Global Trends in Clinical Trial Data Sharing (CTDS)

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30th June, 2015 @ 2nd PhUSE SDE Japan

Agenda

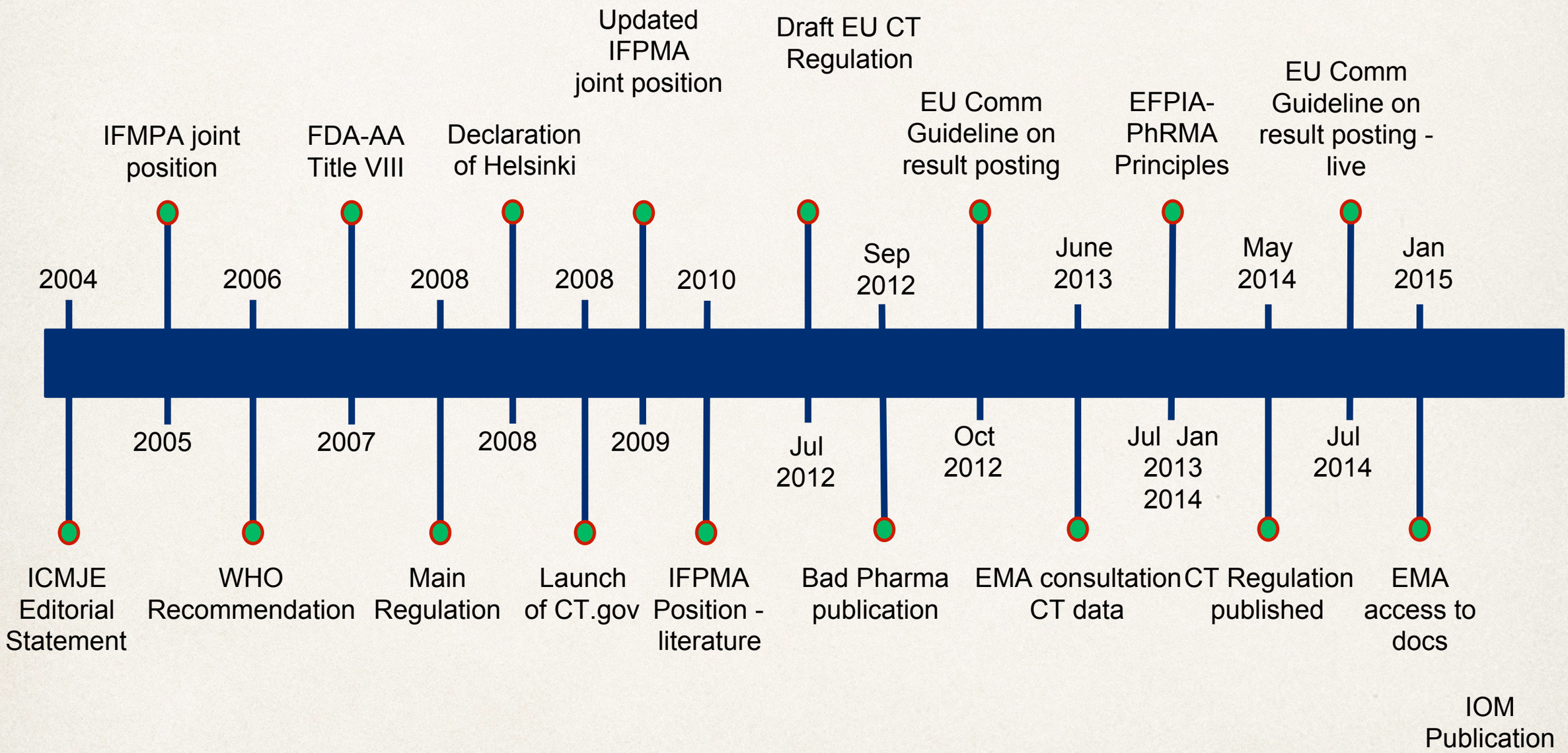
- Background
  - Clinical Trial (data) Transparency
- History
  - Pre 2012
  - Post 2012

Clinical Trial (data) Transparency

1. Registration of clinical trials（治験情報の登録）: ClinicalTrials.gov, JapiCTI, EudraCT, 自社Web site等
2. Disclosure of clinical study results（治験結果の公開）
    1. Disclosure of summary （治験結果概要）： ClinicalTrials.gov, JapiCTI等
    2. Study result publication（治験結果の論文化）
    3. CSR synopsis and full CSR（CSRシノプシスあるいはCSR全文の公開）
3. Sharing clinical study data (individual patient data: IPD)（治験データの共有）

- 2012年頃から、治験（データ）の透明性、特にデータ共有への要望が高まってきている。この潮流は医療産業界のみならず、医学界全体へ影響を及ぼしている。また、この潮流の背景として、薬事規制、医薬品産業に加え第三者の動向がある。

History


2004
ICMJE Editorial Statement
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IFMPA joint position
2006
WHO Recommendation
2007
FDA-AA Title VIII
2008
Main Regulation
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Declaration of Helsinki
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EMA access to docs
IOM Publication

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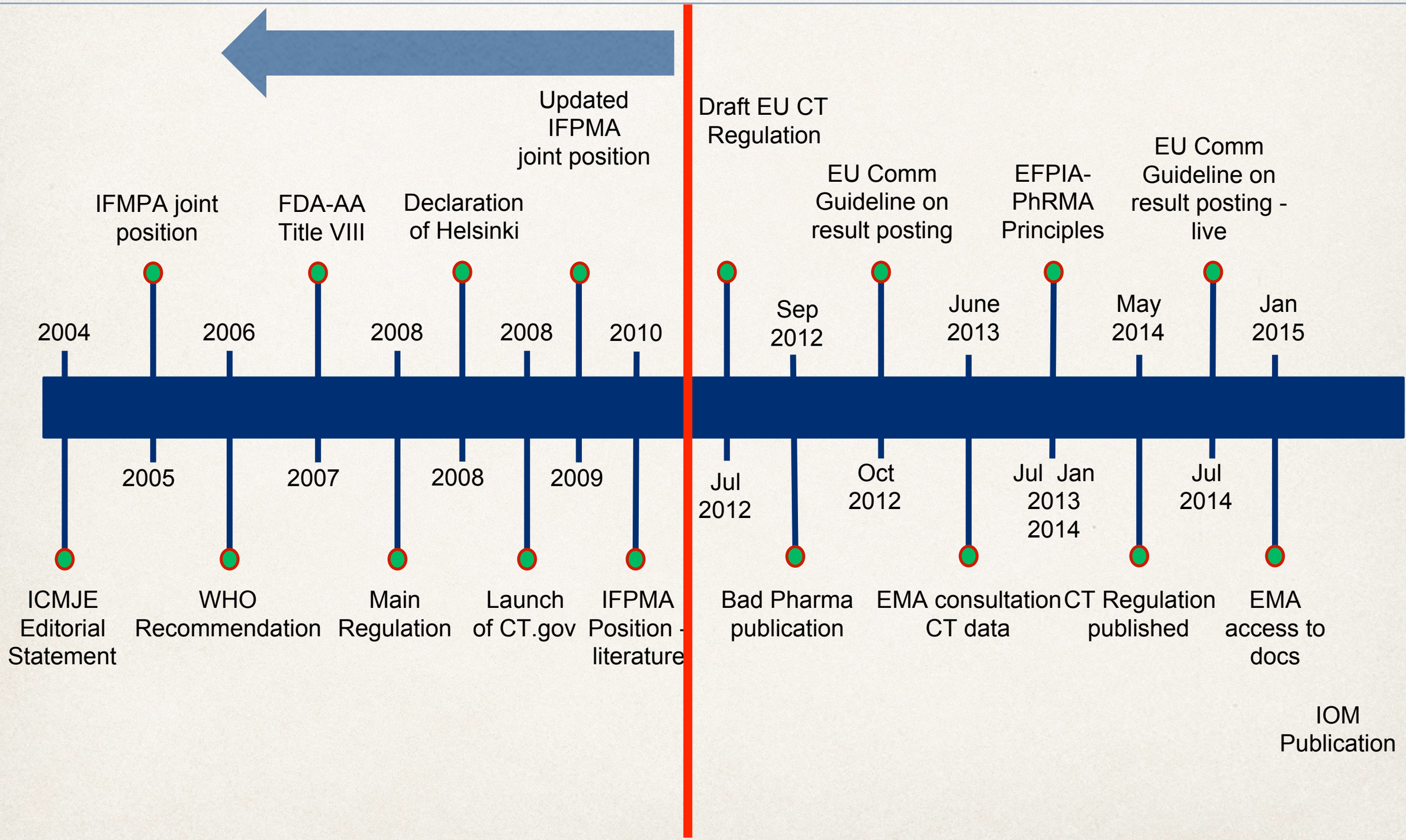
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2012年までの歴史まとめ

治験情報（プロトコール）登録と治験結果の公開中心の時代

2004　ICMJE（医学雑誌編集者国際委員会）声明

- 論文掲載条件として誰でも無料でアクセスできる非営利団体が運営するシステムに事前登録し、結果の開示を求める。

2005　IFPMA（国際製薬団体連合会）共同指針

- 加盟会社が依頼する臨床情報の透明性を約束する
- 全ての治験（探索的治験を除く）の情報を患者登録後21日以内に臨床試験登録簿に掲載
- 試験結果は、承認・販売されてから1年以内に公開、1ヶ国以上で承認されている場合は治験終了後1年以内に公開

2006　WHO勧告

2007　FDA改正法 Title VIII

2008　Maine州制定法改訂

2008　ヘルシンキ宣言のソウル改訂

- 19. すべての臨床試験は、最初の被験者を募集する前に、一般的にアクセス可能なデータベースに登録されなければならない。
- 33. 研究終了後、その研究に参加した患者は、研究結果を知る権利と、例えば、研究の中で有益であると同定された治療行為へのアクセス、または他の適切な治療あるいは利益へのアクセスなどの、研究結果から得られる利益を共有する権利を有する。

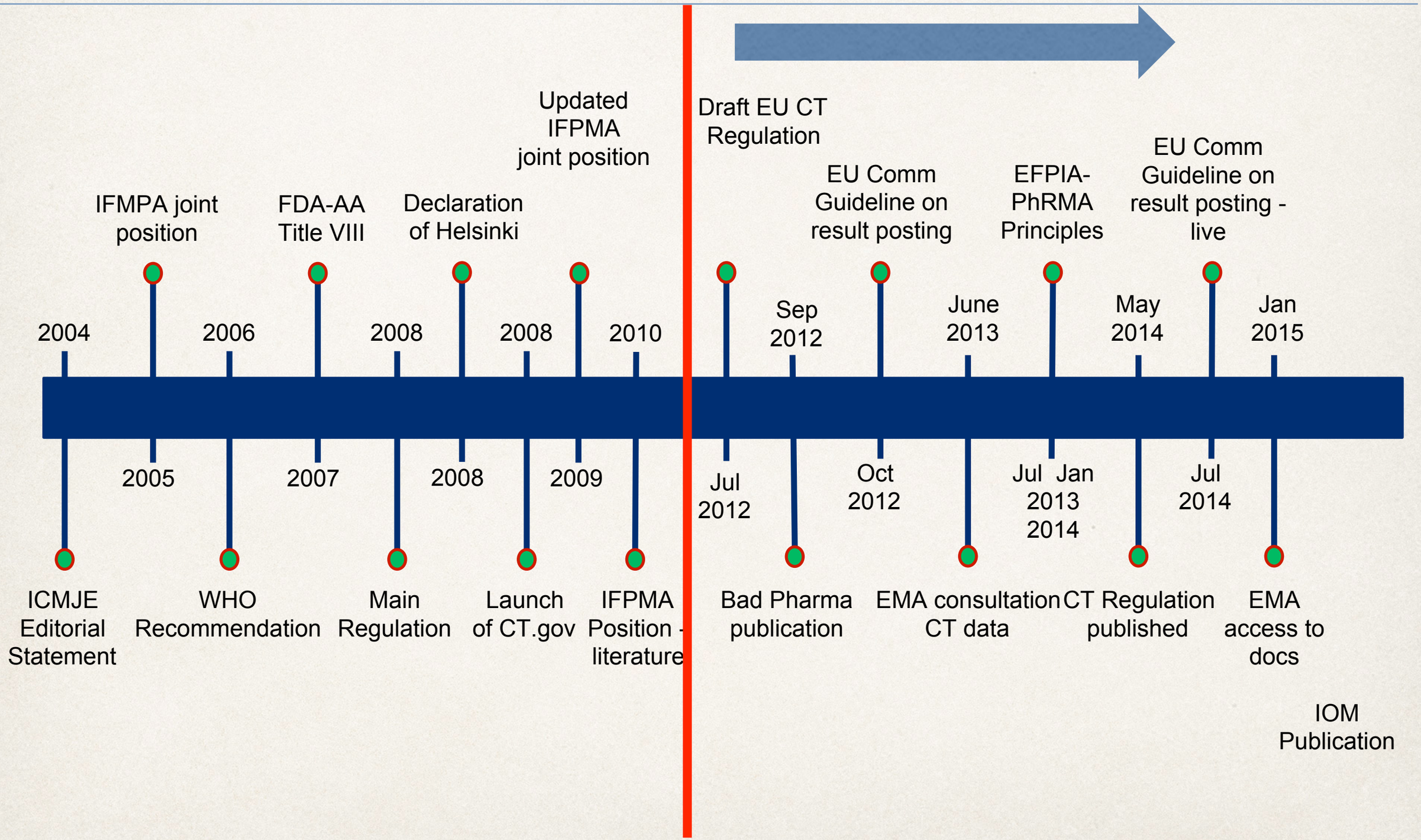
2008　IFPMA共同指針改訂

- 対象となる試験の種類の拡大（登録、結果公開とも）；すべての検証的試験およびすべての有効性をみる探索的試験

2009　IFPMA共同指針改訂

- 対象となる試験の種類の拡大（登録、結果公開とも）；薬剤に関して実施された患者を対象としたすべての臨床試験（最低限）

History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EMA's Action to Disclose Trial Data

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA commits to disclosure of data from trials

Seeks feedback on clinical trial data access policy

The European Medicines Agency (EMA) Released a draft policy on access to clinical trial data as it tries to strike a balance between transparency and confidentiality of sensitive information

- **July 2012 Draft EU CT Regulation**
  - 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
    http://ec.europa.eu/health/human-use/clinical-trials/index_en.htm#rlctd
- **Oct 2012**
  - 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 (October 2012)
    http://ec.europa.eu/health/files/eudralex/vol-10/2012_302-03/2012_302-03_en.pdf

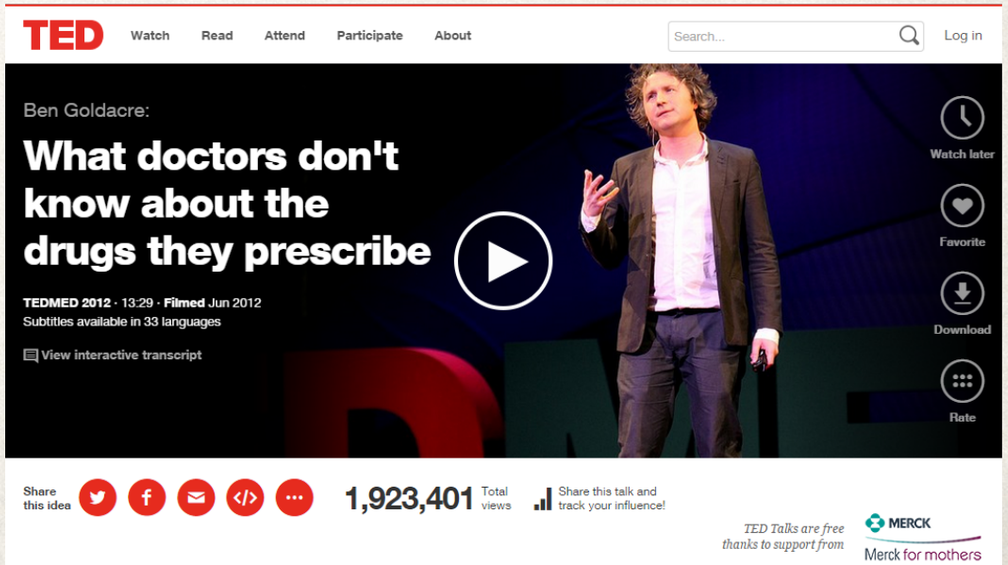
EMA policy on publication of clinical data for medicinal products for human use -Policy 0070-

- EMA will proactively publish clinical reports of applications submitted after **1 January 2015** following the European Commission Decision granting or refusing the marketing authorisation or post- authorisation submission outcome
- As far as extensions of indication and line extensions relating to existing centrally authorised medicinal products are concerned the new policy will apply to applications submitted after date for publishing is **1 July 2015**
- EMA has set up Terms of Use, which govern how data may be accessed, by whom and what is prohibited (Annex 1 and Annex 2 of the Policy)
- EMA has set up a number of redaction principles to protect CCI which may be contained in clinical reports (Annex 3)
- EMA has also set up a process for the publication of a Clinical Report, which gives the applicant the opportunity for an individual consultation regarding what is to be considered CCI (Annex 4).

もう一つのBackground

- 製薬会社への｜医学界への 批判から始まった?
  - Bad Pharma Publication, Ben Goldacre, 2012
    (https://en.wikipedia.org/wiki/Bad_Pharma)
  - AllTrials Campaing
    (http://www.alltrials.net/)
  - What doctors don’t know about the drugs they prescribe @TEDMED 2012
    (http://www.ted.com/talks/ben_goldacre_what_doctors_don_t_know_about_the_drugs_they_prescribe)

- ネガティブデータの共有（Publication Bias）
  →不要な試験の繰り返しを無くす
- ICMJE声明、FDA改訂法への遵守率の低さ
  →全ての治験結果の公開を提言



Recent Public and Academic Call for Sharing of Clinical Trial data

Experts call for broad sharing of clinical trial data

By: ALICIA AULT, ACS Surgery News Digital Network OCTOBER 22, 2013

FROM THE NEW ENGLAND JOURNAL OF MEDICINE

The NEW ENGLAND JOURNAL of MEDICINE

HEALTH LAW, ETHICS, AND HUMAN RIGHTS

Mary Beth Hamel, M.D., M.P.H., *Editor*

Preparing for Responsible Sharing of Clinical Trial Data

Michelle M. Mello, J.D., Ph.D., Jeffrey K. Francer, J.D., M.P.P., Marc Wilenzick, J.D., Patricia Teden, M.B.A., Barbara E. Bierer, M.D., and Mark Barnes, J.D., LL.M.

The NEW ENGLAND JOURNAL of MEDICINE

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EDITORIAL

Participant-Level Data and the New Frontier in Trial Transparency

Deborah A. Zarin, M.D.

N Engl J Med 2013; 369:468-469 | August 1, 2013 | DOI: 10.1056/NEJMe1307268

PhRMA/EFPIA principle

PhRMA
RESEARCH • PROGRESS • HOPE

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DATA SHARING COMMITMENTS WILL ENHANCE RESEARCH AND SCIENTIFIC KNOWLEDGE, ADVANCE PATIENT CARE AND IMPROVE PUBLIC HEALTH

EFPIA and PhRMA Release Joint Principles for Responsible Clinical Trial Data Sharing to Benefit Patients

Washington, D.C. and Brussels (July 24, 2013) — The Europ
Associations (EFPIA) and the Pharmaceutical Research and
their long-standing commitment to enhancing public health
Data Sharing: Our Commitment to Patients and Researcher

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**

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

1	**Share anonymized patient level and study level data with qualified investigators** • For medicines and indications approved in US and EU • Develop process to qualify investigators • Identify external review body
2	**Publish Study Synopsis online** At a minimum, make publicly available the synopsis of CSR filed with regulators as of Jan 2014, for medicines or indications approved in US and EU
3	**Share study results with patients** Work with regulators to adopt mechanism to share clinical trial results with patients
4	**Certify** on pubic web site we have processes in place to follow principles
5	**Publish results** regardless of outcome, particularly for Phase 3 studies; studies with medically significant findings; discontinued program

IOM publication

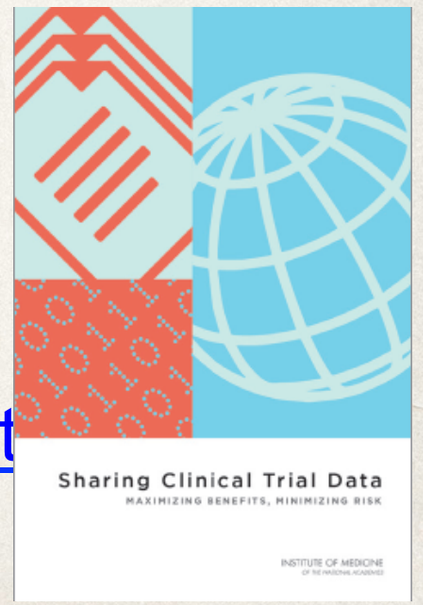
Sharing Clinical Trial Data, Maximizing Benefits, Minimizing Risk

"Data sharing could advance scientific discovery and improve clinical care by maximizing the knowledge gained from data collected in trials, stimulating new ideas for research, and avoiding unnecessarily duplicative trials."

Guiding Principles

- Maximize the benefits of clinical trials while minimizing the risks of data sharing.
- Respect individual participants whose data are shared.
- Increase public trust in clinical trials and the sharing of trial data.
- Conduct the sharing of trial data in a fair manner.

https://www.iom.edu/Reports/2015/Sharing-Clinical-Trial-Dat



IOM Publication Recommendation

http://iom.edu/~/media/Files/Report%20Files/2015/SharingData/CompleteRecommendations.pdf

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RECOMMENDATION 1: Stakeholders in clinical trials should foster a culture in which data sharing is the expected norm, and should commit to responsible strategies aimed at maximizing the benefits, minimizing the risks, and overcoming the challenges of sharing clinical trial data for all parties.

RECOMMENDATION 2: Sponsors and investigators should share the various types of clinical trial data no later than the times specified below. Sponsors and investigators who decide to make data available for sharing before these times are encouraged to do so.

RECOMMENDATION 3: Holders of clinical trial data should mitigate the risks and enhance the benefits of sharing sensitive clinical trial data by implementing operational strategies that include employing data use agreements, designating an independent review panel, including members of the lay public in governance, and making access to clinical trial data transparent. Specifically, they should take the following actions:

RECOMMENDATION 4: The sponsors of this study should take the lead, together with or via a trusted impartial organization(s), to convene a multistakeholder body with global reach and broad representation to address, in an ongoing process, the key infrastructure, technological, sustainability, and workforce challenges associated with the sharing of clinical trial data.

What’s next?

- IPDの“公共財: Public Property”としての活用
  - *“Data sharing could advance scientific discovery and improve clinical care by maximizing the knowledge gained from data collected in trials, stimulating new ideas for research, and avoiding unnecessarily duplicative trials.”*

- **Ideas/concepts/keywords**
  - Wikinomics/Macrowikinomics
    - Life Science Dataのオープン化
  - Big Data in the Healthcare Industry

Backup

IOM Report: Recommendation 2
Timing of Sharing Information

- **Trial registration:**
  - The data sharing plan for a clinical trial (i.e., what data will be shared when and under what conditions) should be publicly available at a third-party site that shares data with and meets the data requirements of WHO's International Clinical Trials Registry Platform; this should occur before the first participant is enrolled.
- **Study completion:**
  - Summary-level results of clinical trials (including adverse event summaries) should be made publicly available no later than 12 months after study completion.
  - Lay summaries of results should be made available to trial participants concurrently with the sharing of summary-level results, no later than 12 months after study completion.
  - The full data package (including the full analyzable data set, the full protocol,1 the full statistical analysis plan, and the analytic code) should be shared no later than 18 months after study completion (unless the trial is in support of a regulatory application).
- **Publication:**
  - The post-publication data package (including the subset of the analyzable data set supporting the findings, tables, and figures in the publication and the full protocol, full statistical analysis plan, and analytic code that supports the published results) should be shared no later than 6 months after publication.
- **Regulatory application:**
  - For studies of products or new indications that are approved, the post-regulatory data package (including the full analyzable data set and clinical study report redacted for commercially or personal confidential information, together with the full protocol, full statistical analysis plan, and analytic code) should be shared 30 days after regulatory approval or 18 months after study completion, whichever occurs later.
  - For studies of new products or new indications for a marketed product that are abandoned, the post-regulatory data package should be shared no later than 18 months after abandonment. However, if the product is licensed to another party for further development, these data need be shared only after publication, approval, or final abandonment.

IOM Report: Recommendation 3 Points to consider for data holders

- Employ data use agreements that include provisions aimed at protecting clinical trial participants, advancing the goal of producing scientifically valid secondary analyses, giving credit to the investigators who collected the clinical trial data, protecting the intellectual property interests of sponsors, and ultimately improving patient care.

- Employ other appropriate techniques for protecting privacy, in addition to de-identification and data security.

- Designate an independent review panel—in lieu of the sponsor or investigator of a clinical trial—if requests for access to clinical trial data will be reviewed for approval.

- Include lay representatives (e.g., patients, members of the public, and/or representatives of disease advocacy groups) on the independent review panel that reviews and approves data access requests.

- Make access to clinical trial data transparent by publicly reporting

  - the organizational structure, policies, procedures (e.g., criteria for determining access and conditions of use), and membership of the independent review panel that makes decisions about access to clinical trial data; and

  - a summary of the decisions regarding requests for data access, including the number of requests and approvals and the reasons for disapprovals.

- Learn from experience by collecting data on the outcomes of data sharing policies, procedures, and technical approaches (including the benefits, risks, and costs), and share information and lessons learned with clinical trial sponsors, the public, and other organizations sharing clinical trial data.

Glossary for CTDT

- CTDT: Clinical Trial Data Transparency
- CCI: Commercially Confidential Information
- FOI: Freedom of Information
- IOM: Institute of Medicine (of the National Academies)
- IPD: Individual Patient Data
- PPD: Protection of Personal data
- Reduction: So-called “マスキング” in Japanese-English
- TRIPs: Trade Related Aspects of Intellectual Property Rights

- Transparency vs. Disclosure: Ref to PhUSE
- Data Sharing | Disclosure | Publication | Registration