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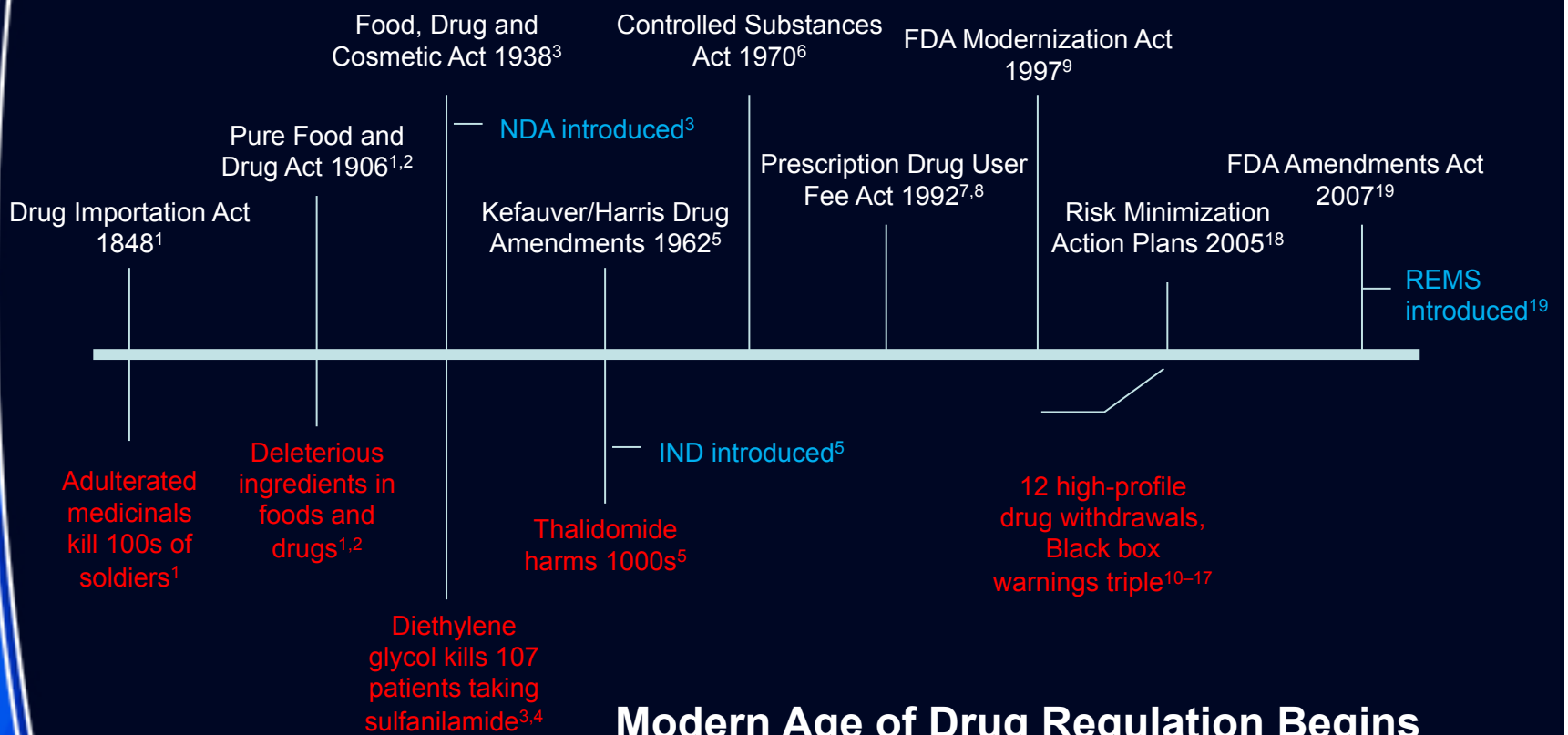
The (Brief) History of Drug Safety



Modern Age of Drug Regulation Begins
Risk Management Efforts Begin

Before the Era of Risk Management

- Drug Importation Act (1848)[1]
  - Prevent adulteration of medicines
- Pure Food & Drug Act (1906)[1,2]
  - Close loopholes in the Drug Importation Act
- Food, Drug and Cosmetic Act (1938)[3]
  - Close loopholes in the Pure Food & Drug Act
  - NDA to confirm safety
- Kefauver/Harris Drug Amendments (1962)[5]
  - Required proof of efficacy in addition to safety
  - IND introduced

In the Era of Risk Management

- Controlled Substances Act (1970)[6]
  - Restricted prescribing, dispensing and patient access to certain drug classes
    - Opioid analgesics
    - Hypnotics
    - Tranquilizers
  - Increase accountability for drugs with higher potential for misuse, abuse and diversion

In the Era of Risk Management (continued)

- Patient Prescribing Information (1976)[6]
  - Began with manufacturers of oral contraceptives
  - Required communication of risk and safety information to patients
  - Dawn of the PPI

In the Era of Risk Management (continued)

- Prescription Drug User Fee Act (PDUFA) (1992)[7,8]
  - Authorized FDA to collect fees from manufacturers
  - Facilitated FDA staffing
    - Modernize FDA technology
    - Enhance drug approval process
    - Support post-marketing safety activities

In the Era of Risk Management (continued)

- FDA Modernization Act (FDAMA) (1997)[9]
  - Reauthorized PDUFA
  - Encouraged collaboration between government and industry
  - Goals:
    - Increase patient access to experimental drugs and devices
    - Accelerate review of important new medications

In the Era of Risk Management (continued)

- Risk Minimization Action Plans (RiskMAPs) (2005)[18]
  - First plan to make safety an ongoing process
    - Step 1: Access benefit-risk profile
    - Step 2: Develop and implement tools to minimize risks and preserve benefits
    - Step 3: Evaluate tool effectiveness and impact on risk-benefit profile
    - Step 4: Adjust as necessary
  - 3 Categories of tools
    - Level 1: targeted education and outreach
    - Level 2: Reminder systems
    - Level 3: Performance-linked access systems

In the Era of Risk Management (continued)

- FDA Amendments Act (FDAAA) (2007)[19]
  - Paradigm shift
  - Transformed RiskMAPs into a mandatory and enforceable program
  - Ensure drug safety and ongoing pharmacovigilance throughout drug lifespan
  - Mandatory components:
    - Risk Evaluation and Mitigation Strategies (REMS)
    - Post-marketing studies
  - Compliance enforcement:
    - Civil monetary penalties

REMS Components[20]

Level	Element	Description
1	Medication Guide	• Paper handout given to patients with Rx • Prevent serious AEs, aid patient decision-making, enhance adherence to safe use and handling • Address drug/class-specific issues
	PPI	• Lay language of PI • Emphasize and instruct patients on side effects, precautions, dosage and administration
2	Communication Plan	• HCP letters • HCP education to encourage REMS implementation • Inform HCPs of drug risks and REMS
3	Elements to Assure Safe Use (ETASU)	• Specialized HCP training, experience, certification • Certification of pharmacies, HCPs, HC settings • Restrictions on dispensing • Evidence/documentation of patient safe use • Patient monitoring • Patient registry

Opportunities for Medical Writers

- Development of REMS programs
- Implementation of REMS elements
  - Medication Guide
  - PPI
  - Communication Plan
  - Elements to Assure Safe Use
- Publication of post-marketing study results

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Thank You

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