Clinical Trials Data Transparency: The Regulatory Barriers

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Industrial Knowledge Production
Post-Thalidomide

- Creation of > $5 billion research “service” industry: CROs, Commercial RECs/IRBs, Communication Agencies
- Extraordinary reliance on data produced and submitted by industry, primarily at regulatory approval stage
- Integration of academic science (investigators & literature) in industrial data protection: recruitment patients & credentializing industry-controlled science
- Little regulatory control on public presentation science
Data Transparency

- Pushed for at international level by WHO, PAHO, WMA, ICMJE, ... since 2004 following Paxil & Vioxx controversies

- Statutory Changes, Regulations or guidelines in Argentina, Brazil, Canada, Cuba, India, Japan, US, Europe, ...

- Canada: Vanessa’s Law 2014 - Transparency as part of improved Post-Marketing Surveillance; Draft Guidelines for Disclosure of Confidential Business Information
Legal barriers remain:

Art. 39.3 TRIPS Undisclosed Data:

Undisclosed tests or data submitted to regulatory agencies as condition of approval is to be protected against unfair commercial use and against disclosure, except:

- where necessary to protect the public

OR:

+ unless steps are protect against unfair commercial use
“Necessary in Public Interest” - Interpretations

Narrow interpretation: only disclosure of specific data sets that are immediately ‘necessary’ for action

Broad Interpretation: full transparency of all clinical trials data & study reports

+ Regulatory data as ‘public goods’

+ Full transparency as essential component of “Right to Health” or other Human Rights related rights (e.g. ECHR & EU right to protection of private & family life)
Section 21.1: discretionary authority of Minister of Health to disclose CBI

(2) If serious risk of injury to human health

(3) Disclosure to government, person who provides advice, or a person who carries out functions relating to the protection or promotion of human health or the safety of the public if: for Protection of Promotion of Human Health or the Safety of the Public
CONFIDENTIALITY AGREEMENT

BETWEEN:

HER MAJESTY THE QUEEN IN RIGHT OF CANADA,
as represented by the Minister of Health ("Health Canada")

- and -

DR. NAVINDRA PERSAUD
Terms of Confidentiality Agreement

- Very Broad Definition of Confidential Business Information: not publicly available; protected by holder; commercial value

- Obligation of Confidentiality: including
  - Not to be reproduced in whole or in part in any document, paper, manuscript
  - Not to be disclosed to third parties

- Obligation to submit any draft document at least 15 days before submission for publication for verification

- Destruction of all information at end of project

- Obligation to indemnify HC for any claim resulting from breach
European Data Access EMA

- EMA Policy 2010: Shift in Presumption in Data Access Decisions
  - From Secrecy & Access to data as Exception
    - Access = Rule; Restriction = Exception to be justified by industry
  - Result: Release of 1,9 million pages data between 2011-2013

- New Clinical Trials Regulation 2014

- EMA New Policy on Prospective Sharing of Data 2014
Access Challenges European General Court 2013/14
ECJ Appeal of Interim Decision (Dec. 2013)

+ Vice-president ECJ annuls interim measure General Court: EMA can publish data Humira and Esbriet
  + Damages resulting from potential breach of commercial secrecy interest in data can be calculated ex post
  + Even if data would be protected as part of right to protection of private life, not all breaches of fundamental right have same consequences and are irreparable with financial damages
Final Policy: 3 Different Data Categories

+ Category 1: Data containing Commercial Confidential Information: considered to be exceptional (clinical trials data is considered CCI only in exceptional circumstances—duty on industry to provide evidence)

+ Category 2: Data without Protection of Personal Data Concerns

+ Category 3: Data with PPD Concerns: raw clinical trials data:
  + de-identification needed before release
  + Only for public health purpose
  + No use for market authorization in non-EU jurisdiction
“Clinical trial (and other) data from the European Medicines Agency (EMA) offers the best available opportunity to address the extensive reporting bias in pharmaceutical trial literature. Data are requested via freedom of information requests, but 5 years on, little is known about how the system is working.”
International Trade Context

- Nov. 2013 Draft European Directive “on the protection of undisclosed know-how and business information (trade secrets) against their unlawful acquisition, use and disclosure”: very broad definition of trade secrets

- Final Trade Secret Directive April/May 2016

- US: congressional initiatives
  - Coons/Hatch Bill: Defend Trade Secrets Act
  - Lofgren Bill: Private Right of Action against Trade Secrets
  - Future of American Innovation and Research Act 2013: federal civil liability for trade secret misappropriation
Almost every aspect of the drug development process involves the generation and application of substantial amounts of technical information and know-how, including the (...) clinical trials phase.”

“disclosure of companies’ non-public data submitted in clinical and pre-clinical dossiers and patient-level data sets risks damaging public health and patient welfare. PhRMA and its members urge the U.S. government to engage with the EU in every available venue to ensure responsible data sharing that protects patient privacy, maintains the integrity of the regulatory review process, and preserves incentives for biomedical research by adequately shielding confidential commercial information from inappropriate disclosure. The EMA’s current and proposed data disclosure policies jeopardize these principles.”

(PhARMA submission to Douglass Bell, Chair US Trade Policy Staff Committee May 10, 2013)
Industry Opinions 2

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Europe Directive Trade Secrets (2016)

Companies are subject to legal obligations to disclose information of public interest, for example, in the chemical and pharmaceutical sectors. Such regulations, which ensure a high level of transparency, will not be affected. The draft directive does not provide any grounds for companies to hide information that they are obliged to submit to regulatory authorities or to the public at large.

European Commission Internal Market, Industry, Entrepreneurship
Concerns

This vote weakens recent efforts by European Institutions to increase sharing and transparency of essential health data. Clinical trials data transparency is key for patient safety, for access to affordable medicines, for public health research and innovation. Today’s vote is clearly designed to undermine the Clinical Trials Regulation, on which the ink is barely dry, which was huge progress for patient safety and access to medicines, but has always been opposed by the pharmaceutical industry which prefers to conduct trials in secrecy. It also seems to be aiming at smoothing the way for the pharmaceutical industry in the EU-US TTIP negotiations, and would lower transparency requirements in the EU to be closer in line with much weaker rules in the US.

Nina Renshaw, Secr Gen European Public Health Alliance
Concerns

+ Very Broad Definition Trade Secrets:
  + Information is Confidential
  + Commercial Value because of its confidentiality
  + Reasonable efforts to keep it confidential

+ No need for companies to identify which information is considered a trade secret
(a) for exercising the right to freedom of expression and information as set out in the Charter of Fundamental Rights of the European Union, including respect for freedom and pluralism of the media

(b) for revealing a misconduct, wrongdoing or illegal activity, provided that the respondent acted for the purpose of protecting the general public interest

© the trade secret was disclosed by workers to their representatives as part of the legitimate exercise of their representative functions in accordance with Union or national law, provided that such disclosure was necessary for that exercise;

(d) for the purpose of protecting a legitimate interest recognised by Union or national law
Concerns

- Precautionary measures to prohibit the disclosure of TS during legal procedures

- Directive sets minimum standards: Countries can impose more stringent measures E.g. France proposed criminal penalties including jail for violation.

- Whistleblowers (employees): need to demonstrate that they acted with “the purpose of protecting the public general interest”: Onus is on whistleblowers to provide evidence
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