

*Public Hearing on CDER's
Current Risk Communication
Strategies for Human Drugs
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- *How easily accessible and understandable are FDA's Internet-based sources of drug information?*
- *What are the strengths and weaknesses of communication tools listed:*
 - Patient and Healthcare Professional Information Sheets
 - Talk Papers
 - Public Health Advisories (PHAs)
 - Press Releases
 - MedWatch Safety Updates
 - Patient Safety News program

- *What information is available about awareness, use, and perceptions of effectiveness by health care professionals and by public in general?*
- *Do these tools provide right kind and amount of risk and other information that*
 - Health professionals need to make informed decisions about whether to prescribe drug products,

AND

 - Public needs to make informed decisions about whether to use those products?

“Fellow citizens, we cannot escape history.”

– Abraham Lincoln, President of the United States,
Second Annual Message to Congress (December 1,
1862)

Accessibility

- Documents readily available on FDA website, so apparently follows they are easily accessible
 - However, health professionals and consumers need to know material posted and how to navigate website
- Methods
 - MedWatch Partners:
 - Expands notification and information dissemination
 - FDA's free e-mail listservs, e.g.,
 - MedWatch
 - CDER Consumer Information
 - FDA Drug Information
 - FDA Consumer

**Goldman SA. Communication of medical product
risk: how effective is effective enough?**

Drug Safety 2004;27:519-534¹

Critical Questions¹

- Labeling changes/large-scale health professional notification: *are they effective, and what is standard for effectiveness?*
- Interventions to improve medication use: *do they actually result in modified behavior?*
- Educational efforts regarding medical product risk: *do they make any difference?*

Labeling Changes/Large-Scale Health Professional Notification¹

Disparate Categories of Risk

- *Drug-drug interactions* (terfenadine; cisapride)
- *Off-label use* (bromfenac)
- *Recommended blood test monitoring* (troglitazone)
- *Teratogenicity* (acitretin)

Drug-Drug Interactions: Cisapride

Coprescription with Contraindicated Meds

- *After notification:*
 - 3.4% overlap of cisapride with at least 1 contraindicated drug²
 - 3.1% of patients used ≥ 1 potentially interacting drug(s)³
- *After implementation of computerized alerting system⁴*
 - Decrease from 9% to 3.1% in proportion of patients receiving contraindicated drug with cisapride
 - Discharge on potentially hazardous drug combination: 36.2% to 7.7%

²Jones JK, et al. *JAMA* 2001;286:1607-1609

³De Bruin ML, et al. *Ann Pharmacother* 2002;36:338-343

⁴McMullin ST, et al. *Arch Intern Med* 1999;159:2077-2082

Drug-Drug Interactions: Cisapride

- Impact on desired standard of care seen as demonstrating notification to have been almost total failure⁵
- Effect of notification content⁶
 - 1998: 58% ↓ in concomitant dispensing w/drugs specifically denoted as contraindicated, but not those exemplifying/implied as members of drug class
 - 1999 letter stressing proscribed medical conditions had no discernible effect on coprescription

Findings seen as indicative of tantamount importance of wording to actual content in altering physician behavior

⁵Smalley W, et al. *JAMA* 2000;284:3036-3039

⁶Weatherby LB, et al. *Clin Pharmacol Ther* 2002 Dec;72:735-742

Notification Wording/Content

- Apparent key features of successful drug notification:
 - Specificity Prominence
 - Brevity Does not depend on secondary information
 - Publicity Personal discussions⁶
- Do content, organization and formatting of Dear Doctor letters affect physician response?
 - Deficient areas identified
 - Clarity
 - Readability
 - Proportion of perceived relevant information to supporting information
 - Easy discernability of critical information
 - Preference for letters with formatting that highlights key information⁷

⁷Mazor KM, et al. *Pharmacoepidemiol Drug Saf* 2005;14:869-875

Information Provided to

Health Professionals and Consumers

Low Molecular Weight Heparins (LMWHs)/Heparinoids

- **12/97:** FDA releases PHA of reported epidural/spinal hematomas in association with LMWHs and spinal/epidural or LP, w/subsequent neurologic injury (including long-term/permanent paralysis)⁸
- **2/98:** 2/5/98 Advisory Committee transcript posted on website
- **5/98:** Q & A's re LMWHs/heparinoids and spinal/epidural anesthesia released, with updated safety information provided⁹:
 - Common clinical aspects
 - Signs/symptoms of spinal/epidural hematoma in reports
 - Factors to consider in performing procedures
 - Where to find further information

⁸Lumpkin MM. FDA Public Health Advisory. December 15, 1997

⁹FDA. Q & A's: Low Molecular Weight Heparins/Heparinoids and Spinal/Epidual Anesthesia. May 6, 1998

Information Provided to Health Professionals and Consumers

COX-2 Selective and Non-Selective NSAIDs

- **April 7, 2005:** FDA announces planned regulatory actions for valdecoxib, celecoxib & prescription/OTC NSAIDs¹⁰
 - **Public Health Advisory**
 - **Drug Information Page**
 - **Q's and A's**
 - Product-specific information, including
 - Perceived benefit/risk profiles
 - Requested labeling changes (including boxed warnings)
 - Related issues (e.g., Advisory Committees; informational basis for FDA decisions)

¹⁰www.fda.gov/medwatch/SAFETY/2005/safety05.htm

Information Provided to Health Professionals and Consumers

NSAIDs

- ***June 15, 2005***: FDA issues supplemental request letters to sponsors of all NSAIDs asking for labeling changes for their products, and posts on website¹¹
 - ***Prescription***:
 - Supplemental request letter
 - Labeling template
 - Medication Guide (which uses Q's and A's format)
 - ***OTC***:
 - Supplemental request letter and labeling template

¹¹www.fda.gov/cder/drug/infopage/COX2/default.htm

Teratogenicity: Acitretin¹²

- Adequate dissemination from health authorities/company/professional association to health professionals, but despite use of multi-media approach to inform those at risk:
 - Personal contact with health professional (35% never contacted), *and/or*
 - Media (press, radio, TV)
 - 45% read in newspaper (57% of regular readers couldn't recall message)
 - 60% followed message on radio and TV (35% couldn't recall message)
 - 9% of women at risk did not use any contraception method
- Effect seen as moderate, with recall of message 6-12 months after warning low

Overall effectiveness deemed poor because of insufficient personal communication with those at risk¹²

¹²Sturkenboom MCJM, et al. *Eur J Clin Pharmacol* 1994;47:125-132

Multifacted Approach¹³

- Notable decrease in flucloxacillin use (desired due to association with adverse hepatic reactions) in relation to various interventions seen as resulting from combination of actions, rather than any individual event
 - Caution that evaluation by any one organization of its intervention without consideration of other factors might lead to false conclusion, in either very positive or negative direction
- Sustaining of desired change entails coordination of activities and ensuring concordance of all (educational, regulatory, promotional) disseminated messages¹³

¹³Roughead EE, Gilbert AL, Primrose JG. *Soc Sci Med* 1999;48:845-853

Risk Communication

Effectiveness: Physician to Patient

- Social influences on responses to health risk information about which physicians should be aware:
 - Extent to which informational source is trusted
 - Relevance of information to everyday life/decision-making
 - Relation to other understood risks
 - Concordance with prior knowledge/experience
 - Difficulty/significance of choices/decisions¹⁴
- Improvement in risk communication entails building of trust and awareness of patients' access to varied and conflicting sources of risk information

¹⁴Alaszewski A, Horlick-Jones T. *Br Med J* 2003;327:728-731

Risk Communication

Effectiveness: Physician to Patient

- Physicians need to be aware of possible confusion in relaying medical statistics with health risk information¹⁵:
 - Single event probabilities, e.g., statement of “30% chance of rain tomorrow” can be interpreted by some people as:
 - Tomorrow it will rain in 30% of area, or
 - Tomorrow will see rain 30% of the time, or
 - There will be rain on 30% of days like tomorrow
 - Conditional probabilities (specificity; sensitivity)
 - Relative risk
- Confusion can be reduced or eliminated with good, simplified representation of risk

¹⁵Gigerenzer G, Edwards A. *Br Med J* 2003;327:741-744

Lessons Learned: Labeling Changes and Large-Scale Notification¹

- In choosing communication methods/assessing effectiveness, major categor(ies) of perceived risk must also be part of evaluative process
 - As behaviors associated with each category of risk may well differ, so may communication methods optimally utilized

Given that all risks are NOT the same, one size of risk notification tool may NOT fit all

Lessons Learned: Labeling Changes and Large-Scale Notification¹

- Multiple modes of risk communication and maximal publicity may well heighten overall effectiveness
- In assessing effectiveness of risk communication, desired results **MUST** be clearly stated
 - A fair degree of achieved success may not be seen as effective enough to prevent market withdrawal

Lessons Learned: Labeling Changes and Large-Scale Notification¹

- Medical products differ in perceived benefit/risk, based on such factors as
 - Disease entity or population treated
 - Availability of other products
 - Reversibility of AE(s) in question
- Thus, each case merits individualized assessment, rather than formulaic, “cookie-cutter” approach

Lessons Learned: Labeling Changes and Large-Scale Notification¹

- Understanding how HPs use risk information critical to improvement in communication methods
 - Examine varied information sources and related factors impacting practitioner behavior
- Optimum use of promising new communication technologies (e.g., Internet; computerized pharmacy systems) is global learning process
- Information overload/increasing time demands on HPs must be acknowledged and considered when planning/assessing risk communication

Lessons Learned: Information Provided¹

- Risk information intended for health professionals should be as clinically oriented and relevant to patient care as possible
- FDA generation/dissemination of Q's & A's based on latest safety information for particular drug of concern should be encouraged/modeled
 - Specifically targeted to treating healthcare community and consumers
 - Address perceived leading concerns/issues for both sectors

Lessons Learned: Risk Communication¹

- For optimal risk communication effectiveness:
 - Awareness of social and psychological factors that impact risk information receipt and perception
 - Clarity of presentation and minimization of ambiguity/possible sources of confusion
 - Establish deserved trust in informational sources
 - Critically evaluate sources of risk information

“The speed of communication is wondrous to behold. It is also true that speed can multiply the distribution of information that we know to be untrue.”

– Edward R. Murrow (1908-1965)

Lessons Learned: Health Professional Education¹

- Drug safety/risk management education for HPs should not be exclusively product-specific
- Goals should include
 - Greater awareness of medical product-induced disease
 - Recognition
 - Management
 - Reporting
 - Enhanced knowledge/application of pharmacotherapy, and of impact individual patient factors can have on pharmacotherapy

Lessons Learned: Health Professional Education¹

- Education efforts need to involve
 - ALL levels and health professional disciplines
 - Professional schools
 - Training programs
 - Post-graduate continuing education
- Based in care delivery setting (e.g., hospitals; clinics)
- MUST be ongoing
 - One-shot programs not nearly enough
- No quick fix -- must be commitment of resources
 - Partnerships/cooperation among stakeholders

Conclusion¹

- Do these risk communication modalities result in desired outcomes?
 - Based on current knowledge/experience gained, answer of “yes, but not in all circumstances, not every time, and not always to the ideal extent” appears reasonable
- New methods/novel combinations need to be sought/
tested to minimize preventable AEs/use errors and
protect patients to greatest degree possible

“History repeats itself; that’s one of the things that’s wrong with history.”

– Clarence Darrow (1857-1938)