Health Hazard Evaluation and Recall

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What do we mean by "recall"?

- A removal or correction of a violative product
  - Correction: on-site repair, modification, adjustment, relabeling, inspection, or destruction of a product
  - Excluding market withdrawal (removal or correction of a product with minor or no violation), stock recovery (product that has not been released for use), and routine servicing
- Violative product, if:
  - Not safe and effective for the intended use – e.g., adulterated (FDCA § 501) or misbranded (§ 502)
  - Presenting a health risk to users

21 CFR 7.3

Reasons for recalled

- Recall occurs even for the best designed product
  - Malfunctions due to inadequate (or unanticipated) design, control, manufacturing and labeling issues, or user errors
  - Often prompted by: user complaints, internal findings, MedWatch/international vigilance reports, FDA inspection
- Words of caution:
  - Modification(s) to correct a violative product needs to be valid and/or adequately validated
    - Some modifications may require a regulatory submission
  - When in doubt, talk to OIVD!

Types of recall

- Firm-initiated (voluntary) recall (21 CFR 7.46)
  - Most common and efficient way to recall a product
- FDA-requested recall (21 CFR 7.45)
  - Refusal by firm to conduct a recall
  - Product posing risk of health or gross deception
- FDA Medical Device Recall Authority (21 CFR 810)
  - Reasonable probability of serious health risk or death
  - Stepwise: (1) cease distribution and notification order; (2) regulatory hearing; (3) mandate or vacate the recall order

Types of recall

- Alternative to recall: FDA-initiated court action (e.g., seizure, injunction)
  - If firm refusing to conduct FDA-requested/ordered recall
  - If ineffective recall, or continuing violation
  - Rare but occasionally happens!

Recall process

- Fact gathering (Firm)
  - Root cause investigation
- Assessing potential health hazard (Firm & FDA)
- Formulating an effective recall strategy (Firm & FDA)
- FDA notification: filing an "806" (*Reports of Corrections and Removals* - 21 CFR 806)
- Recall classification (FDA)
- Monitoring recall progress (Firm & FDA)
- Terminating a recall (FDA)

Health hazard evaluation (HHE)

- Firm should conduct an HHE for the product considered for recall
  - To accurately assess health and safety implications
  - To articulate a coherent and effective recall strategy
- FDA also conducts an HHE on the violative product
  - To classify the recall by relative degree of health hazard
  - To evaluate adequacy of firm's recall strategy
  - To guide FDA recall enforcement actions (e.g., public warning, level of effectiveness checks, audit check)

21 CFR 7.41

Elements of an HHE

- Disease or injuries due to the violative product
  - Existing conditions exposing people to the health risk
- Patient populations exposed to the violative product, including those at greatest risk
- Degree of seriousness of health risk
- Likelihood of occurrence of health risk
- Immediate/long-range consequences of health risk

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/default.htm

21 CFR 7.41

Recall classification (assigned by FDA)

- Class I: reasonable probability that use of, or exposure to the violative product will cause serious adverse health consequences or death
- Class II: use of, or exposure to the violative product may cause temporary or medically reversible adverse health consequences, or remote probability of serious adverse health consequences
- Class III: use of, or exposure to the violative product is unlikely to cause *[any]* adverse health consequences

21 CFR 7.3(m)

Recall strategy

- Depth of recall
  - Degree of health risk, extent of product distribution, amount unused, ease of identification
- Targeted public warning/notification when necessary
  - e.g., news media, trade press, "*Dear Doctor*" letter
- Effectiveness checks to verify notification and action
  - Level A: 100%; B: 11-99%; C: 10 %; D: 2%; E: none
  - Audit checks by FDA to monitor recall effectiveness
- Shortage may modify recall strategy (risk-benefit)

21 CFR 7.42

Firm's role in facilitating a recall

- Maintain updated contingency recall plan
  - Customer contact information
  - Complete product distribution records (kept longer than expected product life) to help locate the product
  - Product information and identification, production logs, lot release data, etc.
  - Methods for returning/disposing of violative product
- Follow Quality System Requirements (21 CFR 820)
  - To implement corrective and preventive actions (CAPA)

21 CFR 7.59

Termination of recall

- FDA will terminate a recall when
  - All reasonable efforts have been made to remove or correct the product
  - Reasonable to assume that the violative product has been removed, and proper disposition/correction has been made
- Firm may request FDA to terminate a recall
  - Submit evidence showing recall is effective
  - Provide most current recall status report

21 CFR 7.55

How OIVD approaches an HHE

- What can be considered as health risk?
  - Error in patient management
  - Lengthening or delay in medical intervention
  - Significant psychological/emotional distress to patients
  - Direct injury to device operator
  - Potentially significant public health impact
    - e.g., exposure of laboratorians/others to infectious agents

How OIVD approaches an HHE

- Assessing health risk
  - As if violative product still in the market
  - As if corrective action not yet taken by firm (or FDA)
  - As if users unable to detect product failure or malfunction
  - Assuming worst case scenario if incomplete information
- Risk not necessarily lower, even if:
  - Lack of reported injuries or deaths
  - Failure due to “user error”

How OIVD approaches an HHE

- Risk mitigating factors allowed (nevertheless!)
  - Obviousness of defect
  - Detectability by routine quality control
    - Pitfall: QC values are assigned by the defective device!
    - Detectable by delta check
  - Availability of alternative testing
    - Back-up system, alternative biomarker
  - Good laboratory practice
  - Not critical to immediate/long-term medical decision

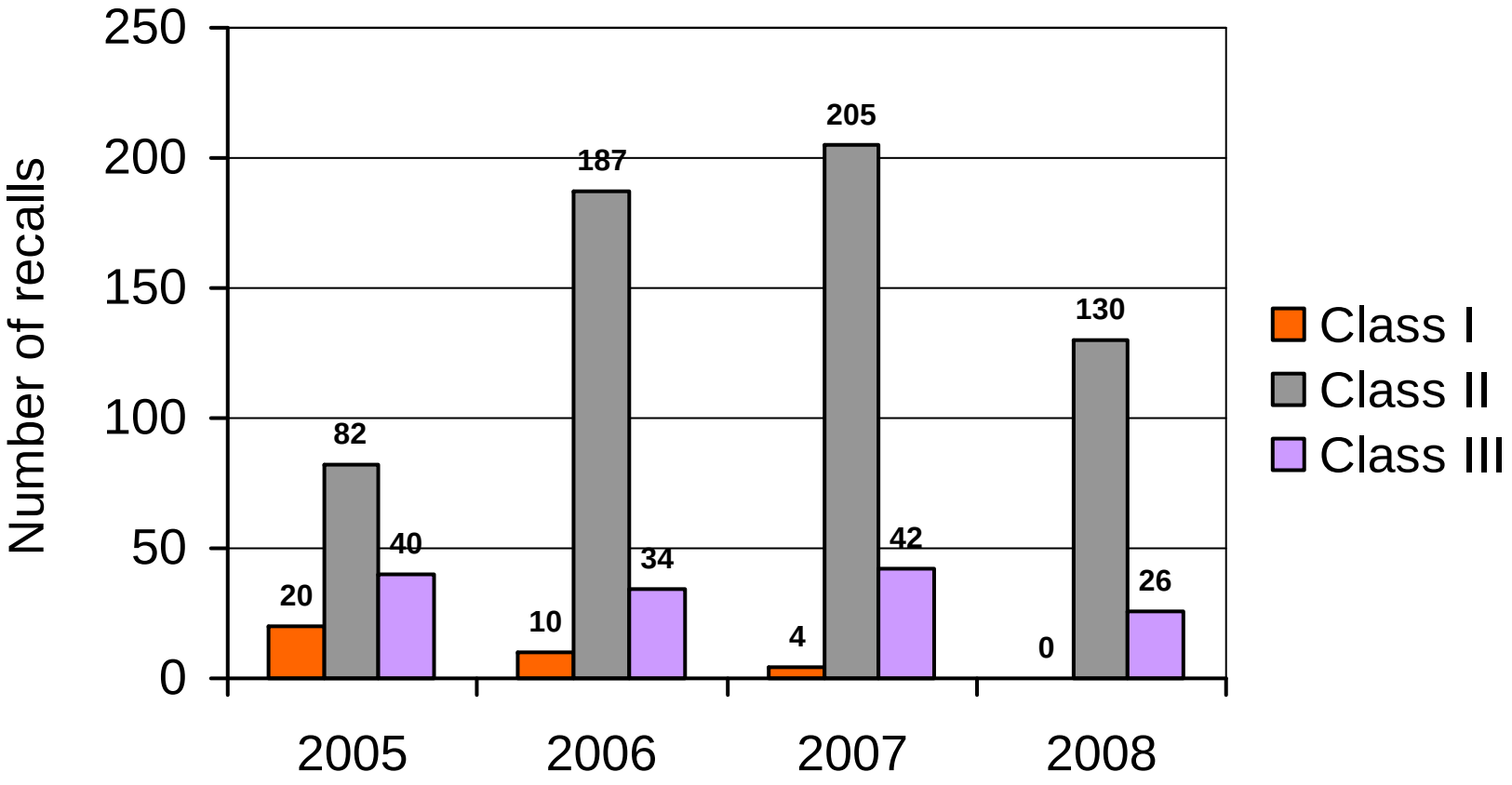
How OIVD approaches an HHE

- Likelihood of health risk
  - Often difficult to estimate frequency of device failure
    - No definition for “unlikely,” “reasonable,” or “remote”
  - Whether test result being the sole basis, a major factor, or a minor contributor to medical decision
- Severity of health risk
  - Magnitude of error in test result
  - Patient population(s) most at risk
  - Permanent and irreversible injury → “serious” injury
- Probability of harm = {likelihood, severity} - mitigation

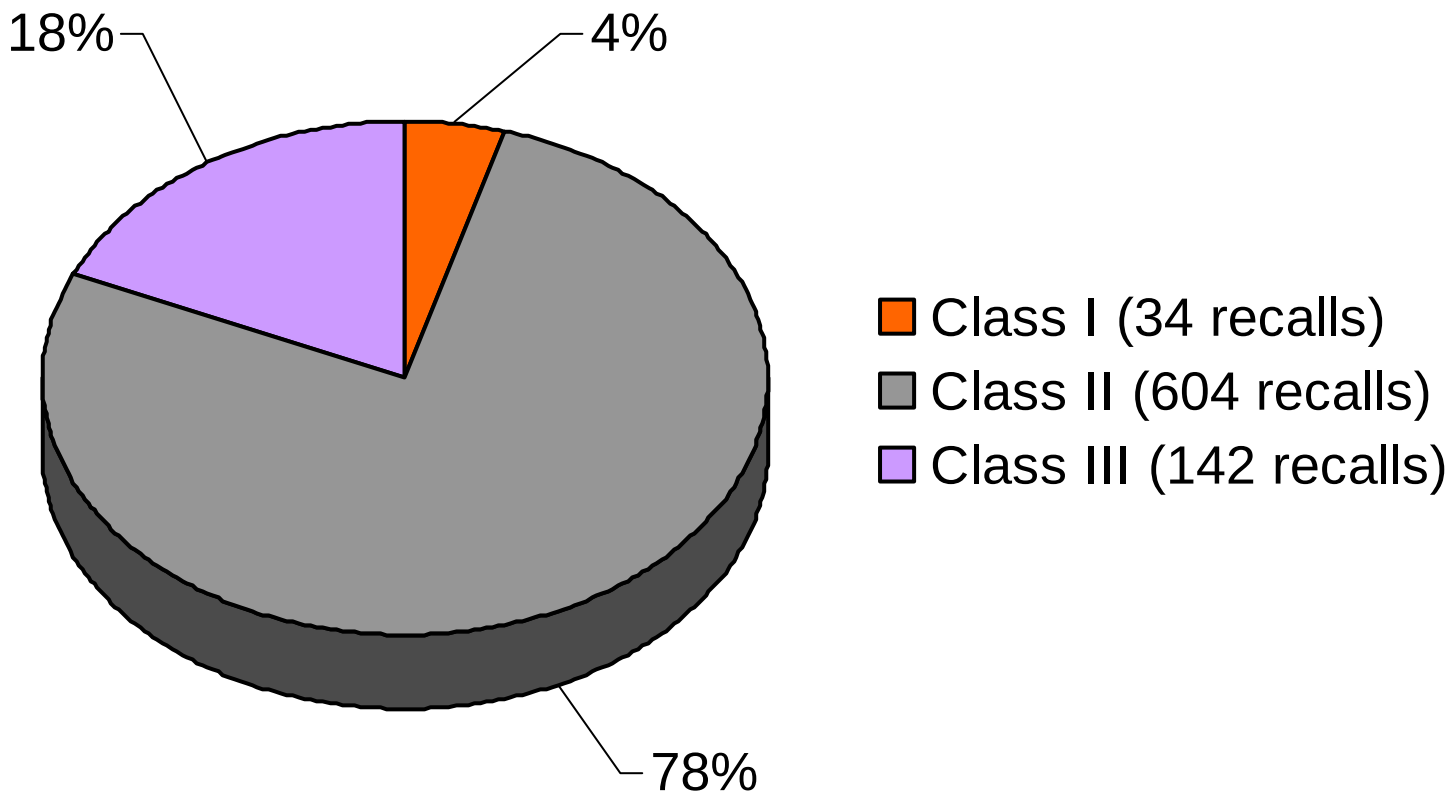
How OIVD approaches an HHE

- Convening *ad hoc* HHE Committee to review HHE, if:
  - Potentially a Class I recall or high visibility case
  - Additional technical/medical expertise needed
- Classification of a recall may be based on
  - A precedent case with similar product problem and risk profile (Class II and III only)
  - A standing "policy"
    - e.g., unless otherwise indicated, removal of an un authorized product is a Class II recall

IVD recalls by year (2005-2008)



IVD recalls by class (2005-2008)



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Thank You!