Sunshine on Europe: impact of recent EFPIA and EU guidelines on publication planners

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Disclaimer

As an independent consultant, the views expressed in this presentation are my own and do not necessarily reflect the views of the conference organisers

Transparency

Agenda

Evolution of data transparency

- Scientific publications & congress abstracts & presentations
- Trial registration, Results posting
- Clinical study report & clinical summary public release
- Individual subject data release, Lay summaries

Response from pharmaceutical industry & industry organisations

- Public policies
- New guidelines – GPP3

Evolution of financial payments transparency

- Sunshine Act
- EfPIA Disclosure Code

New practices

- Publication & disclosure plan
- Impact on protocol, QC processes

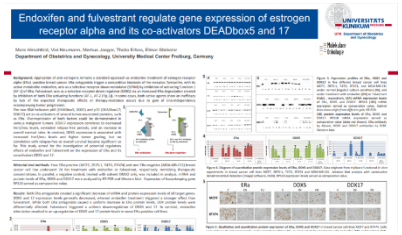
20th century Publication Outlets

Clinical study report

Only to regulatory agency

Publishe d paper

Congress abstract & poster



Publication outlets 2005-2013

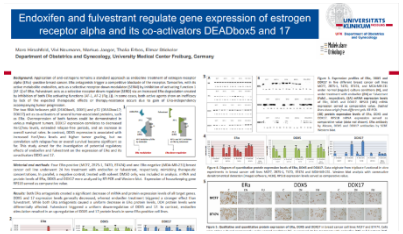
Clinical study report

Only to regulatory agency

Publishe d paper

Trial registry results records CT.gov

Congress abstract & poster



European Medicines Agency policy, June 2014
Mandatory posting of results

- **Interventional clinical trials ending after 21 July 2014**
  - Results must be posted on EudraCT within 12 mo (adult) or 6 mo (paediatric) of study completion
  - Using defined data set
- **Interventional clinical trials ending before 21 July 2014**
  - Results must be posted retrospectively
  - Using defined data set and/or summary
    - Different timeframes dependent on type of trial & date of completion
- **ALL interventional trials**
  - whether drugs approved or not

European Medicines Agency policy, October 2014
Publication of clinical data

- **Make publicly available with redaction of personal identifying and commercially confidential information (CCI):**
  - Clinical overviews
  - Clinical summaries
  - Clinical study reports with
    - Protocols & amendments
    - Sample case report form
    - Documentation of statistical methods
    - Individual patient data (IPD)
- **When decision taken on MAA submitted by centralised procedure (approval or withdrawal)**

PhRMA RESEARCH · PROGRESS · HOPE

efpia European Federation of Pharmaceutical Industries and Associations

Principles for Responsible Clinical Trial Data Sharing

Our Commitment to Patients and Researchers

Biopharmaceutical companies are committed to enhancing public health through responsible sharing of clinical trial data in a manner that is consistent with the following Principles:

- **Safeguarding the privacy of patients**
- **Respecting the integrity of national regulatory systems**
- **Maintaining incentives for investment in biomedical research**

Companies routinely publish their clinical research, collaborate with academic researchers, and share clinical trial information on public web sites at the time of patient recruitment, after new drug approval, and when investigational research programs have been discontinued.

Biopharmaceutical companies will apply these Principles for Responsible Clinical Trial Data Sharing as a common baseline on a voluntary basis, and we encourage all

Each company will establish a scientific review board that will include scientists and/or healthcare professionals who are not employees of the company. Members of the scientific review boards will participate in the review of data requests to determine whether they meet the criteria described below regarding the qualifications of the requestor and the legitimacy of the research purpose, unless a company makes an initial determination on its own to share applicable clinical trial data. Companies

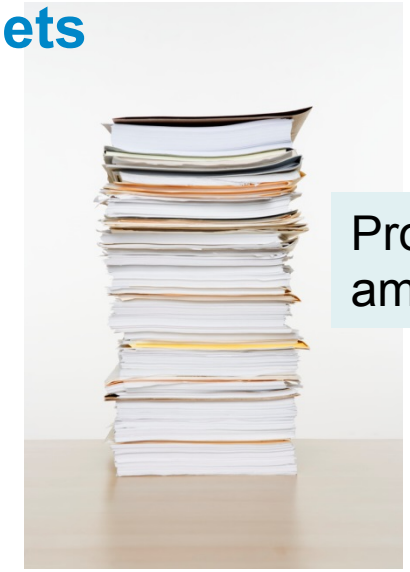
Current disclosure outlets

From 2014/ 2015

Lay Summaries

CSR synopses

Clinical overview & summaries

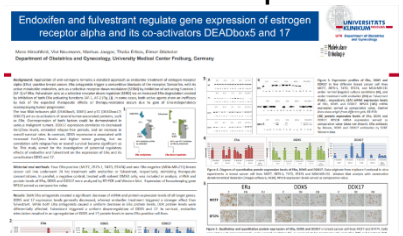


Protocol & amendments

Individual patient data (IPD)

Clinical study report

Congress abstract & poster



Publishe d paper

Trial registry results records CT.gov, EU CTR, others

Discrepancy between published articles and trial registry information

From: **Comparison of Registered and Published Primary Outcomes in Randomized Controlled Trials**

Table 2. Differences Between Primary Outcomes in Trial Registration and in Published
for Studies With a Clear Description of the Primary Outcome in the Registry and Di
Favoring Statistically Significant Results

	No. (%)		
	All (n =)		(n = 72)
Articles with different primary outcomes in trial registration and in published article			24 (33.3)[c]
Registered primary outcome omitted in text		9.7)	7 (9.7)
New primary outcome introduced in te		11 (14.7)	11 (15.3)
Different timing of assessment of		1 (1.3)	3 (4.2)
Published primary outcome outcome in registry	.4)	5 (6.7)	3 (4.2)
Registered primar outcome i	6 (4.0)	4 (5.3)	2 (2.8)
Discrep ng	46	22	24
	19 (41.3)	9 (40.9)	10 (41.7)[e]
	4 (8.7)	1 (4.5)	3 (12.5)
to conclude	23 (50.0)	12 (45.5)	11 (45.8)

ad 2 reasons for difference in primary outcome.
cles had 2 reasons for difference in primary outcome.
pared with general journals: $P=.73$. Two articles had 2 reasons for difference in primary outcome.
discrepancy in primary outcome was said to favor statistically significant results when a new, statistically significant primary outcome was introduced in the article or when a statistically nonsignificant primary outcome was omitted or defined as nonprimary in the published article.
[e] Compared with general journals: $P=.60$.

CONCLUSION: Comparison of the primary outcomes of RCTs registered with their subsequent publication indicated that selective outcome reporting is prevalent.

Sylvain Mathieu, MD; Isabelle Boutron, MD, PhD; David Moher, PhD; Douglas G. Altman, DSc; Philippe Ravaud, MD, PhD
JAMA. 2009;302(9):977-984. doi:10.1001/jama.2009.1242

OPEN ACCESS Freely available online

PLOS | MEDICINE

Timing and Completeness of Trial Results Posted at ClinicalTrials.gov and Published in Journals

Carolina Riveros[1,2,3], Agnes Dechartres[1,2,3]*, Elodie Perrodeau[1,3], Romana Haneef[1,3], Isabelle Boutron[1,2,3,4], Philippe Ravaud[1,2,3,4,5]

1 INSERM U738, Paris, France, 2 Université Paris Descartes—Sorbonne Paris Cité, Paris, France, 3 Centre d'Épidémiologie Clinique, Hôpi... e-Hôpitaux de Paris, Paris, France, 4 French Cochrane Centre, Paris, France, 5 Mailman School of Public Health, Columbia Uni... f America

Abstract

Background: The US Food and Drug Admi... from clinical trials of Food and Drug Administration–approved drugs to ... ter trial completion. We compared the timing and completeness of result... and published in journals.

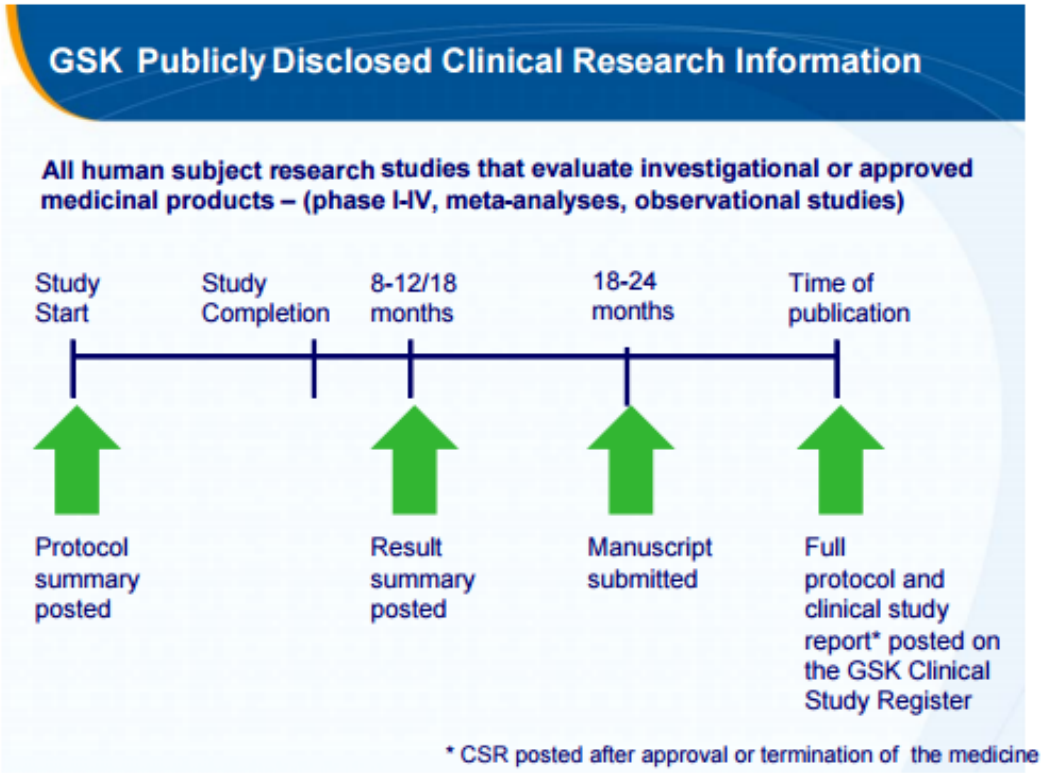
Methods ... on March 27, 2012, for randomized controlled trials of drugs with ... trials, we searched PubMed for corresponding publications. Data were ...rials.gov and from the published articles for trials with results both posted and ...ime to first public posting or publishing of results and compared the completeness of results ...s.gov versus published in journal articles. Completeness was defined as the reporting of all key ...ording to three experts for the flow of participants, efficacy results, adverse events, and serious adverse events

Conclusions: Our results highlight the need to search ClinicalTrials.gov for both unpublished and published trials. Trial results, especially serious adverse events, are more completely reported at ClinicalTrials.gov than in the published article.

PLoS Med. 2013 Dec;10(12):e1001566; discussion e1001566. doi: 10.1371/journal.pmed.1001566. Epub 2013 Dec 3.

PUBLICATION POLICIES

GSK Public policy positions



Trial Data & Results

Other content within Trial Data & Results:

Trial Data & Results
Clinical Study Report Synopses
Data Access Requests
Returning Clinical Data to Patients

Pfizer believes that it is important for researchers, trial participants, regulators, and others acting in the best interest of patients to have access to clinical trial information to advance medical understanding and progress. It's also important that this access works in ways that protect patient privacy, preserve regulatory authority and maintain incentives for those who generate data to conduct new research.

Pfizer publicly shares results from our clinical trials, whether the results are neutral, negative or positive. We also share data gathered in clinical trials we sponsor with trial volunteers, researchers, and others.

There are several ways in which we share trial results and data:

1. We submit clinical trial results for publication in peer reviewed journals within 18 months of primary completion date.

Responsible Data Sharing

Pfizer's practices adhere to the principles for responsible data sharing laid out by the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the Pharmaceutical Research and Manufacturers of America (PhRMA).

- Pfizer Policy: Public Disclosure of Pfizer Clinical Study Data and Authorship
- Read the PhRMA/EFPIA principles (PDF)
- How Pfizer meets or exceeds the PhRMA/EFPIA commitments (PDF)
- A Guide to Requesting Pfizer Patient-Level Clinical Data (PDF)
- Frequently Asked Questions (PDF)
- Statistical Analysis Plan Sample (PDF)

Annals of Internal Medicine RESEARCH AND REPORTING METHODS

Good Publication Practice for Communicating Company-Sponsored Medical Research: GPP3

Wendy P. Battisti, PhD; Elizabeth Wager, PhD; Lise Baltzer; Dan Bridges, PhD; Angela Cairns; Christopher I. Carswell, MSc; Leslie Citrome, MD, MPH; James A. Gurr, PhD; LaVerne A. Mooney, DrPH; B. Jane Moore, MS; Teresa Peña, PhD; Carol H. Sanes-Miller, MS; Keith Veitch, PhD; Karen L. Woolley, PhD; and Yvonne E. Yarker, PhD

- Sets out 10 Good Publication Practice principles for company-sponsored medical research
- Endorses sharing full study reports and appropriately anonymised individual subject data with qualified researchers on request
- Spells out research which should be published, including non-interventional studies
- Expands guidance on interpretation of ICMJE authorship criteria & addresses common authorship issues
- Clarifies appropriate author payments
- Expands on role of medical writers

PERSPECTIVE

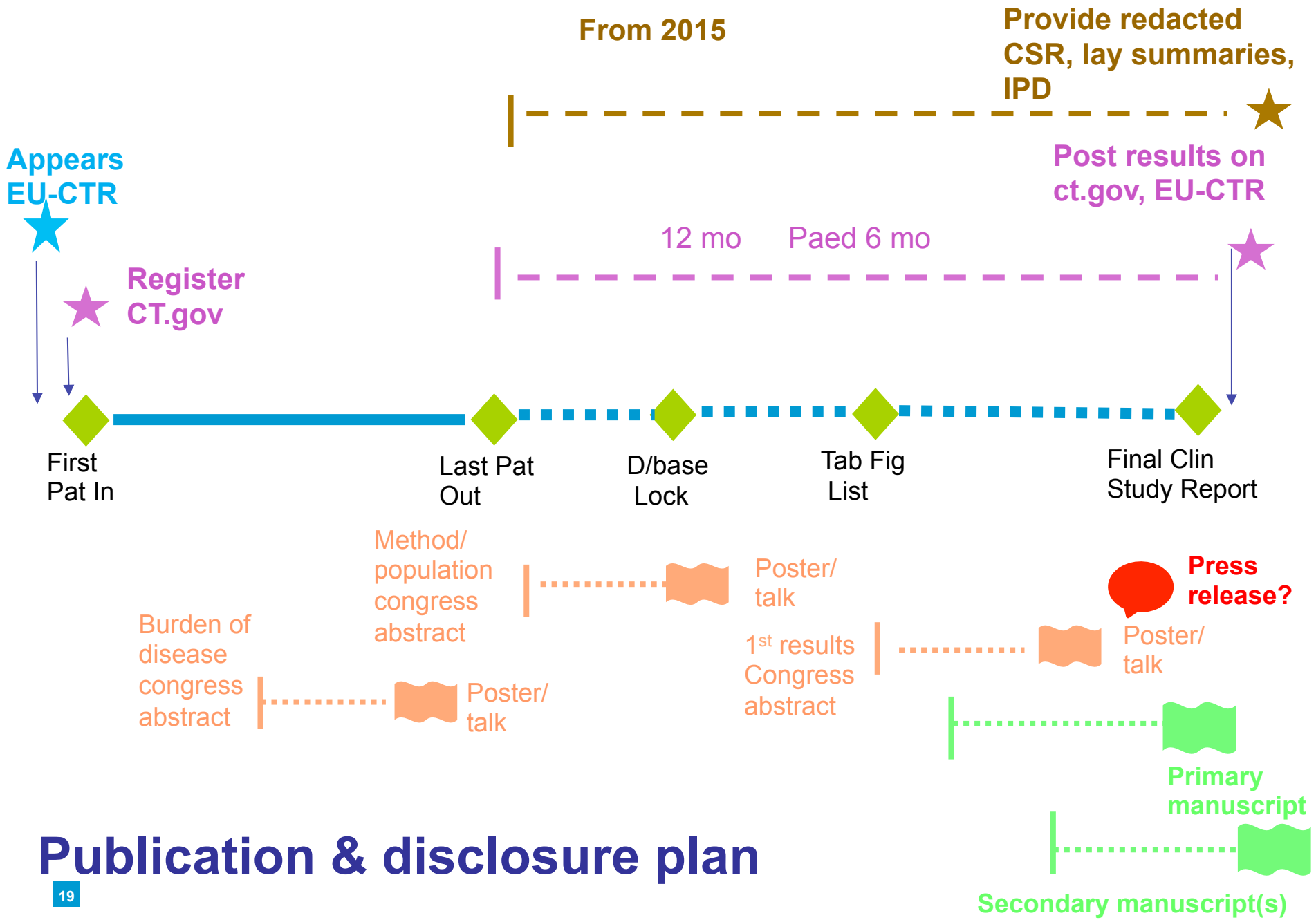
Publication planning: promoting an ethics of transparency and integrity in biomedical research

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE
Editor's Choice

DeTora L, Foster C, Skobe C, Yarker Y, Crawley FP.
Int J Clin Pract, September 2015, 69, 9, 915–921

A supportive and well-organised plan ensuring that the research and its results are communicated clearly to the scientific and healthcare communities as well as the general public is essential

Publication & disclosure plan



FINANCIAL TRANSPARENCY

Physician Payments Sunshine Act - effective Apr 2013

Summary Data for 2014

Total US Dollar Value

$ 6.49 Billion

Total Records Published

11.41 Million

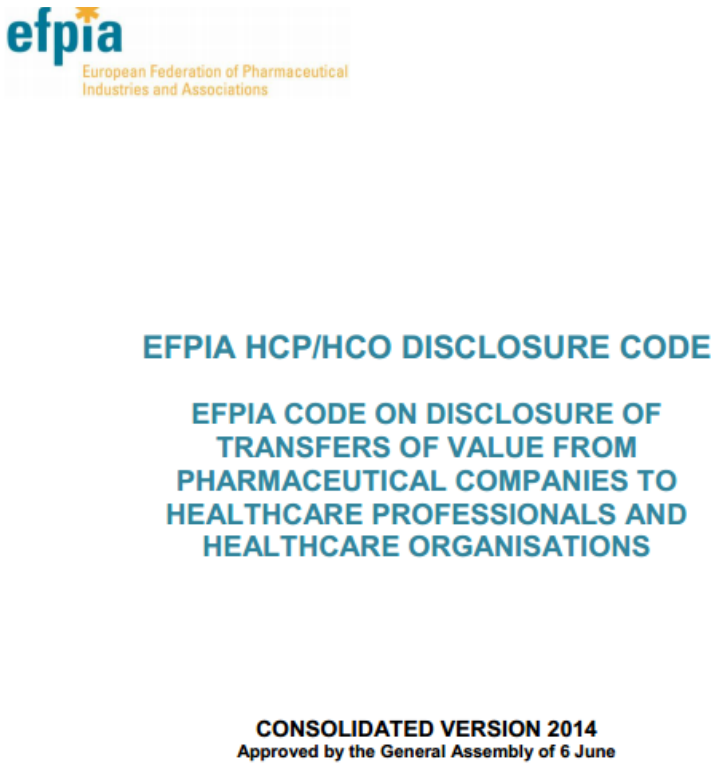
▼ SHOW MORE DETAILS ▼

Total Companies Making Payments
1,444

Total Physicians with Payment Records
607,000

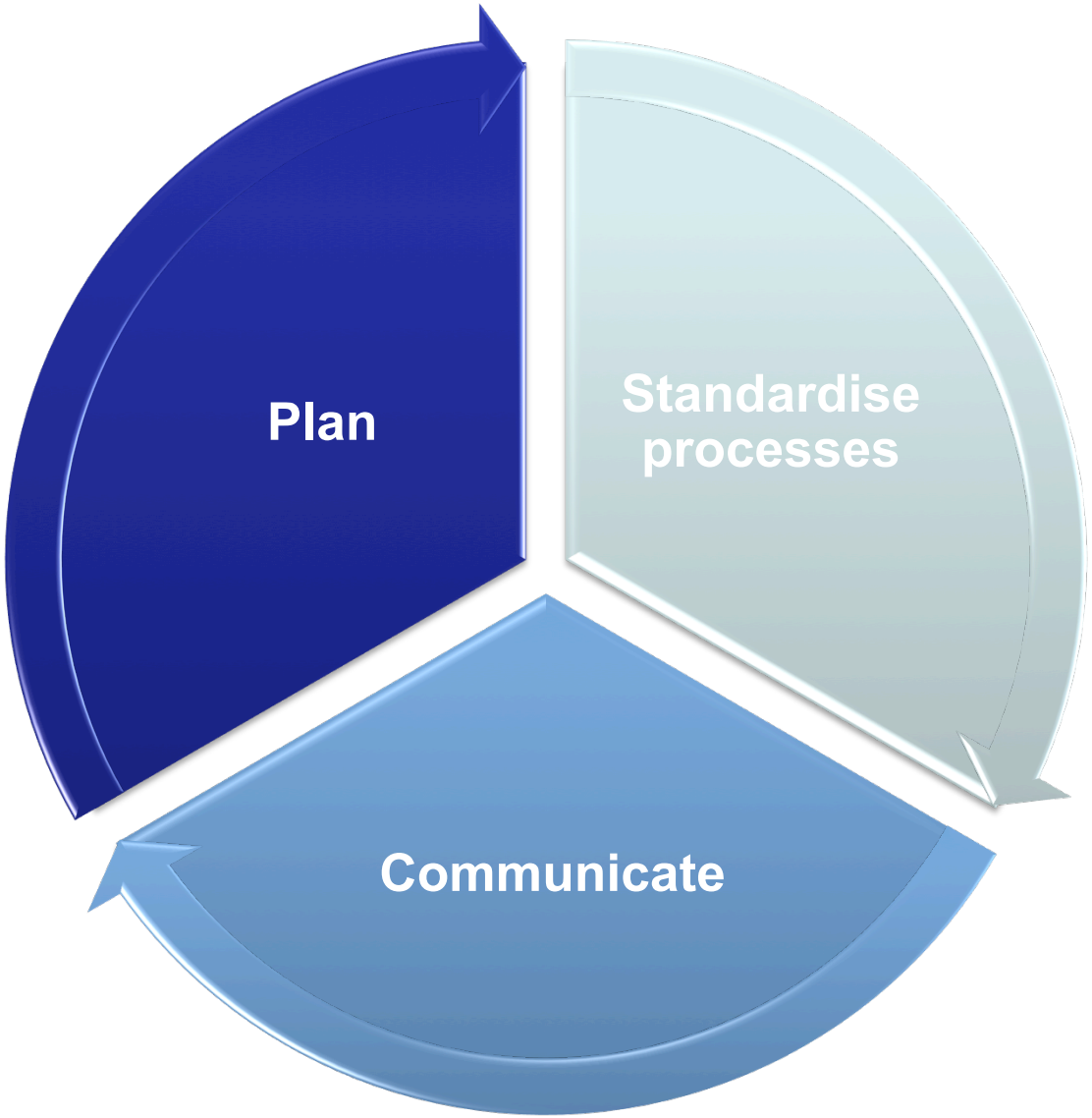
Total Teaching Hospitals with Payment Records
1,121

efpia
European Federation of Pharmaceutical Industries and Associations



- Obliges member companies to disclose direct or indirect Transfers of Value to or for the benefit of an HCP
  - Donations or grants
  - Events costs
  - Service or consultancy fees
- To individual named recipient

- R&D costs reported on aggregate basis
- Annual reporting
- Report on company or government/ association website


Plan
Standardise processes
Communicate

PLAN
PROTOCOL

- Prepare protocol considering it WILL become public
- Clear primary endpoint & timeframe
- Restrict number of secondary endpoints
- Prepare protocol with Company Confidential Information redacted

PLAN

PUBLICATION & DISCLOSURE PLAN

Prepare plan before study recruitment

Plan key scientific content for each

- congress abstract/ poster/ oral & manuscript
- trial registries & results database submission
- press release

Data availability & timelines

Authors, contributors

Target journals (with contingency) & congresses

Review & Approval

- Heads of Publications, Disclosure Team, Med Affairs, Clin Dev, Reg Affairs, Data Mgmt & Stats, Compliance, Public Affairs, Chief Medical Officer NOT Sales/ Marketing

STANDARDISE
QC PROCESSES

Identify one results document as ‘core’

- Final tables, figures & listings?
- ≤ 4mo after study completion (paediatric trials)
- ≤ 10 mo after study completion (adult trials)
- Same data in CSR, Results registries, Congress abstracts, posters &/or oral presentations, Primary manuscripts, Clinical overviews & clinical summaries

Review vs ‘core’ document

- Draft trial & results registrations
- Draft scientific manuscripts & congress materials

Ensure study identifier(s) included in ALL publications

STANDARDISE
PROCESSES

Record costs/ publication project

- Medical writing/ editing
- Journal open access
- Copyright permission
- Congress abstract submission, attendance expenses

Named individual reporting vs aggregate reporting

- part of clinical research?

COMMUNICATE

PUBLICATION & DISCLOSURE PLAN

Present to:

- Project team
- Key internal sponsors eg Clin Dev, Med Affairs, Stats & Data Mgmt
- External study investigators
- Co-development partner

COMMUNICATE

PUBLICATION & DISCLOSURE PROGRESS

Use Publication Management software

- Eg DataVision, PubsHub, PubStrat
- Controlled access to all Publication & Disclosure team members
- Include Disclosure tasks in project activities
- Choose Medical Communications vendor with user capability

COMMUNICATE

PUBLICATION & DISCLOSURE PLANNING MEETINGS

Regular

- F2F/ TC/ videolink

Members

- Disclosure rep, publication manager, medical writer(s) of CSR & publications, Med Affairs, Clin Dev, Reg Affairs, Data Management & Stats, Compliance

Review progress of Publication & Disclosure plan

- timeframe, key content, issues & solutions

For trials on products under joint development

- Key staff from development partners

Change of mindset

Transparency


Consistency

THANK YOU