The United States Drug Safety Paradigm

Stephen A. Goldman, M.D., FAPM, FAPA

Former Medical Director, MedWatch, FDA

Stephen A. Goldman Consulting Services, L.L.C.

Morris Plains, New Jersey, USA

sagcs@aol.com

Evolution of FDA Requirements/Initiatives

International Conference on Harmonization (ICH) and related activities: 1990s to present

- ***1999***: *"Managing the Risks from Medical Product Use"*
  - Report to FDA Commissioner from Task Force on Risk Management
- ***2000***:
  - ICH
    - E2B
    - Common Technical Document
  - Medical Errors
    - Institute of Medicine: "*To Err is Human: Building a Safer Health System*" (1999)

Evolution of FDA Requirements/Initiatives

FDA/ICH-related activities in 2000's:

- ***2001***:
  - Risk Issues (Communication)
  - Medical Errors
- ***2002***:
  - Office of Drug Safety
- ***2003***:
  - The "Tome": Proposed Rule of March 14, 2003
  - Risk Management White Papers
  - E2D (step 4)
  - E2E (step 2)

Evolution of FDA Requirements/Initiatives

FDA/ICH-related activities in 2000's:

- ***2004***:
  - Risk Management Draft Guidances (comment period ended July 6, 2004)
  - E2E (step 4)
- ***2005***:
  - Final Risk Management Guidances issued (March 24, 2005)
  - E2E Guidance issued (April 1, 2005)
  - Proposed Rule becomes Final Rule??

Task Force on Risk Management

- Under FDA Commissioner Henney, Task Force established to assess system for managing risks associated with use of FDA-approved medical products
  - Particular focus on FDA's role
- May 1999: Report to FDA Commissioner
  - ***"Managing the Risks from Medical Product Use: Creating a Risk Management Framework"***[1]

[1]**www.fda.gov/medwatch/articles.htm**

Task Force on Risk Management[1]

- Evaluated risk management in entire healthcare delivery system
- Applied risk management model utilized in other government sectors
- Assessed FDA role
  - Premarketing
  - Postmarketing
- Examined all FDA risk management activities in context of overall system

Task Force on Risk Management: Findings[1]

- Time right for new systems framework
  - Better risk understanding + more system integration = more effective risk interventions
- Each participant's role not clearly defined
- Engage stakeholders to assess current risk management system
- Critical to understand types of risks and sources

Task Force on Risk Management: Findings[1]

Medical product risks: 4 general categories

- Known side effects
  - Most injuries and deaths
  - Estimated more than 50% avoidable[2]
- Medication/device errors
  - Also preventable
- Product defects
  - Uncommon in U.S.
- Remaining uncertainties

[2]Bates DW, Leape LL, Petrycki S. *J Gen Intern Med* 1993:8:289-294

Task Force on Risk Management: Findings[1]

FDA's current role in risk management

- Withdrawal rates and unexpected serious AEs resulting in labeling changes remain low
- Several factors limit discovery of AEs in premarketing
  - Changes would increase costs and slow availability
- Postmarketing surveillance/risk assessment performing as designed

Task Force on Risk Management: Recommendations[1]

Most focused on ways to further improve risk management within current system, including

- Professional education/core competency training for all reviewers
- Integrate current postmarketing systems
  - Uniform application of analytical tools, data entry and editing
  - All information readily available to reviewer
- Intensify surveillance of newly marketed products
- Develop new methodologies for available datasets
- Meeting/series of meetings with stakeholders

Task Force on Risk Management: Options[1]

- Address limitations of premarketing study
  - Large simple trials
  - Restricted exposure early in postmarketing
- Design/implement supplemental ways to obtain postmarketing data, e.g.,
  - ***Sentinel sites***
  - Prospective registries
  - Enhanced external database linkages

Rhode Island ADR Reporting Project[3]

- Designed to increase physician reporting of suspected ADRs via sustained education utilizing several forms[3]
  - After 2 years, > 17-fold increase in Rhode Island direct reports *vs* yearly average prior to project (similar increases not seen in overall U.S. rate)
  - Similar trend seen regarding serious reports
    - *1981 - 1985*: 0.4% of total serious reports to FDA
    - *1988*: 3.6% of all serious direct reports to FDA
      - 31 reports on unlabeled reactions through 1988

[3]Scott HD, et al. *JAMA* 1990;263:1785-1788

Rhode Island ADR Reporting Project[3]

- Pre- and post-intervention surveys found significant gains in knowledge and attitude toward ADR reporting system[3]
  - *Pre-intervention*
    - 55% familiar with FDA ADR reporting program
    - 39% familiar with FDA forms/guidelines for reporting
  - *Post-intervention*
    - 85% familiar with FDA ADR reporting program
    - 69% familiar with FDA forms/guidelines for reporting

MedSun: Medical Product Surveillance Network[4]

- Pilot program begun in 2002
  - Internet-based system designed to be easy/secure way for user facilities to report serious medical device problems mandated under Safe Medical Devices Act
- CDRH contracted CODA to manage program
- Designed to foster important partnership between clinical sites and FDA
  - Used to identify problems and work with manufacturer to produce safer product

[4]www.medsun.net/about2.asp

MedSun[4]

- Serves as two-way communication route between CDRH and clinical community
  - Once problem identified, researchers work with each facility's representatives to clarify situation/fully understand problem
  - Reports later shared without facility identification with rest of MedSun healthcare network so that clinicians can take necessary preventative actions
- Currently ~ 280 hospitals/nursing homes participating, including some of major US teaching hospitals
  - Expected that 300+ healthcare facilities will participate in 2005

MedSun[4]

Benefits of Participation

- Beyond helping ensure medical device safety:
  - **Educational Programs**: at request of several sites, CODA and FDA developed programs designed to encourage staff to report device problems using internal reporting procedures
  - **Feedback**: Facilities report greatest benefit of program is feedback received
    - Includes personal follow-up from MedSun staff members after report filed, as well as information sharing among participating organizations through monthly newsletter
  - **Contribution**: being on forefront of new system designed to yield significant information about medical device safety, facility input is important contributor to system design

Task Force on Risk Management: Options[1]

- Enhance FDA epidemiology/methodology research
- Enhance FDA role/responsibilities in risk communication
- ↑ interventions for special risk products
  - Restricted distribution
  - Mandatory education (providers/patients)
- Legislative changes for risk intervention
  - Suspension authority for drugs

Task Force on Risk Management[1]

- Shared responsibility for risk management
  - FDA
  - Manufacturers
  - Health professionals
  - Patients
  - Other federal groups
  - Healthcare delivery systems
  - Professional societies

2002: Office of Post-marketing Drug Risk Assessment (OPDRA) renamed Office of Drug Safety (ODS)[5]

- ***Division of Drug Risk Evaluation (DDRE)***
  - Safety evaluators detect/assess safety signals
    - Work with Office of New Drugs medical reviewers to place in context
  - Epidemiologists
    - Review epidemiologic study protocols - required Phase 4 commitments
    - Evaluate postmarketing surveillance tools - risk management strategies
    - Estimate public health impact of safety signals (literature; databases)
- ***Division of Medication Errors and Technical Support (DMETS)***
  - **Pre-marketing review of proprietary names, labels and labeling**
  - Post-marketing review/analysis of medication errors received by CDER

[5]**www.fda.gov/cder/Offices/ODS/divisions.htm**

FDA Human Factors Program

What is Human Factors?[6]

- Human factors is study of how people use technology
  - Involves interaction of human abilities, expectations, and limitations with work environments and system design
- "Human factors engineering" (HFE): application of human factors principles to device and systems design
  - NB: often interchanged with such terms as "ergonomics"
- HFE goal: design devices users willingly accept and operate safely in realistic conditions
  - In medical applications, helps improve human performance and reduce risks associated with use error

[6] **www.fda.gov/cdrh/humanfactors/whatis.html**

HFE[6]

- In many cases, focuses on device user interface
  - Includes all components/accessories necessary to operate and properly maintain device, including
    - Controls, displays, software, logic of operation, labels and instructions
- Specific HFE benefits include:
  - Reduced risk of device use error
  - Better understanding of patient's current medical condition
  - Easier to use (or more intuitive) devices
- Should occur early in product development process, and include tools such as
  - Analysis of critical tasks, use error hazard and risk analysis, and realistic use testing

FDA Office of Drug Safety[5]

Division of Surveillance, Research, and Communication Support (DSRCS)

- Data resources
- Outcomes/effectiveness research components of drug safety risk management programs
- Oversees
  - MedWatch
  - Risk communication research and activities, e.g.,
    - Medications Guides
    - Patient Packet Inserts
    - Pharmacy information surveys
    - International regulatory liaison activities for all drug/biologic postmarketing safety issues

FDA Proposed Rule: The "Tome"

"Safety Reporting Requirements for Human Drug and Biological Products: Proposed Rule"

March 14, 2003

Federal Register Volume 68, No. 50, 12405-12497[7]

– *Comment period closed October 14, 2003*

[7]**www.fda.gov/OHRMS/DOCKETS/98fr/03-5204.pdf**

FDA Proposed Rule: Rationale[7]

- Harmonize with ICH and CIOMS standards
- Enhance "worldwide consistency" in safety data collection and safety report submission
- Improve safety report quality
- Speed evaluation of important safety information by Agency
- Protect/promote public health

FDA Proposed Rule[7]

- **Premarketing Expedited Safety Reporting Regulations (IND Safety Reports)**:
  - *21 CFR 312.32 (investigational human drugs or biological products)*
- **Postmarketing Safety Reporting Regulations**:
  - ***Drugs**: 310.305 (marketed w/o approved NDA/ANDA)*

    314.80 (approved NDAs)

    314.98 (approved ANDAs)
  - ***Biological products**: 600.80 (approved BLAs)*

FDA Proposed Rule[7]

Drugs

"Associated with the use of the drug" and

"adverse drug experience" changed to

"suspected adverse drug reaction (SADR)"

Biologics

"Adverse experience" changed to "suspected adverse reaction (SAR)"

FDA Proposed Rule[7]

SADR

"A noxious and unintended response to any dose of a drug ['biological' for proposed 600.80(a)] product for which there is a reasonable possibility that the product caused the response. In this definition, the phrase 'a reasonable possibility' means that the relationship cannot be ruled out."

FDA Proposed Rule: SADR[7]

- With respect to clinical studies of investigational and marketed drugs/biologicals, proposed SADR definition likely to result in ↑ safety reporting to FDA from some studies, as
  - "Reasonable possibility" specifically defined
  - Under proposed definition, AE seen as unlikely or remotely related to study product would still need to be reported (as opposed to typical interpretation of current regulatory requirements)

FDA Proposed Rule: SADR[7]

- FDA recognize possibility of SADR "`over-reporting'" in studies of patients with serious, potentially fatal diseases (e.g., cancer)
  - Any one report may not be informative due to possibility of AE being secondary to disease itself
  - Thus, FDA invites
    - Proposals for alternative(s) ways to handle AE reporting in such cases
    - Comments/suggestions on mechanisms to minimize "'over-reporting'" of uninformative events while insuring reporting of relevant unexpected events

FDA Proposed Rule: 312.32[7]

Expedited Reporting: 15 calendar days

- Sponsor must notify FDA/all investigators of information that "based on appropriate medical judgment, might materially influence the benefit-risk assessment of an investigational drug or that would be sufficient to consider changes in either product administration or in the overall conduct of a clinical investigation"
  - Significant unexpected *in vitro*, animal or human (clinical; epidemiological) study safety findings or aggregate data from studies suggesting significant risk to humans (e.g., mutagenicity, teratogenicity or carcinogenicity)

FDA Proposed Rule

[*310.305, 314.80, 314.98, 600.80*][7]

Expedited Reporting: 15 calendar days

- "Always Expedited Reports"
  - Specific SADRs, regardless of expectedness or seriousness, to be reported on expedited basis due to medical gravity:

Congenital anomalies	Acute respiratory failure
Ventricular fibrillation	Torsades de pointe
Malignant hypertension	Seizure
Agranulocytosis	Aplastic anemia
Toxic epidermal necrolysis	Liver necrosis
Acute liver failure	Anaphylaxis
Acute renal failure	Sclerosing syndromes
Pulmonary hypertension	Pulmonary fibrosis

FDA Proposed Rule[7]

Always Expedited Reports: 15 calendar days

- "Confirmed or suspected transmission of an infectious agent by a marketed drug or biological product,"
- "Confirmed or suspected endotoxin shock,"
- "Any other medically significant SADR that FDA determines to be the subject of an always expedited report (i.e., may jeopardize the patient and/or require medical or surgical intervention to treat the patient or subject)."

FDA Proposed Rule[7]

Expedited Reporting: 15 calendar days

- Information sufficient to consider changes in administration of product, based on appropriate medical judgment
  - Significant unexpected *in vitro*, animal or human (clinical; epidemiological) study safety findings or aggregate data from studies suggesting significant risk to humans (e.g., mutagenicity, teratogenicity or carcinogenicity)

FDA Proposed Rule

[*310.305, 314.80, 314.98, 600.80*][7]

Expedited Reporting: 15 calendar days

- Medication errors (*actual/potential*) occurring in US
  - Irrespective of whether actual error results in serious SADR, nonserious SADR, or no SADR
    - Includes "near misses" (medication errors that were prevented before product was actually administered)
  - Includes potential medication errors not involving a patient, but include information/complaint about similarities in product name, packaging or labeling

FDA Proposed Rule[7]

Full Data Set

- Completion of "all applicable elements" on 3500A or CIOMS 1 forms, "including a concise medical narrative of the case (*i.e.,* an accurate summary of the relevant data and information pertaining to an SADR or medication error)"

Active Query

- Healthcare professional (anyone "with some form of health care training") representing manufacturer/ applicant required to speak directly to initial SADR/ medication error reporter if outcome or minimum data set not determinable on first receipt
  - Entails "focused line of questioning" to ascertain "clinically relevant information"

FDA Risk Management White Papers

- *June 12, 2002*: Prescription Drug User Fee Amendments of 2002 [Public Law 102-571] (PDUFA III) signed
  - In exchange for receipt of user fees under PDUFA III, FDA agreed to specific performance goals, including drafting industry guidance on risk management activities
- FDA planned to finalize three guidance documents for industry by September 30, 2004

FDA Risk Management White Papers

- ***2003***: FDA drafted/released for comment three concept papers that outlined Agency's preliminary thinking on
  - "Premarketing Risk Assessment"
  - "Risk Management Programs"
  - "Risk Assessment of Observational Data: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment"*
- Public workshop held April 2003 (Washington, DC) to present FDA's thoughts/solicit input from stakeholder groups

***www.fda.gov/cder/meeting/riskmanagement.htm**

FDA Risk Minimization Guidances

- *May 5, 2004*: FDA released for comment three draft guidances for industry:
  - "*Premarketing Risk Assessment*"
  - "*Development and Use of Risk Minimization Action Plans*"
  - "*Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment*"*
- *March 24, 2005*: Final risk minimization guidances issued**

***www.fda.gov/cder/guidance/index.htm**

****www.fda.gov/bbs/topics/news/2005/NEW01169.html**

Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment[8]

Use of Data Mining to Identify Product-Event Combinations

- Data mining may augment extant signal detection techniques
  - Particular utility in pattern, time-trend and drug-drug interaction assessment
- NOT a tool for establishing causal attributions between products and AEs
- ***"Use of data mining techniques is not a required part of signal identification or evaluation. If data mining techniques are submitted to FDA, they should be presented in the larger appropriate clinical epidemiological context."***

[8]**www.fda.gov/cder/guidance/6359OCC.pdf**

Good PV Practices & PE Assessment[8]

Safety Signals That May Warrant Further Investigation

- New unlabeled AEs (esp. serious)
- Apparent increase in severity of labeled event
- Occurrence of serious events thought extremely rare
- New product-product/ product-device/product-food/product-dietary supplement interactions
- Identification of previously unrecognized at-risk population
- Confusion about name, labeling, packaging, or use
- Concerns arising from manner in which product used (e.g., AEs at > labeled doses or in populations not recommended for tx)
- Concerns arising from potential inadequacies of currently implemented risk minimization action plan
- Other concerns identified by sponsor or FDA

Good PV Practices and PE Assessment[8]

Investigating Signal through Observational Studies

- Signals warranting additional investigation can be evaluated through carefully designed observational studies of product's use in "`real world`"
  - Pharmacoepidemiologic safety studies
  - Registries
  - Surveys
- FDA recommends sponsors choose most appropriate method and encourages discussion of plans for studies with agency

Good PV Practices and PE Assessment[8]

Interpreting Safety Signals: From Signal to Potential Safety Risk

- When evaluation of safety signal suggests potential safety risk, recommend sponsor submit synthesis of all available safety information/analyses, including
  - Spontaneously reported/published case reports
    - Denominator or exposure information to assist interpretation
  - Background event rate (general/specific populations) if known
  - Relative risks/odds ratios/other association measures from pharmacoepidemiologic studies
  - Biologic effects seen in preclinical studies, PK or PD effects
  - Safety findings from controlled clinical trials
  - General marketing experience with similar products in class

Good PV Practices and PE Assessment[8]

For most products, routine PV (compliance with postmarketing regulatory requirements) sufficient

- Unusual safety signals may become evident before approval or in postmarketing - could suggest sponsor consider enhanced PV efforts or PV plan may be appropriate
- *PV plan*: developed to focus on detecting new safety signals and/or evaluating identified safety signals
  - Describes PV efforts beyond routine postmarketing spontaneous reporting designed to enhance/hasten sponsor's acquisition of safety information

Development and Use of Risk Minimization Action Plans[9]

- ***The Role of Risk Minimization and RiskMAPs [Risk Minimization Action Plans] in Risk Management***
  - For majority of products, routine risk minimization measures sufficient to minimize risks and preserve benefits
  - Only a few products likely to merit consideration for additional risk minimization efforts
- ***Relationship Between a Product's Benefits and Risks***
  - Product considered safe if it has appropriate benefit-risk balance for intended population and use
  - Assessment/comparison of product's benefits/risks complicated process influenced by wide range of individualized patient factors

[9]www.fda.gov/cder/guidance/6358fnl.pdf

Development and Use of RiskMAPs[9]

Determining an Appropriate Risk Minimization Approach

- Routine risk minimization measures involve, for example, FDA-approved professional labeling periodically updated to incorporate information from postmarketing surveillance or studies revealing new benefits or risk concerns
  - Efforts to improve FDA-approved professional labeling (viz, December 2000 Proposed Rule) reflect Agency's belief that labeling is cornerstone of risk management efforts for prescription drugs
- For most products, routine risk management will be sufficient and RiskMAP need not be considered

Development and Use of RiskMAPs[9]

- Term *tool* as used means risk minimization action in addition to routine risk minimization measures
  - Process/system meant to minimize known risks
- Some may be incorporated into product's FDA-approved labeling, such as medication guides or patient package inserts
  - FDA-approved professional labeling refers to portion of approved labeling directed to health care practitioners

Development and Use of RiskMAPs[9]

Tools For Achieving RiskMAP Goals and Objectives

- Can communicate information regarding optimal use, and also provide guidance on prescribing, dispensing, and/or using product in most appropriate circumstances or patient populations
- Number of tools available - development of more tools encouraged and anticipated by FDA

Categories of RiskMAP Tools

- Targeted Education and Outreach
- Reminder Systems
- Performance-Linked Access Systems

Development and Use of RiskMAPs[9]

Targeted Education and Outreach

- Examples of tools in category:
  - Health care practitioner letters
  - Training programs for health care practitioners or patients
  - Continuing Education (CE) for health care practitioners
  - Prominent professional or public notifications
  - Patient labeling such as medication guides and patient package inserts
  - Focused or limited promotional techniques such as product sampling or direct-to-consumer advertising

Development and Use of RiskMAPs[9]

Description of RiskMAP Tools

- Targeted Education and Outreach
  - FDA recommends sponsors consider tools in category
    - When risks cannot be minimized with routine measures alone, or
    - As component of RiskMAPs using reminder or performance-linked access systems
  - Use specific, targeted education and outreach efforts to increase appropriate knowledge of key people or groups (e.g., health professionals and consumers) with capacity to prevent or mitigate product risks of concern

Development and Use of Risk Minimization Action Plans

Reminder Systems

- FDA recommendation
  - Use tools in reminder systems category in addition to targeted education and outreach tools when latter insufficient to minimize risks
- Tools in category include systems that prompt, remind, double-check or otherwise guide health professionals and/or patients in prescribing, dispensing, or receiving product in ways that minimize risk

Development and Use of Risk Minimization Action Plans

Reminder Systems

- Examples of tools in category:
  - Patient education (acknowledgment and agreement forms)
  - Healthcare provider training programs
    - Testing or other documentation of physician knowledge/understanding
  - Enrollment of physicians, pharmacies, and/or patients in special data collection that reinforces appropriate use
  - Limited # of doses in any single prescription or refill
  - Specialized packaging to enhance safe use
  - Specialized systems or records attesting to safety measures having been satisfied (e.g., prescription stickers; physician attestation of capabilities)

Development and Use of Risk Minimization Action Plans

Performance-Linked Access Systems

- Include systems that link access to product to laboratory testing results or other documentation
- FDA recommends tools in category be used when
  - Products have significant or otherwise unique benefits in particular patient group or condition, but unusual risks such as irreversible disability or death also exist, and
  - Routine risk minimization measures, targeted education and outreach tools, and reminder systems insufficient to minimize risks

Development and Use of Risk Minimization Action Plans

Performance-Linked Access Systems

- Examples of tools in category include:
  - Sponsor's use of compulsory reminder systems
  - Prescription only by specially certified health care practitioners
  - Dispensing only by pharmacies or practitioners that elect special certification
  - Dispensing only to patients with evidence or other documentation of safe-use conditions (e.g., lab test results)

Development and Use of Risk Minimization Action Plans

Selecting and Developing the Best Tools

- FDA recognizes once product out on market, health professionals are most significant managers of its risks
- Agency believes that via FDA-approved professional labeling information on safe and effective use for intended population and use(s), FDA and sponsor encourage prescribing that yields favorable benefit-risk balance
  - However, FDA does not have authority to control prescribing decisions by qualified health care practitioners, or to otherwise regulate medical or surgical practice

Development and Use of Risk Minimization Action Plans

Mechanisms Available to FDA to Minimize Risks

- FDA has variety of risk management measures at disposal under FDCA and FDA regulations
- FDA must occasionally invoke other mechanisms to minimize risks from medical products that pose serious public health risks, including:
  - FDA-requested product recalls, warning and untitled letters, and import alerts
  - Safety alerts, guidance documents, and regulations
  - Judicial enforcement procedures such as seizures or injunctions

Goldman SA. Communication of medical product risk: how effective is effective enough? *Drug Safety* 2004;27:519-534

Critical Questions

- Labeling changes/large-scale health professional notification: *are they effective?*
- 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 Notification

Disparate Categories of Risk

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

Lessons Learned: Labeling Changes and Large-Scale Notification (I)

- In choosing communication methods/assessing effectiveness, major categor(ies) of perceived risk must also be part of evaluative process
  - Behaviors associated with each category of risk may well differ - so may communication methods optimally utilized
  - *One size may NOT fit all*
- Multiple modes of risk communication and maximal publicity may well heighten effectiveness of overall effort

Lessons Learned: Labeling Changes and Large-Scale Notification (II)

- 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
- Medical products differ in perceived benefit/risk
  - Based on such factors as
    - Disease entity/population treated
    - Availability of other products
    - Reversibility of AE(s) in question

  each case merits individualized assessment, rather than formulaic, "cookie-cutter" approach

Lessons Learned: Labeling Changes and Large-Scale Notification (III)

- Understanding how HPs use risk information critical to improvement in methods
  - Examine varied information sources and related factors impacting treatment 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 when planning/assessing risk communication

Lessons Learned: Information Provided

- Risk information intended for health professionals should be as clinically oriented as possible
- FDA efforts such as generating/disseminating Q's & A's based on latest safety information for particular medical product of concern should be encouraged/modeled
  - Specifically targeted for treating healthcare community

Lessons Learned: Health Professional Education (I)

- Medical product 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 Education (II)

- 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

Lessons Learned: Risk Communication

- Need to be aware of social/psychological factors that impact health risk information receipt and perception
- Need for clarity and minimization of ambiguity/ possible sources of confusion
- Need to establish deserved trust in informational sources
- Need to critically evaluate sources of risk information

Conclusion

- 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

New FDA Drug Safety Initiative

Drug Safety Board[10]

- Management of important drug safety issues
  - Identification, tracking and oversight
  - Adjudication of organizational disputes
  - Establishment of policies
- ***Drug Watch***
  - Selection of drugs for placement
  - Updating status (including removal) as appropriate
- Oversight of development of patient/professional information sheets

[10]**www.fda.gov/cder/mapp/4151-3.pdf**

New FDA Drug Safety Initiative

Drug Safety Board[10]

- Tracking important emerging safety issues
  - Ensure resolution in timely manner
- Ensure CDER decisions about drug's safety benefit from input/perspective of internal and external experts who did not
  - Conduct primary review, or
  - Serve as deciding official in ongoing pre-market evaluation or post-marketing activities with respect to drug

New FDA Drug Safety Initiative

Drug Watch Web Page[11]

- New communication channel proposed by FDA
  - Inform public of latest information possible on emerging safety issues, even before FDA fully determines significance of data or decides whether regulatory action appropriate
  - NOT intended to identify specific drugs as being particularly risky
- Not yet active
  - May 2005 draft guidance released explaining proposed Drug Watch program in more detail
  - FDA thus soliciting public input before implementation

[11]**www.fda.gov/cder/drug/DrugSafety/drugSafetyQA.pdf**

New FDA Drug Safety Initiative

Drug Watch Web Page[11]

- As proposed, ***emerging*** safety information would become available to public
  - Factual information about new potential side effects and/or risks avoidable through such measures as appropriate patient selection or adequate patient monitoring
- FDA preliminary review of emerging information to determine which data warrants dissemination to public while scientific evaluation by Agency continues
  - Agency would work towards as quick a resolution of identified safety issues as possible
  - Status of FDA analyses of emerging information would be posted

CDRH Safety Notification Program

- In 2002, CDRH added new form of notification to existing program, *Web Notifications*[12], for posting of safety information on its website
  - Intended to supplement other forms of notification
  - Provide mechanism for quick dissemination of device safety information of benefit to health professionals, but not appropriate for other forms
  - May be used when available information limited, changing, and/or CDRH unable to make specific recommendations, but timely provision to healthcare community desired
  - Updated upon availability of further information

[12]www.fda.gov/cdrh/safety.html