Division of Compliance Risk Management and Surveillance

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Food and Drug Administration

DCRMS MISSION

- **Reduce public health risks associated with the quality, safety, and effectiveness of the nation's marketed drugs**
  - -Use results-driven, risk based approaches to develop and implement strategies to increase industry compliance with regulations and conformance with good practices
  - -Utilize science-based surveillance programs and strategic problem solving to identify, evaluate, and prioritize risk related to drug quality, safety, and effectiveness
  - -Use both our surveillance and strategic problem solving expertise to develop and support innovative compliance and risk reduction activities

Promoting Public Health through influencing Drug Availability

- Our goal is to advance public health through increasing availability of safe, effective, & quality drugs; and conversely, through limiting exposure to unsafe, ineffective, & poor quality drugs.
- Our focus is on DATA support for decision-making
  - Surveillance
  - Pre-inspection information
  - Evaluation
  - Data supporting compliance/regulatory activities

DCRMS FOCUS

- Surveillance – Monitor public health impact and drug industry compliance to improve drug quality and safety reporting
- Identify and target compliance problem areas, based upon public health impact
- Enhance coordination and prioritization of inspection processes for both GMP and ADE inspections through data support

DIVISION TEAMS

- Drug Registration and Listing Team
- Surveillance Programs Team
- Data Analysis & Information Management Team
- Risk Management & Strategic Problem Solving Team

Drug Registration and Listing Team Functions

- Manage Drug Establishment Registration and Drug Product Listing processes and data systems (DRLS), and manage NDC Directory
- Sponsor electronic drug facility registration through FURLS/DFRM and drug product listing through SPL/eLIST [eDRLS]
- Provide data support for Drug Efficacy Study Implementation (DESI) compliance activities
- Monitor marketed unapproved new drugs and provide data support for regulatory activities

Drug Registration and Listing (DRL Team)

- Register all drug establishments with FDA
  - Manufacturers, Packers, Relabelers
  - Assign NDC labeler code & FEI number (FACTS)
- List all marketed drug products with FDA
  - Repository of all drug product NDC numbers
  - Includes all ingredients & each establishment
- DRLS team (15 contractors) enters & reviews data
- DRLS accessible to ORA investigators
- DRLS contact: 301-210-2840

http://www.fda.gov/cder/drls/registration_listing.htm

Future → e-DRLS

- Provide electronic submission/updating of Registration and drug Listing information
- Improve data accuracy, minimize data input, and allow more focus on regulatory and safety issues
- FDA issue (and control) all valid NDC numbers
- Utilize FURLS (DFRM – patterned after FFRM)
- Integrate eLIST with Structured Product Labeling (SPL), and provide electronic label access through DailyMEDS at NLM

Drug Efficacy Study Implementation – DESI Support

- 1962 Amendments required all marketed drugs to be approved for both safety and effectiveness
  - manufacturers required to provide proof of effectiveness based upon "substantial evidence."
- DESI reviews started in 1966; include 3,443 drug products approved between 1938 and 1962, and approximately 15,000 unapproved drugs that were similar to DESI drugs
- DRL Team provides data support and identifies DESI pending and final drug products for CMS that are not reimbursable under CMS's Drug Reimbursement Program
- We will soon provide a searchable database of relevant Federal Register notices related to DESI drugs

Surveillance Program Team Functions

- Enhance industry compliance with the Postmarketing Adverse Drug Experience (ADE) regulations for accurate, complete and timely surveillance, receipt, evaluation, and submission of ADE data to the agency
- Identify potential risks associated with manufacturing, labeling, and packaging of pharmaceuticals through the Drug Quality Reporting System (DQRS) and NDA/ ANDA Field Alert Reporting (FAR) program.
- Monitor the quality of the nation's drug supply through the identification and coordination of drug product sampling and analysis.

Drug Quality Reporting System

- Central reporting system for marketed drug quality problems to identify areas or trends requiring corrective action.
- Drug quality reports are received from consumers & health professionals – primarily pharmacists.
- Reports are prioritized and forwarded to district offices, other CDER offices, and manufacturers for appropriate follow-up

NDA/ANDA Field Alerts

- Applicant holders submit NDA/ANDA Field Alert Reports on drug labeling, manufacturing, safety, effectiveness, or other quality issues for products on the market.
- Firms must notify District office within three working days of awareness of potential problem
- Districts submit FARs to DCRMS, and follow-up investigational findings

Biologics Product Defect Reporting

- In 2003 CBER transferred to CDER certain therapeutic biological product oversight responsibilities
- Biologics Product Defect Reports for CDER products are now integrated with the DQRS and FARs programs
- CDER Biologics website: http://www.fda.gov/cder/biologics/

Drug Product Quality Sample Survey

- Monitor the quality of the nation's drug supply through chemical and microbiological analyses of selected marketed drugs
- Include domestic and foreign finished dosage forms and bulk ingredients (APIs)
- Utilize a risk-based sample surveillance approach to select products for analysis that have greatest risk of quality problems and/or health impact

Drug Product Quality Sample Survey – Sample Collection

- Drug products are selected for sampling each year through a risk-based approach with a different emphasis each year
- Survey results are intended for publication and address broad issues that are used to focus regulatory efforts and set priorities
- Individual drug quality issues are followed-up by Districts

ADE Reporting Compliance – Inspections

- Develop and maintain risk profiles associated with drug products and ADE reporting processes
- Manage inventory of establishments responsible for submitting ADE data to FDA
- Issue inspectional assignments using risk-based approach based upon risk profiles
- Review inspectional findings and corrective actions by firms, and support/initiate regulatory actions

ADE Reporting Compliance – Education

- Public forums and individual interactions to educate industry on regulatory reporting obligations and industry best practices
- Formal on-line and classroom training for ORA field staff, as well as technical support for investigators and compliance personnel
  - Training video available on web at: http://www.fda.gov/cder/learn/ade/ade_page.htm

RiskMAP Compliance

- Review Risk Minimization Action Plans for procedural issues, enforceability, and barriers to successful implementation
- Review RiskMAPs for adequate ADE reporting procedures by all involved personnel and firms
- Monitor ADE reporting and RiskMAP implementation, develop strategies for corrective action if RiskMAP variance is noted during inspections or other surveillance activities
- Monitor achievement of risk minimization goals

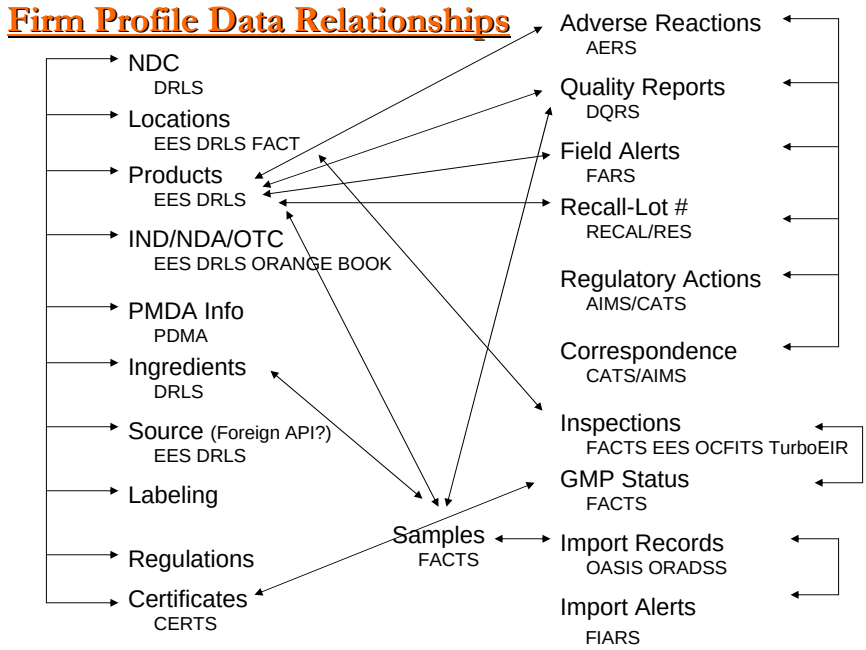
Data Analysis & Information Management Team – Functions

- Identify relevant internal and external data and databases that may support risk-based compliance programs and decisions
- Manage or understand compliance-related databases, including AERS, EES, DRLS, PDMA, Recalls and Shortages, DQRS, FARs, FACTS, OASIS, Turbo EIR.
- Perform quantitative and qualitative analyses of data collected in and generated from surveillance programs and other relevant internal and external databases.
- Work with other DCRMS teams and other FDA organizations to identify trends and patterns of non-compliance to help target specific interventions.

Surveillance Steps

- Identify universe of source data for assessment of problems related to drug quality, drug safety monitoring, and related well-being of the public and industry
- Select sources to utilize in identifying drug and industry surveillance and establish access
- Develop surveillance systems and approaches
- Assure that public health issues relative to drug safety and quality, and to related public and industry well-being, are adequately monitored

Firm Profile Data Relationships



Risk Management & Strategic Problem Solving Team – Functions

- Utilize quantitative and qualitative data analysis and strategic problem solving techniques to focus compliance and regulatory activities, and develop innovative compliance strategies for reducing public health risks
- Work with other DCRMS teams and CDER/OC divisions, identifying patterns of non-compliance, assessing public health risk, and developing strategies for risk minimization
- Work closely with other agency units in areas of strategic planning, program targeting, and compliance prioritization

Strategic Problem Solving

- Utilize surveillance data to identify problem areas
- Analyze surveillance & other data to identify potential risk factors and root causes
- Identify strategies for prevention/protection and develop control measures
- Evaluate potential impact of control programs
- Implement control programs using the best strategies
- Monitor outcomes and assess impact of the implementation programs

ADE Inspection Site Selection Risk Model

- **New NDA/ANDA Approval**
- **NME/New Indication**
- **Patient Population/RiskMAP**
- **Narrow Therapeutic Range**
- **Narrow Risk-Benefit Profile**

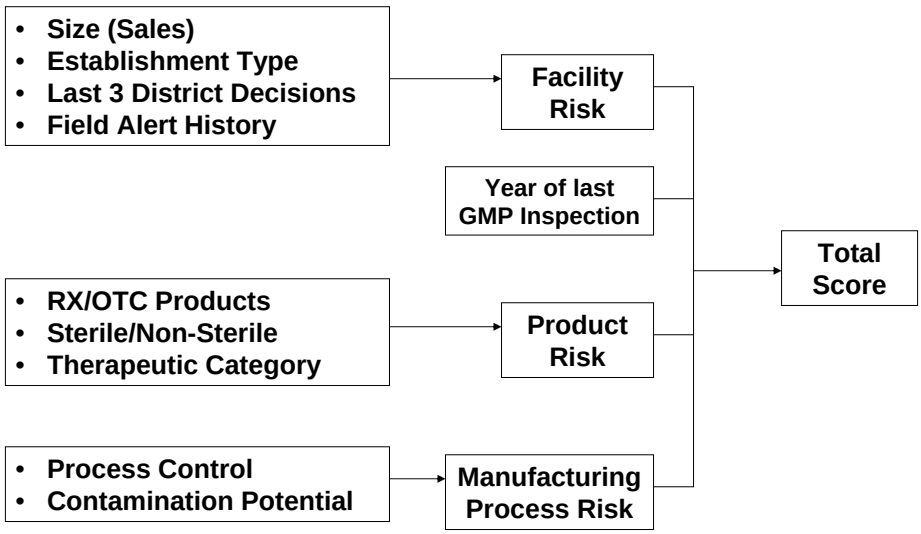
→ **Product Risk**

- **Written Procedures**
- **Observed Performance**
  - •From submissions
  - •From inspections
- **Data Transfer**
  - •Internal
  - •External
- **Corporate Structure**
- **Inspectional History**

→ **ADE Reporting Process Risk**

→ **Total Score**

GMP Inspection Site Selection Risk Model



Challenges

- Strengthen communications and working relationships with OND/OGD and ODS
- Strengthen communications and working relationships with the field offices and investigators
- Use field and DCRMS skills and resources to support and strengthen compliance program areas
- Enhance ingenuity and outside-the-box thinking
- Enhance strategic problem solving