Post-Market Drug Safety

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Drug Safety Program: Overview

- ## CDER's Post-Marketing Drug Safety Risk Assessment Program:
  - tracking adverse events of marketed drugs (note: includes medication errors)
  - monitoring the utilization of marketed drugs
  - soliciting/performing population-based epidemiologic studies

Drug Safety Program: Overview (Cont'd)

- ## Role expanding/evolving
  - pre-marketing safety assessment
  - pharmacovigilance planning
  - risk minimization action plans (RiskMAPs)
  - risk communication
    - MedWatch
    - patient information
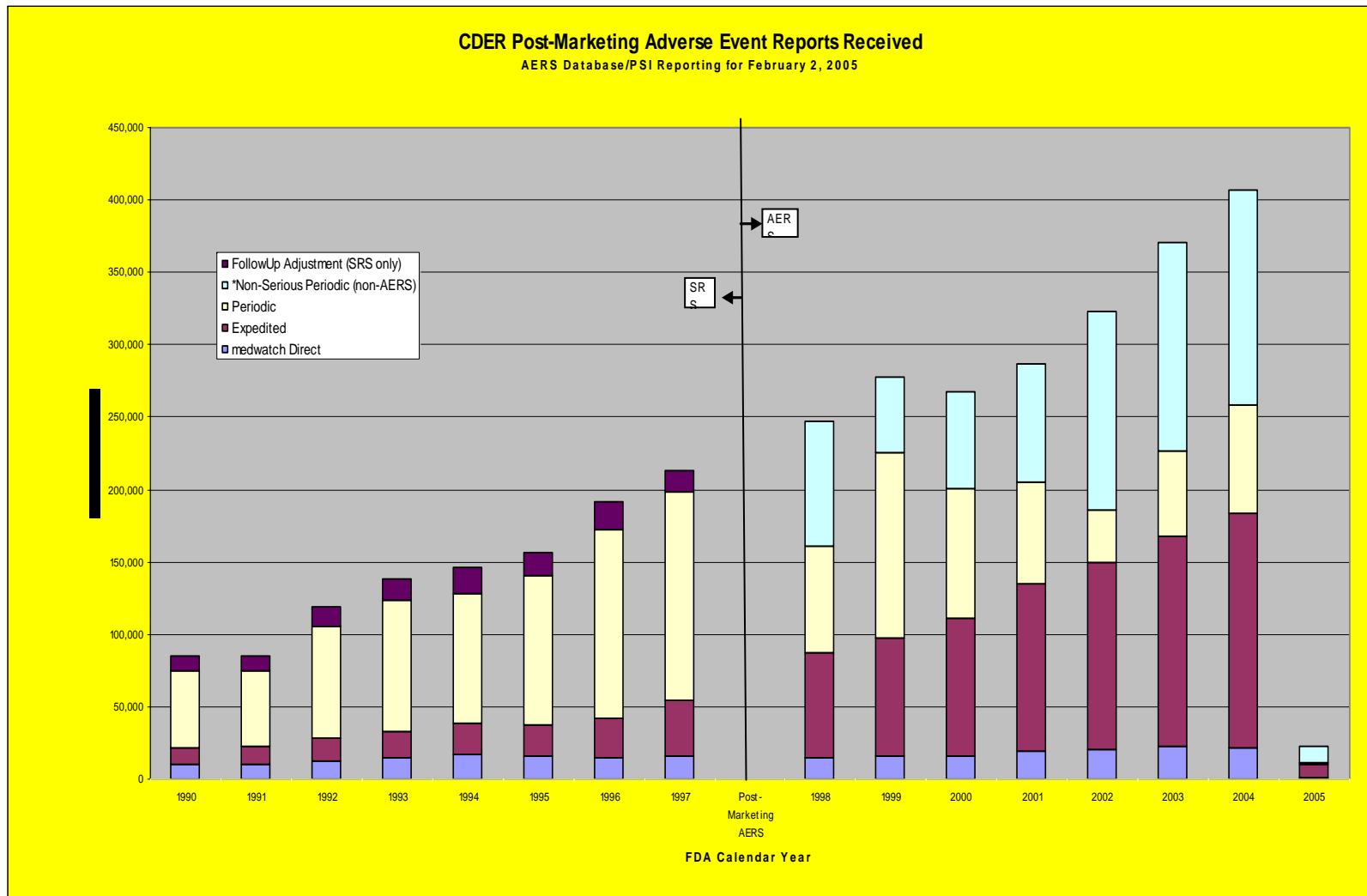 - medication error prevention (names, packaging)

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: 407,234 reports submitted

FDA

AERS Reports By Year

CDER Post-Marketing Adverse Event Reports Received

AERS Database/PSI Reporting for February 2, 2005

Legend:
- FollowUp Adjustment (SRS only)
- *Non-Serious Periodic (non-AERS)
- Periodic
- Expedited
- medwatch Direct

AERS

SRS

FDA Calendar Year

Years shown: 1990, 1991, 1992, 1993, 1994, 1995, 1996, 1997, Post-Marketing AERS, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005

Drug Utilization Data Sources
Estimates of Actual Drug Use

- Outpatient
  - dispensed prescriptions
  - sales
  - longitudinal data / concomitant use
  - physician office-based surveys
- Inpatient
  - adult and pediatric - hospital data
  - sales data

Drug Utilization Data: Value

– **Denominators for putting AERS reports into context (reporting rates)**

– **Description of prescribing patterns**

  - physicians' specialty

  - patient demographics

  - associated diagnoses/procedures

– **Insight into concomitant use of multiple drugs**

– **Surveillance of risk management practices to restrict drug use**

Postmarketing Drug Safety Studies

- ## Sponsors
  - Phase IV
  - Ad hoc postmarketing studies

- ## FDA
  - Cooperative agreement program
  - National database (GPRD)
  - Other resources
    - Kaiser Permanente, California
    - Veterans' Administration

Population-Based Data Resources

- **Cooperative Agreement Program**
  - HMO network: 1.8M*
  - TN Medicaid: 1.5M
  - UnitedHealth: 2M
- **GPRD:**   3M
- **Kaiser California:**   6M
- **VA Medical System:**   3.4M
  - * "covered lives"

Post-marketing Safety Challenges

- ## Spontaneous Reporting
  - collects only a percentage of cases
  - variable quality (missing data)
  - lack denominator

- ## Case identification
  - linked databases
  - analytic tools (e.g., data mining)
  - electronic medical record

Challenges (cont'd)

- ## Make reporting easier for the practitioner
  - interactive
  - "push a button to populate a MedWatch form and submit to the FDA"

- ## Electronic reporting initiative
  - more timely receipt and and efficient processing of data

Challenges (cont'd)

- ## Access to databases
  - timely surveillance
  - population-based studies

- ## Weighing evidence obtained by different methods
  - RCTs, case reports, observational studies

- ## Benefits and risks

Challenges (cont'd)

- ## Need for metrics to evaluate regulatory actions
  - label changes, messages, RiskMAPs

- ## Science of safety
  - mechanistic understanding of drug injury processes
  - population variability, who is at risk
  - assessment "circumstantial" until we have markers for drug-induced injury

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