Safety and Risk Management

Safer medicine. Sound business.

IOM Drug Forum Symposium on Drug Safety: Public/Private Partnerships



Pfizer

Drug Safety – Process of Continuous Improvement

- Manufacturers are continually seeking to add to our armamentarium of safety tools
- Industry also supports the development and validation of new sources of data for the purposes of evaluating drug safety
- Government funding along with support from private entities is critical
- To best serve patients, public/private partnerships must:
  - Be transparent and get input from all parties
  - Provide more opportunities for quality care, not limit patients' access to medicines
  - Assessment of benefit/risk should be science-based

Automated Databases – cornerstone of PPPs

- Automated databases are an important resource for epidemiology studies
  - Cohort and nested case control designs
  - Prospectively collected prescription and medical data
  - Large sample sizes
  - Completed more rapidly than many primary data collection
  - Real world data – customary clinical practice
- Resource for estimating background rates and drug effects
  - Background rates
    - Mortality and serious cardiovascular events among patients with schizophrenia (Saskatchewan, UHC, Medicaid)
  - Drug effects
    - Triptan use and cardiovascular risk (UHC, GPRD)

Issues to Consider

- Scientific safety question should drive the process, not what data are available
  - Data not collected for research purposes (billing, reimbursement)
  - Lack of specificity in coding of public use data make them less useful for answering specific safety issues
  - May not be collected uniformly across sites
- Public use data may have skewed populations that make them problematic for answering safety questions
  - VA data – military population
  - Medicare – elderly population
  - Medicaid- on government assistance
  - UHC – insured population (working healthy)
- Ability to adjust for important confounders limited, such as sociodemographic factors, health behaviors and OTC use

Issues to Consider continued

- Need to validate safety endpoints with medical records
- Medicine may not be reimbursed (e.g. Viagra) or use restricted (e.g. Cox-2s)
- Potential for channeling bias if other medications available for indication (e.g. Geodon, Exubera)
- Some diagnostic or procedural codes inconsistently or rarely used

Epidemiology Post Approval Commitment Studies

Completed, Ongoing and in Regulatory Review

Study	Agency	Safety Objective	Population	Start Date	Total Length of Study	Total Cost of Study
Exubera THIN Lung Cancer Cohort	EMEA FDA	Lung cancer mortality	THIN UK database (n=80,000)	2Q 2007	12 yrs	$8 M
Exubera VOLUME LST	EMEA FDA	Mortality, Pulmonary, CV	5,000 patients from 24 countries, EXU vs. usual care	3Q 2006	8 yrs	$110 M
Celebrex JRA Registry	FDA	General	400 JRA patients <18 yrs, CEL vs. NSAID	1Q 2008	3.5 - 4 yrs	$3 M
Celebrex FAP Registry	EMEA FDA	General	200 FAP patients vs. 200 FAP historical/concurrent controls in US & EU	3Q 2004	6 yrs	$8 M
Celebrex SCOT LST	EMEA	Mortality, CV	20,000 patients, CEL vs. NSAID	1Q 2007	5 yrs (incl. 1 yr pilot)	$10 M
Macugen MISSION Cohort	EMEA	Ocular infection from IVT procedure	550 patients from 16 EU countries	3Q 2006	3 yrs	$7 M
Macugen US Medicare Cohort	FDA	Endophthalmitis from IVT procedure	Medicare patients 2000-2006	4Q 2004 (Ph. I) 4Q 2006 (Ph. II)	4 yrs	$.5 M
Viagra IMHS	EMEA	Mortality, CV	3813 ED patients in France, Germany, Spain & Sweden	Completed	3 yrs	$14 M
Viagra NAION Natural History Case Control	EMEA FDA	NAION	US Data Source	Under regulatory review	3 - 8 yrs	$3 M $10 – 15 M
Chantix Pregnancy Cohort	EMEA FDA	Birth defects	Denmark & Sweden National Registry Data	Under regulatory review	4 - 10 yrs	$1 - 3.5 M
Geodon ZODIAC	FDA MPA	Mortality, CV	18,000 schizophrenia patients from 18 countries	1Q 2007	5 yrs	$77 M
Viracept HAART OC Cohort	EMEA	CV, Hepatoxicity	20,000 patients from US, EU & Australia	1Q 2000	7+ yrs	$4-5 M (Pfizer)

Select Lipitor Clinical End-point Trials

Study	Study Objective	Population	Study initiation/ Completion Dates	Study duration (median follow-up time)	Total Cost
TNT	Reduction of CV events with aggressive lipid lowering in CHD patients, using atorvastatin 80mg vs atorvastatin10mg	10,001 patients; 246 sites in 14 countries	1998-2004	4.9 years	$156 M
IDEAL	Reduction of CV events with aggressive lipid-lowering in CHD patients, using atorvastatin 80mg vs simvastatin 20/40mg	8,888 patients; 190 sites in 6 countries	1999-2005	4.8 years	$55 M
SPARCL	Reduction of repeat stroke in patients without CHD, using atorvastatin 80mg vs placebo.	4,731 patients; 205 sites in 27 countries	1998-2005	4.9 years	$98 M

Clinical Trial Disclosure: IOM's Recommendation and Pfizer's Policy

IOM Report Recommendation:

- Congress should require industry sponsors to register in a timely manner at clinicaltrials.gov, at a minimum, all Phase 2 through 4 clinical trials, wherever they may have been conducted, if data from the trials are intended to be submitted to the FDA as part of an NDA, sNDA, or to fulfill a postmarket commitment.
- Posting should include a structured field summary of the efficacy and safety results of the studies.

Pfizer's Policy for Clinical Trial Disclosure (eff. 1/1/07):

- All studies in patients are registered at clinicaltrials.gov prior to the start of the study. This includes Phase 1 trials conducted in patients as well as Phase 4 observational trials with prospective data collection.
- Study results are made public for the same scope of studies described above at clinicalstudyresults.org (with hyperlinks to the registry data). In addition, studies included in approved applications and studies with results that are considered medically significant will also have study results disclosed. Therefore, Phase 1 studies that were included in an approved application and were conducted using healthy volunteers would have results disclosed.

Clinical Trial Disclosure: Other IOM Recommendations and Pfizer's Position

IOM Suggests:	Pfizer Position:
Study registration site should accommodate results.	Pfizer currently adds hyperlinks between study registration on clinicaltrials.gov and study results on clinicalstudyresults.org to help ease of use.
Disclosed data should be structured and leverage the WHO and ICH E3 synopsis standards.	Pfizer follows the IFPMA Joint Position which commits members to register clinical trials using the 20 data fields established by the WHO, with the sponsor reserving the right to delay disclosure of 5 fields (e.g. interventional name, primary and key secondary endpoints, official scientific title, target sample size) in rare cases when competitive reasons dictate. The Joint Position also commits Industry to post summary results for these studies using the ICH format.
The FDA and NLM share the task of reviewing all clinical trial information submitted for completeness and accuracy.	Pfizer stands behind the completeness and accuracy of the information it discloses about our clinical trials. Practicality needs to be considered, especially with regard to the impact on the timely disclosure of information.
Posting of raw data is not recommended.	Pfizer agrees with this recommendation.