



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# Open trial data for all? An EMA perspective

Amsterdam, HAI, Oct 2012  
Hans-Georg Eichler





# Did EMA have a transparency problem?

“To regulate the pharmaceutical industry behind closed doors is the antithesis of science.

But the EMA have made their decisions about this, so we are left with blind faith, at an inevitable cost.”

Drug trial secrecy leaves us dependent on blind faith



**Ben Goldacre**

The Guardian, Saturday 5 March 2011

[Article history](#)

“The EMA has been given a rap over the knuckles by the European Ombudsman for a perceived lack of transparency.”

<http://www.inpharm.com/news/ema-transparency-criticised>



BMJ

BMJ 2011;342:d2686 doi: 10.1136/bmj.d2686

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# Opening up data at the European Medicines Agency

Widespread selective reporting of research results means we don't know the true benefits and harms of prescribed drugs. **Peter Gøtzsche** and **Anders Jørgensen** describe their efforts to get access to unpublished trial reports from the European Medicines Agency

Peter C Gøtzsche *professor*, Anders W Jørgensen *PhD student*

Nordic Cochrane Centre, Rigshospitalet and University of Copenhagen, Dept 3343, Blegdamsvej 9, DK-2100 Copenhagen Ø, Denmark



# A change of minds and hearts

“Clinical trial data is not  
commercial confidential information”

EMA position



# The evolution of transparency

- Clintrials.gov
- Summary of results to be published
- Access to documents – retroactive availability of trial reports
- Proactive publication of trial reports
- ? Public availability of ‘raw’ data ? (pre-licensing RCT, pharmacovigilance, observational data)

**“Playing with data”**



# Data is like children...



**You like your own best, and do not like  
strangers to play with them**



# Transparency and the division of labor

“Historically, observation and analysis have been yoked together, the person who does the experiment analyses the data. ...

M. Nielsen. Reinventing Discovery. Princeton Press 2011

Exceptions: regulated products, e.g. medicines

“...a new division of labor.”

M. Nielsen. Reinventing Discovery. Princeton Press 2011



# Playing with data: boon or bane for drug development and public health?

## Cons:

- Data protection issues
- Phantom risks, health scares
- Industry and regulators will be blind-sided





# The brave new world of data transparency...

“We have entered an era of increasingly frequent publication of meta-analyses, some of which identify potential safety signals. Such publication commonly leads to urgent calls to take immediate regulatory action....”

Michele TM et al; NEJM 363:1097-1099; September 16, 2010

**Third party (publications) will drive the agenda; many drugs will come under attack**

## Safety Data from Pooled Analysis of Tiotropium Trials and UPLIFT.\*

Attribute	29 Pooled Trials (N = 13,544)
Study duration	1–12 mo
Patient-years (placebo group)	3065
Patient-years (tiotropium group)	4571
Relative risk (95% CI)	
Stroke	
Myocardial infarction	
Death from cardiovascular causes†	
Death from any cause	

**Singh et al, 2008:  
“relative risk of  
cardiovascular events of  
1.60 (95% CI, 1.22 to  
2.10)”**

\* Data from UPLIFT (Understanding Potential Long-Term Impacts on Function with Tiotropium) are for the treatment period plus 30 days of follow-up, not including vital status for patients who withdrew from the trial. Data may be found at [www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Pulmonary-AllergyDrugsAdvisoryCommittee/ucm190461.htm](http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Pulmonary-AllergyDrugsAdvisoryCommittee/ucm190461.htm). CI denotes confidence interval.

## Safety Data from Pooled Analysis of Tiotropium Trials and UPLIFT.\*

Attribute	29 Pooled Trials (N = 13,544)	UPLIFT (N = 5992)
Study duration	1–12 mo	48 mo
Patient-years (placebo group)	3065	8499
Patient-years (tiotropium group)	4571	9222
Relative risk (95% CI)		
Stroke	1.37 (0.73–15.6)	0.95 (0.70–1.29)
Myocardial infarction		0.71 (0.51–0.99)
Death from cardiovascular causes†	0.97 (0.54–1.75)	0.73 (0.56–0.95)
Death from any cause		0.85 (0.74–0.98)

\* Data from UPLIFT (Understanding Potential Long-Term Impacts on Function with Tiotropium) are for the treatment period plus 30 days of follow-up, not including vital status for patients who withdrew from the trial. Data may be found at [www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Pulmonary-AllergyDrugsAdvisoryCommittee/ucm190461.htm](http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Pulmonary-AllergyDrugsAdvisoryCommittee/ucm190461.htm). CI denotes confidence interval.

*Michele et al, NEJM 363; 12:1097-99, 2010*



# How many good drugs will we lose?

“... there are challenges to achieving meaningful informed consent in postmarketing trials of drugs for which there is a signal indicating the possibility of drug-related harm.”

Mello MM, Goodman SN, Faden RR. Ethical considerations in studying drug safety-the Institute of Medicine report. N Engl J Med. 2012 Sep 6;367(10):959-64.



# Playing with data: boon or bane for drug development and public health?

## Pros:

“open science” could support development of:

- predictive models for patient selection to appropriate treatments/doses
- machine learning systems
- matching patient history to clin trial data set
- enable Comparative Effectiveness Research



## **Comparative Efficacy and Safety of New Oral Anticoagulants in Patients With Atrial Fibrillation**

Sebastian Schneeweiss, MD, ScD; Joshua J. Gagne, PharmD, ScD; Amanda R. Patrick, MS;  
Niteesh K. Choudhry, MD, PhD; Jerry Avorn, MD

- three new active substances compared individually against warfarin; ca 45.000 patients in 3 large trials
- common comparator indirect comparison based on publicly available information

Circ Cardiovasc Qual Outcomes. 2012 Jul 1;5(4):480-6.



# Next steps for EMA?



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

20 July 2012  
EMA/406355/2012  
Senior Medical Officer

## Workshop on access to clinical trial data and transparency

Send your expression of interest to [ctdataworkshop@ema.europa.eu](mailto:ctdataworkshop@ema.europa.eu)

The European Medicines Agency is hosting a workshop on access to clinical trial data and transparency on 22 November 2012 from 12.30 to 17.00 in meeting room 2A at the Agency's offices in Canary Wharf, London, UK.



## Next steps for EMA?

Purpose of meeting:

- EMA to listen to all its stakeholders
- be informed when drafting our policy
- establish a working relationship with those stakeholders who are willing to engage





## Next steps for EMA?

While protecting the decision making process,  
develop ...

- standards for storing and sharing of data
- level of data to be released
- standards for protection of personal data
- quality standards
- rules of engagement (open but filtered access?, pre-registration of protocols?)

# Thank you!

(EMA, London, Canary Wharf)

