



Safety Activities in the Office of Drug Safety

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Drug Safety Program

- Pre-Marketing Activities
- Post-Marketing Activities

■ ■ ■ Drug Safety Program

- Key functions in Pre-Marketing Drug Safety
 - review of foreign post-marketing safety data if available
 - participation in meetings where safety concerns are addressed
 - preNDA and FDA preapproval safety conferences

■ ■ ■ Drug Safety Program

- Key functions in Post-Marketing Drug Safety :
 - track adverse events and medication errors of marketed drugs = safety “signaling”
 - monitor the utilization of marketed drugs
 - solicit/perform population-based epidemiologic studies
 - pilot active surveillance initiatives
 - design, review, and evaluate RiskMAPs to handle identified safety problems

■ ■ ■ Safety “Signaling”

- Medication errors
 - 14 SEs led by 2 TL (DMETS)
- USP, ISMP, and med errors noted in AE reports
 - ≈300 per month
- Methods and processes
 - focus on name, label, labeling and packaging to identify contributing factors
 - share findings with review division to make and implement recommendations

■ ■ ■ Safety “Signaling”

- Adverse events
 - 28 SEs led by 5 TL
 - each SE assigned specific products or classes
- Adverse Event Reporting System (AERS)
 - electronically delivers serious cases to evaluators’ inbox
 - facilitates review, enumeration, and detailed examination of case reports

■ ■ ■ Tracking Adverse Events

- Adverse Event Reporting System (AERS)
 - an Oracle database repository containing more than 3 million AE reports
 - steady increase in numbers of reports submitted each year
 - CY04: Total 407,234 reports submitted, with >180,000 routed to SE inboxes

■ ■ ■ Triggers for a Closer Safety Look

- Safety concerns from premarketing safety database
- Notable case reports
- Literature reports
- Systematic reviews of AE term hierarchies
- Displays of disproportionality of drug/event combinations or “datamining”

■ ■ ■ Safety “Signaling”

- Case reports or series
 - thorough and collaborative clinical review of drug relationship to AE
 - primary, secondary, and tertiary review within ODS
 - cases often are incomplete
 - primary basis for reconsideration of R/B balance and regulatory actions ranging from labeling changes to withdrawal

■ ■ ■ Safety “Signaling”

- Context/magnitude of problem
 - use drug utilization data to estimate exposure
 - “reporting rates” per Rx or person-time
 - context of AE background rate in disease or general population

■ ■ ■ Safety “Signaling”

- Drug utilization patterns may also signal a potential safety problem
 - populations or subpopulations
 - indications
 - contraindications
 - staging of drug use
 - drug-drug interactions

■ ■ ■ Safety “Signaling” Follow-Up

- Observational studies in populations
 - refine and quantify drug/AE hypotheses
 - assess and compare relative risks
 - examine risk factors
- Challenges
 - access and timeliness of data resources
 - weighing post-marketing “observational” data and pre-marketing “experimental” data

■ ■ ■ Safety “Signaling” Frontiers

- Federal surveillance resources
 - “Active” or purposeful surveillance
 - emergency room visits (NEISS)
 - HMO data (AHRQ CERT)
 - CMS and VA
- Sponsor-supported pharmacovigilance plans
 - abuse and diversion of opioids



Design, Review, and Evaluation of RiskMAPs

- Participation in periapproval safety discussions (pre- and postmarketing)
 - Recommendation of educational or programmatic interventions (RiskMAP)
 - Design and conduct RiskMAP performance evaluations
 - alosetron, isotretinoin
- Extensive collaboration with other CDER components including OND



Post-Marketing Safety: Overview

- Wide scope
 - all prescription, OTC, and generic drugs
 - therapeutic biologics
- Observational data often incomplete or confounded
- Matrixed expertise and regulatory decision-making environment requiring close communication and collaboration