaceutical Industries and Associations; PhRMA=Pharmaceutical Research and Manufacturers of America.

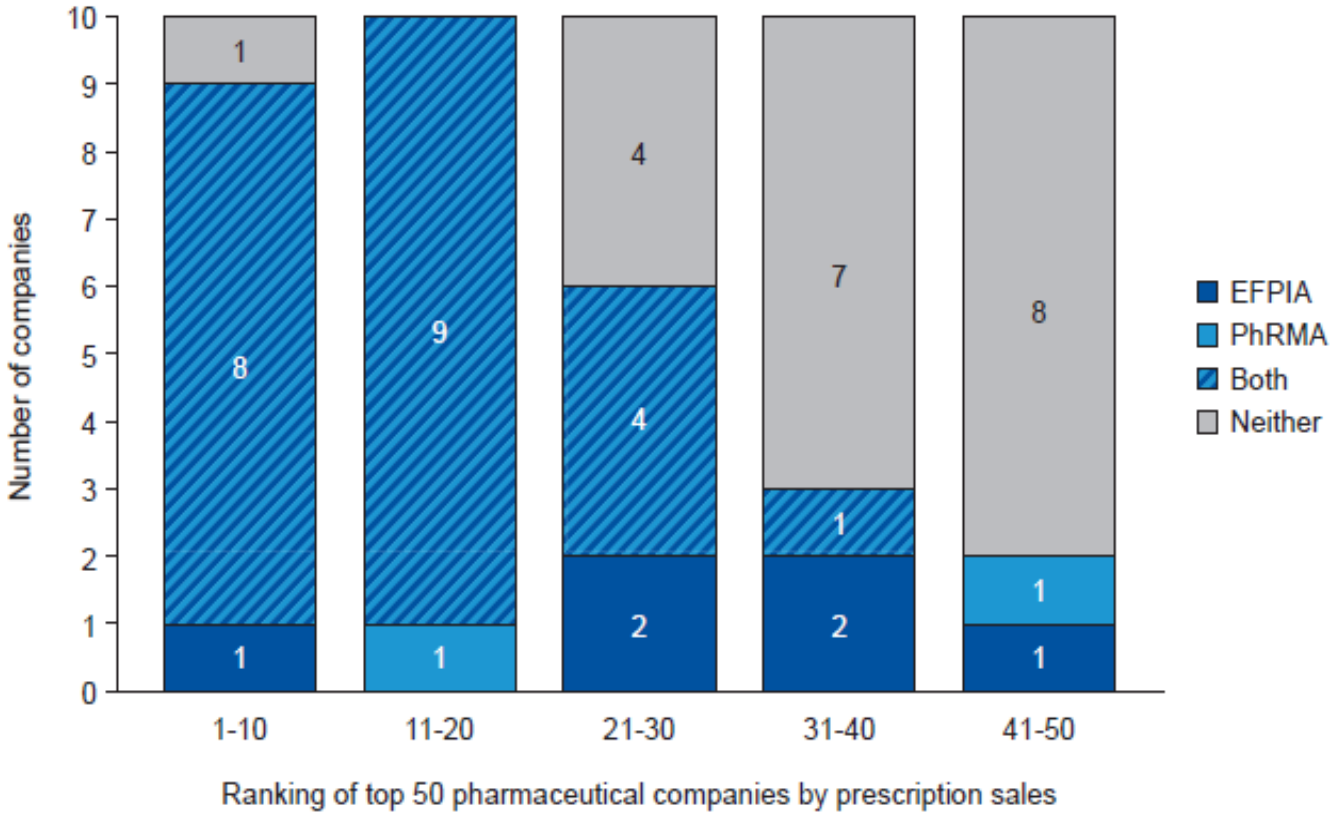

Fig 1 Membership of EFPIA/PhRMA according to worldwide prescription sales

EFPIA=European Federation of Pharmaceutical Industries and Associations; PhRMA=Pharmaceutical Research and Manufacturers of America.

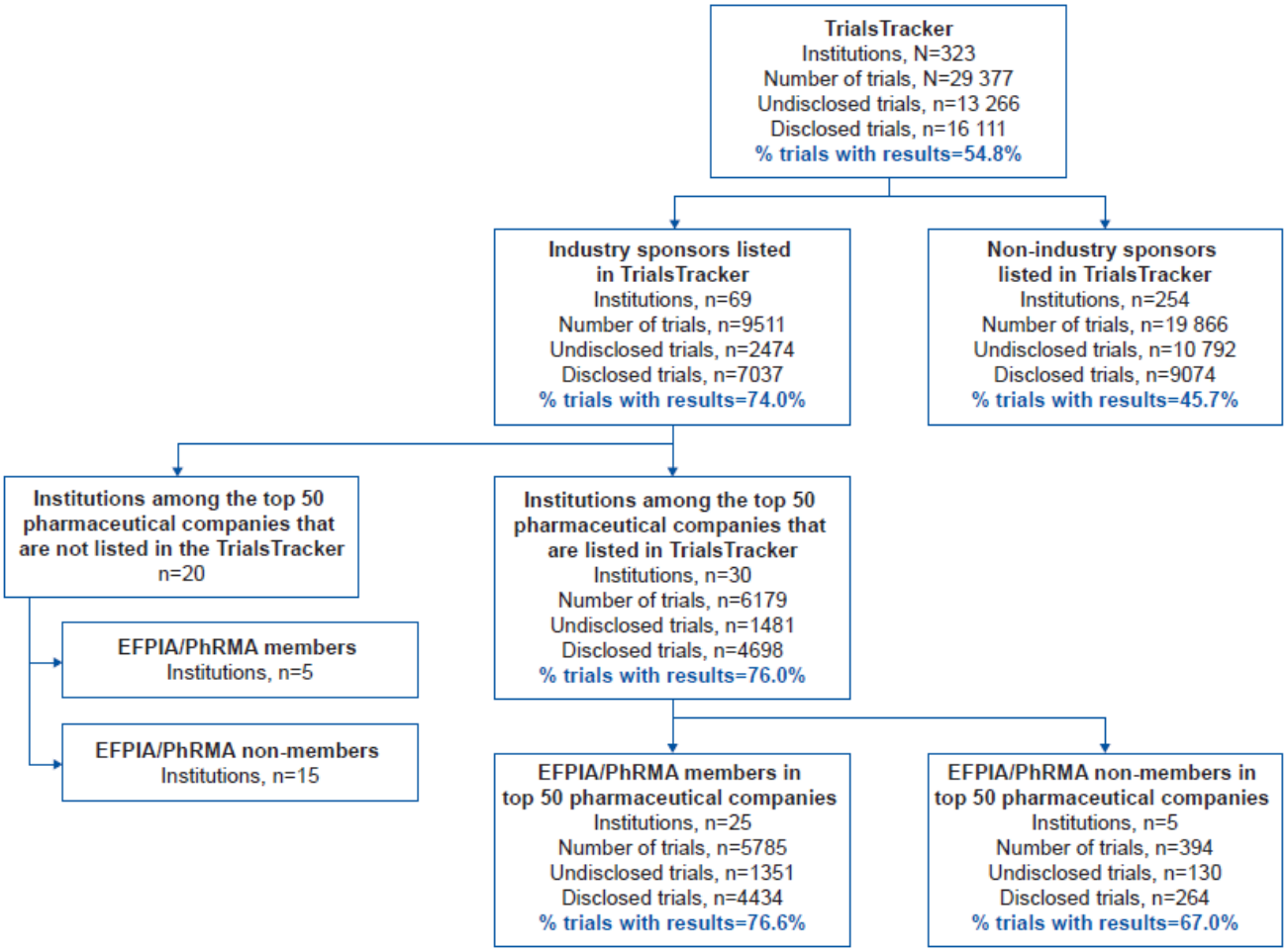

Fig 2 Types and numbers of sponsors represented in TrialsTracker, with their disclosure rates

EFPIA=European Federation of Pharmaceutical Industries and Associations; PhRMA=Pharmaceutical Research and Manufacturers of America.

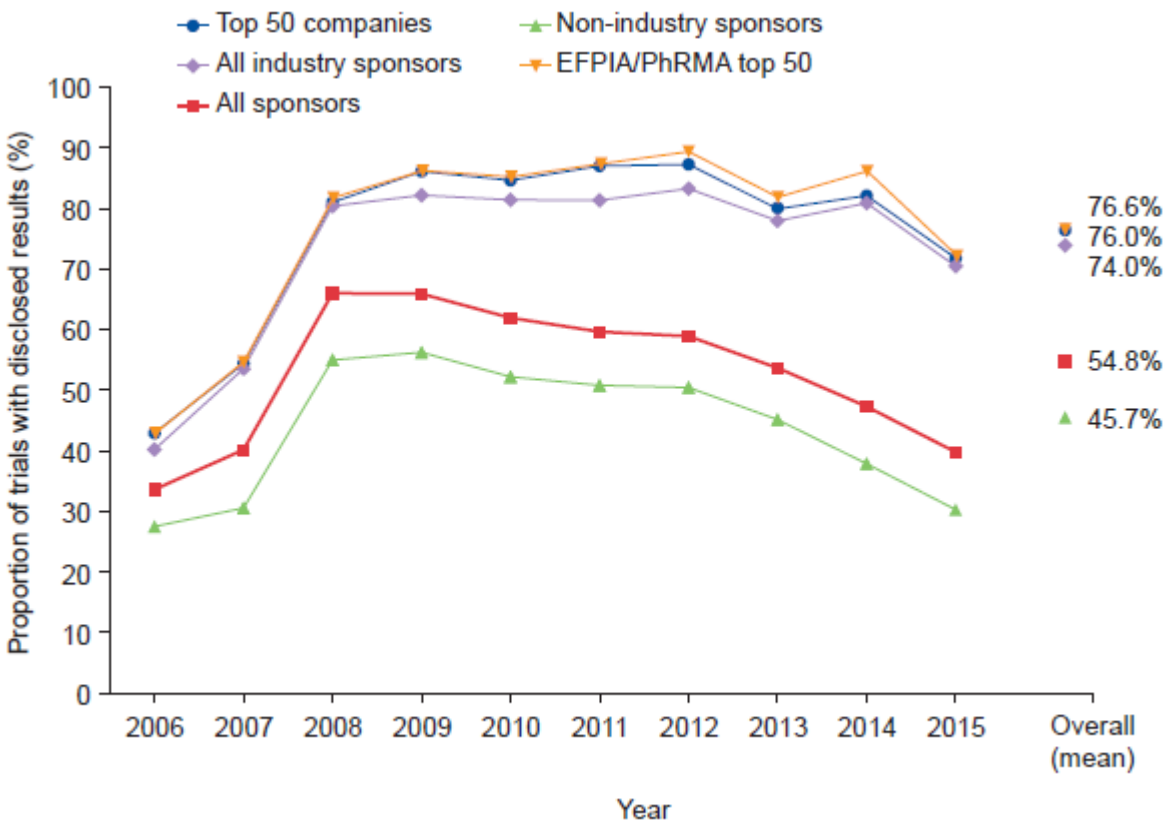

Fig 3 Disclosure of clinical trial results by sponsor type

EFPIA=European Federation of Pharmaceutical Industries and Associations; PhRMA=Pharmaceutical Research and Manufacturers of America.

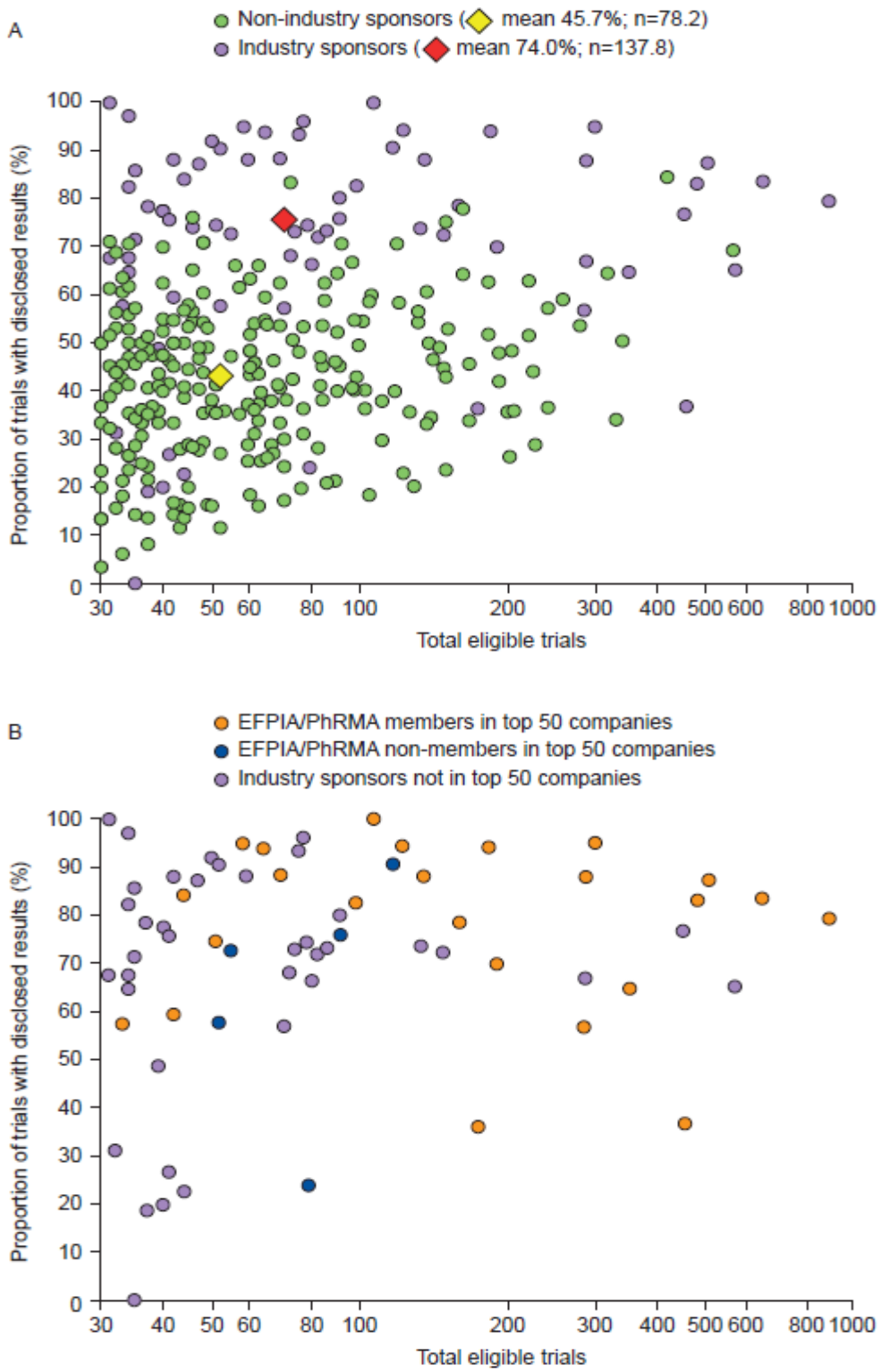

Fig 4 Disclosure rates versus total eligible trials for (A) biopharmaceutical industry and non-industry clinical trial sponsors and (B) industry-only sponsors, highlighting EFPIA/PhRMA members and non-members in the top 50 companies, and industry sponsors not in the top 50 companies

EFPIA=European Federation of Pharmaceutical Industries and Associations; PhRMA=Pharmaceutical Research and Manufacturers of America.

Supplementary material

Data analysis

A comparison of proportions (e.g. all industry, the top 50 companies, and EFPIA/PhRMA members in the top 50 companies compared with non-industry clinical trial sponsors, EFPIA/PhRMA members *v* non-members in the top 50 biopharmaceutical companies with statements committing to responsible data transparency) was calculated as follows (note that the comparison of clinical trial disclosure for industry and non-industry sponsors is used as an example):

- proportion of trials disclosed by industry (p^1) = $\frac{\text{disclosed industry trials } (n^1)}{\text{total industry trials}(N^1)}$
- proportion of trials disclosed by non-industry (p^2) = $\frac{\text{disclosed non-industry trials } (n^2)}{\text{total non-industry trials}(N^2)}$
- sample proportion ($\hat{p}$) = $\frac{((p^1 \times N^1)+(p^2 \times N^2))}{(N^1 + N^2)}$
- standard error (SE) = $\sqrt{((\hat{p} \times (1 - \hat{p}\,)) \times \frac{(N^1 + N^2)}{(N^1 \times N^2)})}$
- *z*-score = $\frac{(p^1 - p^2)}{SE}$

Confidence level	*z*-score (standard deviations)	P value
90%	< –1.65 or > +1.65	< 0.10
95%	< –1.96 or > +1.96	< 0.05
99%	< –2.58 or > +2.58	< 0.01

- 95% confidence interval for the difference in the proportion of disclosed clinical trials ($p^1 - p^2$):
  - lower limit = $(p^1 - p^2) - (1.96 \times SE)$
  - upper limit = $(p^1 - p^2) + (1.96 \times SE)$

The null hypothesis (H_0) was for no difference in the proportions of disclosed trials between industry and non-industry sponsors.

Table S1 Comparison of disclosure rates for all industry, the top 50 biopharmaceutical companies, and EFPIA/PhRMA members in the top 50 biopharmaceutical companies compared with non-industry sponsors

Year	Sponsor	Proportions	N	$\hat{p}$	$1-\hat{p}$	SE	z-value	Lower 95% CI	Upper 95% CI	Significance
2006	All industry	0.402	851	0.336	0.664	0.022	5.664	0.083	0.171	Proportions significantly different at 99%
	Non-industry	0.275	921							
2007	All industry	0.535	1063	0.401	0.599	0.020	11.674	0.192	0.269	Proportions significantly different at 99%
	Non-industry	0.305	1478							
2008	All industry	0.804	1361	0.660	0.340	0.017	14.892	0.221	0.288	Proportions significantly different at 99%
	Non-industry	0.550	1774							
2009	All industry	0.822	1223	0.659	0.341	0.017	15.165	0.226	0.293	Proportions significantly different at 99%
	Non-industry	0.562	2063							
2010	All industry	0.814	1108	0.619	0.381	0.018	16.356	0.257	0.327	Proportions significantly different at 99%
	Non-industry	0.522	2217							
2011	All industry	0.813	997	0.596	0.404	0.018	16.579	0.270	0.342	Proportions significantly different at 99%
	Non-industry	0.508	2444							
2012	All industry	0.833	914	0.589	0.411	0.019	17.384	0.291	0.365	Proportions significantly different at 99%
	Non-industry	0.504	2630							
2013	All industry	0.779	916	0.536	0.464	0.019	17.144	0.291	0.366	Proportions significantly different at 99%

	Non-industry	0.451	2609							
2014	All industry	0.809	763	0.473	0.527	0.020	21.033	0.390	0.470	Proportions significantly different at 99%
	Non-industry	0.378	2712							
2015	All industry	0.705	315	0.398	0.602	0.032	12.747	0.340	0.464	Proportions significantly different at 99%
	Non-industry	0.303	1018							
Overall	All industry	0.740	9511	0.548	0.452	0.006	45.626	0.271	0.295	Proportions significantly different at 99%
	Non-industry	0.457	19866							
	Top 50	0.760	6179	0.529	0.471	0.007	41.749	0.289	0.318	Proportions significantly different at 99%
	Non-industry	0.457	19866							
	EFPIA/PhRMA	0.765	5785	0.526	0.474	0.007	41.267	0.293	0.322	Proportions significantly different at 99%
	Non-industry	0.457	19866							

CI=confidence interval; EFPIA=European Federation of Pharmaceutical Industries and Associations; $\hat{p}$=sample proportion; PhRMA=Pharmaceutical Research and Manufacturers of America; SE=standard error.

Table S2 Comparison of the proportion of EFPIA and PhRMA members versus that of non-members in the top 50 biopharmaceutical companies as ranked by 2015 worldwide prescription sales with statements committing to responsible data transparency

EFPIA and/or PhRMA membership	Proportions	N	$\hat{p}$	$1-\hat{p}$	SE	z-value	Lower 95% CI	Upper 95% CI	Significance
General data sharing statement									
EFPIA only	1	6	0.231	0.769	0.196	5.099	0.616	1.384	Proportion significantly different from non-EFPIA/PhRMA at 99%
PhRMA only	0.5	2	0.045	0.955	0.154	3.237	0.197	0.803	Proportion significantly different from non-EFPIA/PhRMA at 99%
EFPIA and PhRMA	0.864	22	0.453	0.547	0.154	5.618	0.563	1.165	Proportion significantly different from non-EFPIA/PhRMA at 99%
EFPIA and/or PhRMA	0.867	30	0.520	0.480	0.144	6.012	0.584	1.150	Proportion significantly different from non-EFPIA/PhRMA at 99%
Non-EFPIA/PhRMA	0	20							
EFPIA/PhRMA principles									
EFPIA only	0.667	6	0.154	0.846	0.168	3.971	0.338	0.996	Proportion significantly different from non-EFPIA/PhRMA at 99%
PhRMA only	0	2	0.000	1.000	0.000	0.000	0.000	0.000	**Proportion not significantly different from non-EFPIA/PhRMA**
EFPIA and PhRMA	0.727	22	0.381	0.619	0.150	4.846	0.433	1.021	Proportion significantly different from non-EFPIA/PhRMA at 99%
EFPIA and/or PhRMA	0.667	30	0.400	0.600	0.141	4.716	0.390	0.944	Proportion significantly different from non-EFPIA/PhRMA at 99%
Non-EFPIA/PhRMA	0	20							
Commitment to sharing clinical trial data with researchers									
EFPIA only	1	6	0.231	0.769	0.196	5.099	0.616	1.384	Proportion significantly different from non-EFPIA/PhRMA at 99%
PhRMA only	0.5	2	0.045	0.955	0.154	3.237	0.197	0.803	Proportion significantly different from non-EFPIA/PhRMA at 99%

EFPIA and PhRMA	0.818	22	0.428	0.572	0.153	5.350	0.518	1.118	Proportion significantly different from non-EFPIA/PhRMA at 99%
EFPIA and/or PhRMA	0.833	30	0.500	0.500	0.144	5.771	0.550	1.116	Proportion significantly different from non-EFPIA/PhRMA at 99%
Non-EFPIA/PhRMA	0	20							
Public availability of CSR synopsis as a minimum									
EFPIA only	1	6	0.269	0.731	0.206	4.601	0.545	1.355	Proportion significantly different from non-EFPIA/PhRMA at 99%
PhRMA only	0	2	0.045	0.955	0.154	-0.324	-0.353	0.253	**Proportion not significantly different from non-EFPIA/PhRMA**
EFPIA and PhRMA	0.727	22	0.405	0.595	0.152	4.464	0.380	0.974	Proportion significantly different from non-EFPIA/PhRMA at 99%
EFPIA and/or PhRMA	0.733	30	0.460	0.540	0.144	4.747	0.401	0.965	Proportion significantly different from non-EFPIA/PhRMA at 99%
Non-EFPIA/PhRMA	0.05	20							
Availability of results for trial participants									
EFPIA only	0.667	6	0.154	0.846	0.168	3.971	0.338	0.996	Proportion significantly different from non-EFPIA/PhRMA at 99%
PhRMA only	0	2	0.000	1.000	0.000	0.000	0.000	0.000	**Proportion not significantly different from non-EFPIA/PhRMA**
EFPIA and PhRMA	0.636	22	0.333	0.667	0.146	4.367	0.351	0.921	Proportion significantly different from non-EFPIA/PhRMA at 99%
EFPIA and/or PhRMA	0.6	30	0.360	0.640	0.139	4.330	0.328	0.872	Proportion significantly different from non-EFPIA/PhRMA at 99%
Non-EFPIA/PhRMA	0	20							
Public certification of adoption of EFPIA/PhRMA commitments									
EFPIA only	1	6	0.231	0.769	0.196	5.099	0.616	1.384	Proportion significantly different from non-EFPIA/PhRMA at 99%
PhRMA only	0	2	0.000	1.000	0.000	0.000	0.000	0.000	**Proportion not significantly different from non-EFPIA/PhRMA**

EFPIA and PhRMA	0.682	22	0.357	0.643	0.148	4.607	0.392	0.972	Proportion significantly different from non-EFPIA/PhRMA at 99%
EFPIA and/or PhRMA	0.7	30	0.420	0.580	0.142	4.913	0.421	0.979	Proportion significantly different from non-EFPIA/PhRMA at 99%
Non-EFPIA/PhRMA	0	20							
Commitment to publish clinical trial data (phase III minimum)									
EFPIA only	1	6	0.231	0.769	0.196	5.099	0.616	1.384	Proportion significantly different from non-EFPIA/PhRMA at 99%
PhRMA only	0.5	2	0.045	0.955	0.154	3.237	0.197	0.803	Proportion significantly different from non-EFPIA/PhRMA at 99%
EFPIA and PhRMA	0.773	22	0.405	0.595	0.152	5.097	0.476	1.070	Proportion significantly different from non-EFPIA/PhRMA at 99%
EFPIA and/or PhRMA	0.8	30	0.480	0.520	0.144	5.547	0.517	1.083	Proportion significantly different from non-EFPIA/PhRMA at 99%
Non-EFPIA/PhRMA	0	20							
All five principles									
EFPIA only	0.667	6	0.154	0.846	0.168	3.971	0.338	0.996	Proportion significantly different from non-EFPIA/PhRMA at 99%
PhRMA only	0	2	0.000	1.000	0.000	0.000	0.000	0.000	**Proportion not significantly different from non-EFPIA/PhRMA**
EFPIA and PhRMA	0.545	22	0.285	0.715	0.140	3.906	0.272	0.818	Proportion significantly different from non-EFPIA/PhRMA at 99%
EFPIA and/or PhRMA	0.533	30	0.320	0.680	0.135	3.959	0.269	0.797	Proportion significantly different from non-EFPIA/PhRMA at 99%
Non-EFPIA/PhRMA	0	20							

CI=confidence interval; CSR=clinical study report; EFPIA=European Federation of Pharmaceutical Industries and Associations; PhRMA=Pharmaceutical Research and Manufacturers of America; $\hat{p}$=sample proportion; SE=standard error.

Table S3 Availability of reference to transparency in clinical trial data disclosure for non-industry institutions

Institution	Total eligible trials	Proportion of trials disclosed, %	Reference found to transparency in clinical trial data disclosure?
1	570	69.1	Yes
2	418	84.4	No
3	339	50.4	No
4	329	34.0	No
5	318	64.5	No
6	278	53.6	No
7	259	59.1	No
8	241	36.5	No
9	241	57.3	No
10	226	28.8	No