Association of the British Pharmaceutical Industry
7th Floor, Southside, 105 Victoria Street, London SW1E 6QT
t +44 (0)870 890 4333 www.abpi.org.uk

abpi

Bringing medicines to *life*

Clinical Trial Transparency: Technical standards for data sharing for old, current and future clinical trials

Report of a technical workshop organised by the ABPI in partnership with the PSI, December 2013

Preface

On 5 December 2013, the ABPI, in partnership with the PSI (Statisticians in the Pharmaceutical Industry) organised a stakeholder workshop to examine the practicalities of data sharing for current, future and past clinical trials. The workshop was a follow up to an event held in March 2013, which examined definitions and guiding principles and established a framework for further discussions[1].

The workshop brought together a range of stakeholders from industry, academia, funding bodies, data analysis organisations and other fields, to discuss the key practical challenges to greater data sharing and how they might be addressed.

Executive summary

The desirability of wider clinical data sharing is now widely recognised by all parties. However, while the principle is well established, how it can best be achieved remains the subject of much discussion.

Increasingly, companies are establishing mechanisms that will make recent and future clinical trial data easier to access. However, accessing information from historical trials becomes more complex as the time elapsed since study conduct increases.

Practical difficulties, along with the volume of data that could theoretically be made available, may necessitate an incremental approach to the delivery of data from historical studies. The workshop discussed what systems could support that incremental delivery and how efforts should be prioritised.

A possible avenue is to create routine mechanisms to provide access to recent data and defined historical data, while responding to specific requests for datasets linked to other trials. This is the approach that has been adopted by, for example, GSK and Roche.

The question of the scope of the original informed consent to a study has been cited as a significant barrier to the sharing of data from clinical studies. Some companies expressed the view that once data are anonymised they fall outside the scope of current data protection legislation and there is, therefore, no barrier for sharing this data in a secure fashion with qualified researchers.

Companies are developing mechanisms to enable suitably skilled groups to access clinical trial data for bona fide purposes; however, these systems may be difficult for small companies to emulate. There is also varying levels of access to clinical data generated by academic research funders. There may be advantages to an industry-wide platform, potentially also able to handle data from academic trials.

An increased focus on re-analysis and meta-analysis of clinical trial data is emphasising a need for a more coordinated approach to data capture and management. There may be significant benefits from greater standardisation of protocols, outcome measures and data recording.

Background

Decisions on the use of medicines are best made after analysis of all relevant data. Calls for greater clinical trial transparency over the years has lead industry to be more open, for example, through comprehensive trial registration and improving access to clinical trial data. Indeed, the first industry commitment to register and report results was made in 2005[2] and has been updated a number of times, while the FDA Amendments Act mandating trial registration and results reporting in the USA came into force in 2007.

[1] A report of the workshop is available at www.abpi.org.uk/our-work/news/2013/Pages/190413.aspx
[2] IFPMA Joint position on the disclosure of clinical trial information via clinical trial registries and databases, 6 January 2005, http://clinicaltrials.ifpma.org/clinicaltrials/fileadmin/files/pdfs/FINAL%20Position%20Clinical%20Trials%20Information%20January%2005.pdf

The Pharmaceutical Research and Manufacturers of America (PHRMA) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) in 2013 built on these existing industry commitments and produced a more recent set of Principles for Responsible Data Sharing[3]. In addition, a recent analysis commissioned by the ABPI revealed that, for new medicines approved by the European Medicines Agency (EMA) in 2009–11, some results from 89 per cent of trials had been disclosed by 31 January 2013[4].

Beyond these broad commitments, as discussed at the last workshop, there are additional complexities to consider. The terms 'clinical data' and 'clinical trial information', for example, cover a range of material from synopses and Clinical Study Reports (CSRs) to individual patient level data. In addition, while systems are being put in place to enhance data sharing for trials relating to new or recently launched medicines, historical trials can often present a different set of challenges.

The patient perspective

Dr Síle Lane of Sense About Science described the AllTrials campaign, which argues for registration of all trials, public disclosure of summary results and publication of Clinical Study reports (CSR's) where produced. Launched by Sense About Science and a range of UK and US bodies, AllTrials now has some 60,000 supporters. Its work has been endorsed by more than 400 organisations, including over 200 patient groups.

AllTrials makes the case that failure to publish findings is a betrayal of trust, with patients volunteering to take part in research on the understanding that data would be made available as a public good. The BMA and other bodies argue that clinicians running clinical trials have a responsibility to ensure that results are made available, and failure to do so should be considered professional misconduct. The GMC is currently considering this proposal.

Trial registers have existed for many years and registration has been mandated for certain studies for a number of years. From September 2013, the Health Research Authority (HRA) has required registration of all clinical trials as a condition for ethical approval. Existing registers accepted by the HRA include clinicaltrials.gov, which was made available to the public in 2000 and the EU Clinical Trials Register. Meanwhile, the EMA is adopting policies to ensure wider availability of trial data. While this and other moves continue to ensure that registration is routine, and future disclosure of results is enhanced, access to information from past trials remains a key topic for discussion – not least as this encompasses most of the evidence relating to medicines currently in use.

The academic data-generator perspective

As well as industry, charities and public funding bodies are also important funders of clinical trials, though may not act as the trial sponsor. A key question is the extent to which data-sharing principles and practices established for industry should also apply to academic studies. **Dr Fiona Reddington** described Cancer Research UK (CRUK)'s perspectives and the data-sharing challenges it faces.

CRUK supports research across the entire translational spectrum, including clinical trials. It supports eight clinical trials units, and since 2005/06 more than 210,000 patients have been enrolled into its trials.

CRUK faces a series of key questions. Which studies should data transparency apply to? What does good practice look like? And what practical steps can CRUK take to promote good practice? Furthermore, CRUK does not operate in isolation – it also works with other charities, pharmaceutical companies, public funding bodies and European organisations. Consistency of approaches would, therefore, be highly desirable.

[3] www.phrma.org/phrmapedia/responsible-clinical-trial-data-sharing
[4] Rawal B, Deane BR. Clinical trial transparency: an assessment of the disclosure of results of company-sponsored trials associated with new medicines approved recently in Europe. Curr Med Res Opin. 2013 Nov 11. [Epub ahead of print] PMID: 24168052

CRUK's clinical trials units have a potentially critical role to play. However, CRUK trials also take place outside these units, which may also conduct research in other disease areas. Multiple accreditation bodies and regulatory requirements add further complexity to the conduct of running clinical trials and many trials also have an international dimension.

CRUK does not specify what data management systems should be used, and there is as yet no consensus on the best available approaches. An ideal system would need to be internationally compatible, able to accommodate multiple data-sources from other systems and not be disease-specific. In discussions with trial organisers CRUK emphasises the entire data life cycle, so applicants think about later use of data when designing a trial. Efforts are made to conform to standards where they exist.

In response to requests for data CRUK seeks to identify the level of information required, whether it is being requested for a valid purpose, and how the results of any new analysis will be disseminated. However, CRUK currently has no infrastructure for sharing of clinical data. One possibility would be a partnership with other research funders to establish a shared platform; CRUK has also held discussions with GSK about the possibility of joining a multi-sponsor platform on which a number of organisations list studies.

In an international context, other developments include a multi-stakeholder roundtable meeting organised by the European Forum for Good Clinical Practice (EFGCP) on clinical data sharing[5] which recommended review of requests prior to data access, and accreditation systems for data centres being developed by the European Clinical Research Infrastructures Network (ECRIN; www.ecrin.org/).

Making historical data available would present a major challenge. Organisations such as CRUK need to weigh up the benefits and costs of making retrospective data available, which would consume resources that might be put to better use elsewhere.

Changing approaches to consent may also introduce complexities. New studies are increasingly using more future-proofed but ethically sound consent mechanisms, allowing for future data analyses. A further challenge identified in discussion is the existence of 'non-digital' information assets, such as ECG traces, typically available only in paper form.

The quality of data reporting has been enhanced by standardised approaches such as CONSORT (Consolidated Standards of Reporting Trials) guidelines. Similarly, the quality of protocols may be assured by adherence to SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines, developed following a systematic review and consensus-building discussions to provide a basis for good practice in protocol development (www.spirit-statement.org/).

The data-user perspective

One of the strongest drivers for greater clinical trial transparency has been the need for healthcare decision-making to be made on the basis of all relevant information.

Health policy-makers rely on the specialist skills of those undertaking systematic evidence syntheses. In this area, a key role is played by the Cochrane Collaboration, whose work was described by **Dr David Tovey**, Editor-in-Chief of the Cochrane Library.

The Cochrane Collaboration is an international network spanning more than 31,000 people in over 120 countries, promoting the systematic appraisal of research information to support evidence-based decision-making by health policymakers, healthcare practitioners and others.

[5] Report downloadable from http://bit.ly/1d9bvd8

Systematic reviews lie at the heart of its work. It publishes around 400 new reviews each year, alongside some 450 updates, amounting to more than 5000 systematic reviews in total. It also works to promote use of research evidence to support health decision making, to enhance the systematic reviews skills base, and to support new methodological developments.

The aim of systematic reviews is to capture and assimilate all high-quality evidence, and to assess the risk of bias, particularly to inform the development of clinical guidelines. Publication bias – the non-publication of negative results – can have a significant impact on these analyses. Although methods exist to adjust for publication bias, a more accurate overall picture could be obtained if all relevant data were made available for analysis.

One important role of Cochrane reviewers is to assess the quality of individual studies and the likely risk of bias, by examination of study designs. Hence as well as summary results, it is also important to have access to study protocols and clear descriptions of methods used.

Systematic review methodologies continue to evolve. CSRs, as well as journal articles, are now incorporated into reviews. In some cases, reviews have gone deeper still and analysed individual patient data. Groups have had mixed experience with this level of analysis, some finding it difficult, others more straightforward.

Dr Tovey expressed his support for the principles published by the PHRMA and EFPIA, though he questioned the use of the term 'qualified' to describe those granted access to data – Cochrane reviewers often have specialist skills rather than specific qualifications. In addition, he suggested, the principles were less clear about access to retrospective data and left open the question of who would make decisions on access.

Nevertheless, he argued, there was a need for all parties to work together on issues that would facilitate use of clinical trial data, such as greater consistency in data structure and reporting, standards for data sharing and storing, and sound procedures for ensuring data confidentiality.

The historical data challenge

While systems are being established for comprehensive registration of new trials and improved access to recent data, historical trials raise numerous challenges, summarised by **Sally Hollis** of AstraZeneca.

Many factors change over time, limiting the value or accessibility of historical data. Critical disease endpoints, for example, may change or new ones may be introduced. New or modified regulatory requirements may also be introduced. Technology platforms constantly evolve, and old systems or file formats may hinder data extraction.

The impact of company mergers and acquisitions should also not be underestimated. A less obvious but critical factor is the separation or loss of supporting information. Potentially in a variety of formats, this supporting information may be essential to the understanding of data fields and interpretation of raw data.

Broadly speaking, suggested Sally Hollis, company trials fall into three categories: core or pivotal trials that are central to regulatory submissions; global trials that are not part of a regulatory submission; and local or investigator-led trials, often set up to address local healthcare issues or to satisfy the concerns of local regulatory authorities. While sourcing data retrospectively would generally be straightforward for core trials, it is likely to be progressively more difficult for other types of trial. In particular, data from local trials might be very hard to obtain from studies conducted before centralised registration and reporting of clinical trials became the norm.

Drug development pathways also mean that responsibility for data may shift, for example, after in-licensing. Early development may be carried out within a biotech company, and data management may have been outsourced. Hence it may be difficult to track down data. Data recording approaches, for example, on adverse event coding, may also vary over time.

Hence, while there may be a willingness to share data, in some cases companies may face major practical steps required to make available relevant data, along with all the supporting documentation that enable researchers to make the most use of those data. Such considerations emphasise that there may be constraints on what can be achieved in practice, though lessons can be learnt from those companies who are currently making trial data routinely available to researchers. Hence it may be helpful to think in terms of priority-setting and an incremental approach to historical studies to identify what can be achieved in the short, medium and longer-term by individual companies.

Discussion

Patient consent is a recurring theme, with some concerns that checking consent statements could introduce further obstacles or delays (and re-consenting would not be an option as it would be an enormous and potentially impossible undertaking).The GSK system enables researchers to request access to anonymised data, from which personally identifiable information has been removed and the link back to the original dataset destroyed. For research proposals that are approved by an independent panel, access to these anonymised data is provided in a secure IT environment. GSK has taken an approach that because access is given to anonymised data, from a legal perspective there is no need to seek re-consent of research participants or check individual consent forms. However, they have chosen to require that further research must study the medicine or disease researched in the original study. From an ethical perspective, this requirement is in place to align with the fact that when patients agreed to take part in the original study they gave permission to use their data to study the medicine or disease GSK were researching.

The related issue of confidentiality was also touched upon. Unrestricted public access to data may increase the risk that patients identify data specific to them, which could mean they gain clinical information outside a medical context. There are also growing concerns about re-identification of patients from anonymised data (e.g. genetic data). These possible concerns have to be weighed against the strong desire among patients to see more use made of clinical data to improve health. Provision of access to data in a secured environment to bona-fide researchers would help answer these concerns while still allowing re-use of clinical data.

In these debates, there were notable differences in opinion on how a phased approach should be undertaken. Data users and those representing patients typically argued for public disclosure of the full amount of information generated by trials, e.g. list of specific data sets (even if the data might not be immediately accessible and potentially not accessible at all). Some industry voices, however, argued that this would imply a commitment that could not be guaranteed to be deliverable. From an industry perspective, there was a widely expressed preference for priority to be given to studies where it is known that high quality information exists and can be made available.

The approach taken by GSK broadly follows this model and illustrates how it can be made more flexible over time. An independent board considers requests for access to data from GSK trials listed on the request site. Trials are listed after a medicine has been approved or terminated and the trial accepted for publication. There are approximately 450 studies listed on this site and the list is being regularly updated to include global studies going back to 2000.

Researchers are also able to enquire about the availability of studies that are not yet listed, e.g. other GSK studies that researchers have identified from public Registers. For these enquires, GSK assesses the practicalities of providing data and, if data are available, the researchers are able to submit a research proposal for review by the independent board. Information on the number of research proposals and enquires for studies are listed on the request site.

In January 2014, the initial system established by GSK is being expanded to include studies sponsored by other organisations, including Roche[6]. Although the level of demand is difficult to predict, Roche has committed a number of staff to managing applications – evidence of the significant resource implications. Depending on the commitment made this may be particularly onerous for small firms.

The case for consistency to tackle prospective data sharing

Moving onto the subject of data sharing for future clinical trials, attendees discussed possible changes to current technical standards that may help address some of these data-sharing challenges.

The data life cycle begins with a clinical trial protocol. The quality of clinical trial data is, therefore, heavily dependent on the quality of the associated trial protocol. According to **Dr Beat Widler** of Widler & Schiemann Ltd, the quality and consistency of protocols could be improved to generate data of more general usefulness.

A good approach is to consider the later uses of data, and to use this knowledge to shape the way in which the protocol is designed. There are strong arguments in favour of standardisation as standards can capture good practice and introduce efficiencies, and facilitate meta-analyses. More use could be made of pilot studies to test and refine protocols in specific disease areas. Standardised protocols might also be beneficial, streamlining procedures for investigators and groups such as ethics committees.

What kind of organisation could lead such new ways of working? Dr Widler suggested such an organisation would need to be global, provide resources, guidelines and tools for sponsors and investigators, and be an impartial and trusted body with good links to all stakeholder communities. Possibilities include academic centres, which have studied recurring weaknesses in study design and set-up, funding bodies, or a not-for-profit partnership like ACRES (the Alliance for Clinical Research Excellence and Safety; www.acresglobal.net/).

In addition to improving protocol design, Dr Widler suggested there may also be scope to construct better global systems for data sharing of trial information, with appropriate controls for managing data privacy issues, to ensure requests are being made for legitimate purposes, and to assess the appropriateness of proposed data analyses, using objective and transparent criteria.

Currently, individual companies are establishing their own mechanisms to manage data release, for example, through independently appointed boards. In the interests of efficiency and scalability, Dr Wilder questioned the wisdom of establishing multiple boards operating in isolation and suggested it would be more effective entrusting a central body.

In a shared approach, he proposed that data access could be coordinated by a Central Governance Board which would be resourced to manage requests and provide a specialist service to data users. Such a model would benefit smaller companies that might struggle to develop their own independent systems.

A Central Governance Body would likely need to be a public–private partnership. Companies could come together to discuss with an existing not-for-profit body how such a structure would work, or an academic network like ECRIN could take the lead. Alternatively, a not-for-profit body could independently take steps to develop a suitable infrastructure. Whatever its origins, to achieve public trust the Central Governance Body would need to have transparent processes and clear systems of accountability.

In practice, the Central Governance Body could receive requests for data re-use, including a rationale, methodological summary and timeline for dissemination of findings. It would then assess the merit of the application and either approve or reject it, according to objective criteria. Privacy issues, such as the risk of re-identification or disclosure of sensitive information, would be very low, while a standardised and high-

[6] https://www.clinicalstudydatarequest.com/

quality data-analysis environment could be established. Such an approach would create a one-stop-shop for clinical data, a counter to the current mushrooming of registries. In terms of possible hosts for this Central Governance Body, organisations such as the Wellcome Trust or ACRES could again be considered, as well as other groups such as the Cochrane Collaboration or TransCelerate (www.transceleratebiopharmainc.com/), an industry initiative established to simplify R&D processes through collaboration.

As **Dr Catrin Tudur Smith** from the University of Liverpool pointed out, the most critical data in clinical trials relate to outcomes. Synthesis of data on outcomes is typically made harder by heterogeneity in outcome measures adopted by trials. Furthermore, a lack of standard outcome measures can raise the risk of 'outcome reporting bias' – publication of some but not all the outcomes recorded in a trial. Evidence suggests that statistically significant outcomes are more likely to be reported, which can have a significant impact on later meta-analyses.

A way round this issue is to develop 'core outcome sets', agreed sets of outcome measures for particular conditions. These have been pioneered for rheumatology and related fields by the OMERACT (Outcome Measures in Rheumatology; www.omeract.org/) group, and more recently and more widely through the COMET (Core Outcome Measures in Effectiveness Trials; www.comet-initiative.org/) initiative. The ultimate goal is to improve the likelihood that key outcomes are measured, in an appropriate manner, which will also facilitate later meta-analyses and reduce the risk of outcome reporting bias.

Availability of individual patient data for all outcomes in all trials is a further way in which outcome reporting bias can be addressed, and outcome standardisation may be possible. For example, analysis of individual data may allow more clinically relevant outcome measurements to be extracted from raw study data. More complete analysis of data can be undertaken with individual patient data, and it may also be possible to explore the effects of treatment on different types of patient.

The main disadvantage is that it can be time-consuming and expensive to get hold of individual patient data. Differences in data format may need to be overcome, although this is generally not an insuperable hurdle. Such studies can be used to check the analyses and interpretations made in primary papers and also to clarify queries – good dialogue with data owners is essential.

Meta-analyses using individual patient data may be facilitated by widely used data standards, such as those developed by CDISC (Clinical Data Interchange Standards Consortium; www.cdisc.org/). However, a lack of such standards should not be a barrier for sharing these data and many high impact meta-analyses of individual patient data have already been successfully completed. Analysis of individual patient data depends most critically on availability of trial protocols (including amendments), annotated case report forms, raw data in electronic format, and dataset specifications. A contact point for communication is highly desirable.

Discussion

In discussion, there was some support for the idea of standardised protocols, though they would likely need to be specialty-specific. The SPIRIT guidelines could be a step in this direction.

Standards are more likely to be taken up when there is an incentive for companies to adopt them. Although CDISC standards are widely used, for example, there is also considerable 'personalisation' within companies. The FDA has been supportive of CDISC standards, but a recent decision to adopt them more formally has led to a surge of interest in their application.

There was also some debate over whether academic trials should be subject to the same processes as industry trials, which could impose burdensome demands on academic researchers. There is the same expectation of full disclosure and sharing of data from academic trials. However, some academics may be less willing to share

data because of a desire to publish further data analyses and generate additional academic outputs. Funders have an important role to play in ensuring timely release of data. Ways are being looked at for researchers to gain credit for data deposition, to provide an incentive for timely data sharing.

Although standardisation of outcomes has many benefits, in practice industry has to be sensitive to the requirements of regulatory bodies, which generally have specific preferred outcome measures. In addition, the requirements of bodies such as NICE and Health Technology Assessment (HTA) may introduce other important measures. When the demands of different international regulatory agencies are taken into account, industry already faces considerable constraints on its choice of outcome measures.

In terms of the possible organisers of a globalised and consistent approach to access to clinical trial data, the Wellcome Trust has been mentioned as one possibility. The Wellcome Trust is keen to approach other UK and international parties interested in forming a consortium to discuss possible approaches for facilitating access to data from academic and commercial trials, across a spectrum of types of study. It is in the process of commissioning research into the potential of studies analysing data from previous clinical trials to address new research questions. It is also planning a cross-sector meeting at the end of January to discuss the interim discussion paper from the US Institute of Medicine, due in January 2014, on guidelines for the responsible sharing of clinical trial data.

This workshop included contributions from both data generators and data users – and intermediaries between the two – in both industry and academia. There was a common agreement that clinical data are a valuable resource, the analysis of which could provide significant patient benefits. Attendees felt that the environment with regards to wider access to clinical data was improving, though gaining access to historical studies remains a particular challenge. Although views differ on how this challenge can be best addressed, workshops such as this provide a valuable forum in which these views can be aired and discussed constructively.

Appendix 1

Technical Workshop 2: Clinical Trial Transparency

Technical standards for data sharing for old, current and future clinical trials

Date: 5 December 2013

Time: 10am to 4pm

Venue: Fleming room, ABPI offices, 7th Floor, Southside, 105 Victoria Street, London SW1E 6QT

Introduction:

This is the second in a series of workshops hosted by ABPI to facilitate discussions on clinical trial transparency and how this can practicably be achieved by all trial sponsors for the benefit of research and the public.

Purpose:

Technical Workshop 2 has been convened by the ABPI in partnership with the PSI (Statisticians in the Pharmaceutical Industry) for the main purpose of facilitating discussions on the technical standards required for data sharing for old, current and future clinical trials.

Attendees:

Industry representatives, including trade bodies and individual companies, researchers and statisticians from industry and academia, including the Cochrane collaboration, academic representatives with an interest in sharing data, such as MRC and the Wellcome Trust.

Appendix 2
Agenda:

TIME	TOPIC	SPEAKER / FACILITATOR
10.00	**Welcome and introductions**	Dr Bina Rawal, ABPI, Robert Cuffe, PSI
10.15	**Scene Setting**	
	• AllTrials	Dr Síle Lane, AllTrials
	• Cancer Research UK	Dr Fiona Reddington, CRUK
	• Cochrane Collaboration	Dr. David Tovey, Cochrane Editorial Unit
	Session 1: Accessing information from older studies	
11.00	Introduction	Sally Hollis, AstraZeneca
11.20	*Coffee break (30 minutes)*	
	Breakout session	
11.50	• *Activity incl. question 1* (20 min discussion – 15 min feedback)	
12.25	• *Question 2* (25 min discussion – 15 min feedback)	
13.05	*Lunch (45 minutes)*	
	Session 2: Considerations for future trials	
13.50	Introduction	
	• Developing protocols for registration/results reporting	Dr Beat Widler, Widler Schiemann Ltd:
	• Standardising outcomes	Dr Catrin Tudur-Smith, University of Liverpool
14:20	**Breakout session**	**All**
15.00	*Coffee break (20 minutes)*	
15.20	Feedback from breakout groups	
15.50	**Close and sum-up**	Dr Bina Rawal, ABPI
16.00	**Close**	

Appendix 3
Technical Workshop 2: Clinical Trial Transparency

Technical standards for data sharing for old, current and future clinical trials

Date: 5 December 2013
Time: 10am to 4pm
Venue: Fleming room, ABPI offices, 7th Floor, Southside, 105 Victoria Street, London SW1E 6QT

Attendees:

	NAME	ORGANISATION
Speakers:		
1.	Robert Cuffe	ViiV Healthcare – chair PSI
2.	Sally Hollis	AstraZeneca
3.	Bina Rawal	ABPI
4.	Síle Lane	Sense About Science / AllTrials
5.	Fiona Reddington	Cancer Research UK
6.	David Tovey	Cochrane Editorial Unit
7.	Catrin Tudur-Smith	University of Liverpool
8.	Beat Widler	Widler & Schiemann Ltd
Participants:		
9.	Nigel Brayshaw	Takeda
10.	Tim Crook	Pfizer
11.	Claire Cope	Academy of Medical Sciences
12.	Maria Dilleen	Pfizer
13.	Paul Fardy	Association of Clinical Data Management
14.	Sue Forda	Eli Lilly & Co for EFPIA
15.	Robert Frost	GSK
16.	Will Greenacre	Wellcome Trust
17.	Trish Groves	British Medical Journal
18.	Tony Johnson	Medical Research Council
19.	Ian Jones	Independent
20.	Fraser Lewis	Office of Health Economics
21.	Rebecca Lumsden	ABPI
22.	Frances Lynn	Biogen Idec
23.	Tom Smith	Health Research Authority
24.	Rebecca Sudlow	Roche
25.	Neil Tape	National Institute for Health Research
26.	Liz Tremain	NIHR Evaluation, Trials & Studies Coordinating Centre
27.	Zoe Williams	LeoPharma

Appendix 4

ABPI clinical trial disclosure toolkit

Useful links to regulatory and government publications

Abbreviations

ABPI	Association of the British Pharmaceutical Industry
CONSORT	Consolidated Standards of Reporting Trials
CRUK	Cancer Research UK
EC	European Commission
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
EudraCT	European Union Drug Regulating Authorities Clinical Trials
HRA	Health Research Authority
ICMJE	International Committee of Medical Journal Editors
IFPMA	International Federation of Pharmaceutical Manufacturers and Association
MHRA	Medicines and Healthcare Regulatory Authority
PhRMA	Pharmaceutical Research and Manufacturers of America
PMCPA	Prescription Medicines Code of Practice Authority
UK	United Kingdom
WHO	World Health Organization
WMA	World Medical Association

Registries and portals

Global

WHO International Clinical Trials Registry Platform (ICTRP), www.who.int/ictrp/en/

IFPMA Clinical Trials Portal, http://clinicaltrials.ifpma.org/clinicaltrials

The ISRCTN register, www.controlled-trials.com/isrctn

Current controlled trials, www.controlled-trials.com/mrct/

EU

EU Clinical Trials Register, www.clinicaltrialsregister.eu

European Clinical Trials Database of all clinical trials commencing in the European Union from 1 May 2004 onwards. The EudraCT database has been established in accordance with Directive 2001/20/EC, https://eudract.ema.europa.eu/ENCePP Electronic Register of Studies, www.encepp.eu/encepp/studiesDatabase.jsp

UK

UK Clinical Trials Gateway, www.ukctg.nihr.ac.uk

CRUK clinical trials database, www.cancerresearchuk.org/cancer-help/trials/

USA

US National Institute of Health, www.clinicaltrials.gov

Appendix 4

ABPI clinical trial disclosure toolkit

Useful links to regulatory and government publications

Pharmaceutical industry commitments and statements regarding trial disclosure:

Industry position statements

IFPMA Joint position on the disclosure of clinical trial information via clinical trial registries and databases, 6 January 2005, http://clinicaltrials.ifpma.org/clinicaltrials/fileadmin/files/pdfs/FINAL%20Position%20Clinical%20Trials%20Information%20January%2005.pdf

IFPMA Joint position on the disclosure of clinical trial information via clinical trial registries and databases, updated 18 November 2008, http://clinicaltrials.ifpma.org/clinicaltrials/fileadmin/files/pdfs/EN/Revised_Joint_Industry_Position_Nov_2008.pdf

IFPMA Joint position on the disclosure of clinical trial information via clinical trial registries and databases, updated 10 November 2009, http://clinicaltrials.ifpma.org/clinicaltrials/fileadmin/files/pdfs/EN/November_10_2009_Updated_Joint_Position_on_the_Disclosure_of_Clinical_Trial_Information_via_Clinical_Trial_Registries_and_Databases.pdf

IFPMA Joint position on the publication of clinical trial results in the scientific literature, 10 June 2010, http://clinicaltrials.ifpma.org/clinicaltrials/fileadmin/files/pdfs/20100610_Joint_Position_Publication_10Jun2010.pdf

Codes of Practice

ABPI Code of practice for the pharmaceutical industry second 2012 edition, www.abpi.org.uk/our-work/library/guidelines/Pages/code-2012.aspx

IFPMA Code of Practice 2012, www.ifpma.org/fileadmin/content/Publication/2012/IFPMA_Code_of_Practice_2012_new_logo.pdf

Industry guidelines

ABPI Best practice model for the disclosure of results and transparent information on clinical trials, produced 2007, revised 2008, www.abpi.org.uk/our-work/library/guidelines/Pages/best-practice-model.aspx

PhRMA's Principles on conduct of clinical trials and communication of clinical trial results, 2011, http://phrma.org/sites/default/files/pdf/042009_clinical_trial_principles_final_0.pdf

EFPIA and PhRMA Principles for responsible clinical trial data sharing. Our commitment to patients and researchers, 2013, http://transparency.efpia.eu/uploads/Modules/Documents/data-sharing-prin-final.pdf

Government and regulatory authority – trials transparency

UK

HRA

The HRA interest in good research conduct, Transparent research, May 2013, http://www.hra.nhs.uk/documents/2013/08/transparent-research-report.pdf

HRA confirms its action plan on transparent research, July 2013, www.hra.nhs.uk/hra-news-and-announcements/hra-confirms-its-action-plan-on-transparent-research/

Trial registration to be condition of the favourable REC opinion from 30 September 2013, http://www.hra.nhs.uk/about-the-hra/who-we-are/transparency/

Appendix 4

ABPI clinical trial disclosure toolkit

Useful links to regulatory and government publications

Government and regulatory authority – trials transparency *continued*

UK

Commons Select Committee

Committee to inquire into clinical trials and disclosure of data, 13 December 2012, www.parliament.uk/business/committees/committees-a-z/commons-select/science-and-technology-committee/news/121213-clinical-trials-inquiry-announced/

Science and Technology Committee - Third Report, Clinical Trials, Published 17 September 2013, http://www.publications.parliament.uk/pa/cm201314/cmselect/cmsctech/104/104.pdf

NICE

Health Committee – Eighth Report: National Institute for Health and Clinical Excellence, 2013, www.publications.parliament.uk/pa/cm201213/cmselect/cmhealth/782/78202.htm

EU

EMA

European Medicines Agency policy on access to documents (related to medicinal products for human and veterinary use), 1 December 2010, www.ema.europa.eu/docs/en_GB/document_library/Other/2010/11/WC500099473.pdf

Draft policy 70: Publication and access to clinical-trial data, June 2013, www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500144730

Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency, www.ombudsman.europa.eu/en/cases/decision.faces/en/5459/html.bookmark

Publication and access to clinical-trial data: an inclusive development process, www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000556.jsp&mid

Release of data from clinical trials, www.emea.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000555.jsp&mid=WC0b01ac0580607bfa

Workshop on access to clinical-trial data and transparency kicks off process towards proactive publication of data, November 2012, www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2012/11/news_detail_001662.jsp&mid=WC0b01ac058004d5c1

Access to clinical-trial data and transparency. Workshop report. 2012, www.ema.europa.eu/docs/en_GB/document_library/Report/2012/12/WC500135841.pdf

ENCePP, Electronic Register of Studies aims to provide a publicly accessible resource for the registration of pharmacoepidemiological and pharmacovigilance studies, www.encepp.eu/encepp/studiesDatabase.jsp

European Parliament, Commission and Council of the EU

Commission Guideline — Guidance on posting and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006, http://ec.europa.eu/health/files/eudralex/vol-10/2012_302-03/2012_302-03_en.pdf

EU Public consultation on the protection of business and research know-how, http://ec.europa.eu/internal_market/consultations/2012/trade-secrets_en.htm

Appendix 4

ABPI clinical trial disclosure toolkit

Useful links to regulatory and government publications

Government and regulatory authority – trials transparency *continued*

EU

European Parliament, Commission and Council of the EU

Proposal for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. European Commission. 2012, http://ec.europa.eu/health/files/clinicaltrials/2012_07/proposal/2012_07_proposal_en.pdf

Article 78(1) of the European Commission's EU Clinical Trials Regulation proposal, http://ec.europa.eu/health/files/clinicaltrials/2012_07/proposal/2012_07_proposal_en.pdf

Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use, of 4 April 2001, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:121:0034:0044:en:PDF

Germany

Medicinal Products Act in the version published on 12 December 2005 (Federal Law Gazette [BGBl.]) Part I p. 3394, last amended by Article 1 of the Law of 25 May 2011 (Federal Law Gazette I p. 946), www.gesetze-im-internet.de/englisch_amg/englisch_amg.html#p0930

USA

FDA

Food and Drug Administration Amendments Act (FDAAA) of 2007, www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FoodandDrugAdministrationAmendmentsActof2007/default.htm

Other – trial transparency

About the WHO International Clinical Trials Registry Platform (ICTRP), www.who.int/ictrp/about/en/

The CONSORT Statement, www.consort-statement.org/consort-statement

Good publication practice for communicating company sponsored medical research: the GPP2 guidelines, BMJ2009; 339:b4330, www.bmj.com/content/339/bmj.b4330

International Committee of Medical Journal Editors (ICMJE), 2013. Uniform requirements for manuscripts submitted to biomedical journals: publishing and editorial issues related to publication in biomedical journals: obligation to register clinical trials, www.icmje.org/publishing_10register.html

WMA Declaration of Helsinki – Ethical principles for medical research involving human subjects, www.wma.net/en/30publications/10policies/b3/

Note: All web links accessed in October 2013

ABPI clinical trial disclosure toolkit disclaimer

The information provided in this toolkit for companies is provided in good faith, and every reasonable effort is made to ensure that it is accurate. The toolkit is not intended and should not be construed as regulatory or legal advice. The ABPI cannot in any circumstances accept responsibility for any errors or omissions and users should satisfy themselves as to their legal obligations.

The Association of the British Pharmaceutical Industry
7th floor, Southside, 105 Victoria Street, London, SW1E 6QT Telephone +44 (0) 870 890 4333
Follow us on Twitter@ABPI_UK