U.S. FOOD & DRUG ADMINISTRATION

MDR Reporting Requirements

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AGENDA

- CDRH Vision
- Postmarket Surveillance
- MDR Regulation (21 CFR 803)
- Reporting Timeframes
- Limitations of MDR Data
- Considerations for OPTN

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CDRH VISION

- Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world.
- The U.S. is the world's leader in regulatory science, medical device innovation and manufacturing, and radiation-emitting product safety.
- **U.S. post-market surveillance quickly identifies poorly performing devices, accurately characterizes real-world performance, and facilitates device approval or clearance.**
- Devices are legally marketed in the U.S. and **remain safe, effective, and of high-quality**.
- Consumers, patients, their caregivers, and providers have access to understandable science-based information about medical devices and **use this information to make health care decisions**.

https://www.fda.gov/about-fda/center-devices-and-radiological-health/cdrh-mission-vision-and-shared-values

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DEVICE SURVEILLANCE

- **Medical Device Reporting (MDR)**
- MedSun Program
- Post-Approval Studies (PAS)
- Postmarket Surveillance Studies (522/PSS Studies)
- Signal Management
- National and International Device Registries
- National Evaluation System for Health Technology (NEST)

MEDICAL DEVICE REPORTING (MDR) REGULATION

Medical Device Reporting (MDR, 21 CFR Part 803)

- Establishes the reporting requirements for device user facilities, manufacturers and importers. (Authorized under Section 519 FD&C Act.)
- A mechanism for FDA and manufacturers to identify and monitor adverse events involving marketed medical devices

Types of Events that Must Be Reported to FDA

- If device may have caused or contributed to a death or serious injury.
- Certain malfunctions must also be reported

What is a Reportable Event?

21 CFR 803.3(o)

- An adverse event that **user facilities** become aware of that reasonably suggests that a device has or may have caused or contributed to a death or serious injury, or
- An event that **manufacturers or importers** become aware of that reasonably suggests that one of their marketed devices:
  - May have caused or contributed to a death or serious injury, or
  - Has malfunctioned and that the device or a similar device marketed or manufactured by the manufacturer or imported would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.
  - FDA assumes that once a malfunction has occurred, it will recur.

https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-803/subpart-A/section-803.3

"CAUSED OR CONTRIBUTED"

A death or serious injury may have been attributed to a medical device

or

A medical device may have been a factor in a death or serious injury including events resulting from

- Failure
- Malfunction
- Improper or inadequate design
- Manufacturing (problems)
- Labeling (problems)
- Use error

https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-803/subpart-A/section-803.3

What is a Serious Injury?

A reportable serious injury is defined as an injury or illness that is:

- Life-threatening

or

- Results in permanent impairment or damage to a body function or structure

or

- Requires medical or surgical intervention to preclude permanent impairment or damage to a body function or structure

https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-803/subpart-A/section-803.3

WHAT IS A MALFUNCTION?

- The failure of a device to meet its performance specifications or otherwise perform as intended.
  - Performance Specifications include all claim made in the labeling for the device
  - The intended performance of a device refers to the intended use for which the device is labeled or marketed as defined in 21 CFR 801.4.

https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-803/subpart-A/section-803.3

WHAT IS NOT AN MDR?

- MDR ≠ Complaint

- Complaints (21 CFR 820.198)
  - Written electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.
  - Manufacturers and importers are required to maintain complaint files and establish and maintain procedures for receiving, reviewing and evaluating complaints.

- Complaints are reviewed, evaluated and documented for MDR reportability

- Volume of MDRs ≠ Complaint Rate

REPORTING TIMEFRAMES

REPORTER	WHAT TO REPORT	WHERE	WHEN
Manufacturer	Deaths, Serious Injuries, Malfunction	FDA	Within 30 calendar days
	Events that require remedial action to prevent an unreasonable risk of substantial harm	FDA	Within 5 working days
	Supplements (Follow-up Reports)	FDA	Within 30 calendar days
User Facility	Deaths	FDA and Mfr.	Within 10 working days
	Serious Injury	Mfr. (FDA if unknown)	Within 10 working days
Importer	Deaths and Serious Injuries	FDA and Mfr.	Within 30 calendar days
	Malfunctions	Mfr.	Within 30 calendar days

EMPHASIZING USER FACILITY REPORTING REQUIREMENTS

1. ***Reports of death.*** Submit a report to FDA as soon as practicable but no more than 10 work days after the day that you become aware of information, from any source, that reasonably suggests that a device has or may have caused or contributed to the death of a patient of your facility. Also submit the report to the device manufacturer, if known. (§ 803.32).
2. ***Reports of serious injury.*** Submit a report to the manufacturer of the device no later than 10 work days after the day that you become aware of information, from any source, that reasonably suggests that a device has or may have caused or contributed to a serious injury to a patient of your facility. If the manufacturer is not known, submit the report to FDA (§ 803.32).

What information does FDA consider "reasonably" known to me?

- This information includes information found in documents that you possess and any information that becomes available as a result of reasonable follow-up within your facility.
- You are not required to evaluate or investigate the event by obtaining or evaluating information that you do not reasonably know.

https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-803/subpart-C

TYPES OF MDR SUBMISSIONS

- Individual (initial) Reports (3500/3500A):
  - Contain text narratives
  - Some may describe multiple patients, events or devices

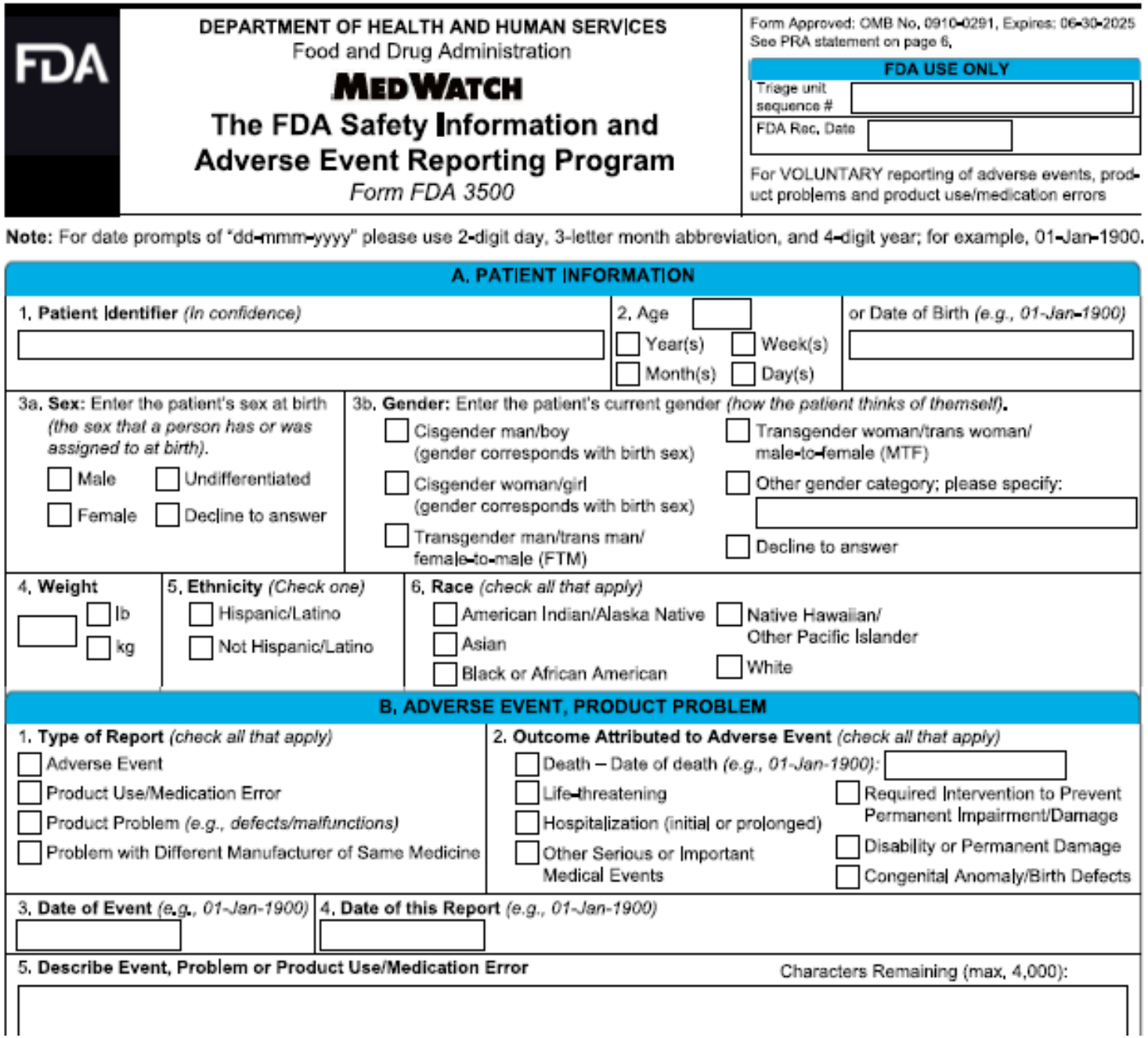
- Supplemental/Follow-up Reports:
  - Filed for individual MDRs when additional information is obtained
    - Manufacturer's evaluation of returned device
    - New or corrected information
    - Follow up with user facility

Where Can I Find Information on How to Prepare And Submit an MDR?

(21 CFR 803.23)

- You may obtain information on how to prepare and submit reports in an electronic format that FDA can process, review, and archive at: *http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm107903.htm*.

- We may sometimes update information on how to prepare and submit reports electronically. If we do make modifications, we will ensure that we alert reporters by updating the eMDR Web page.



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

Form FDA 3500

Form Approved: OMB No. 0910-0291, Expires: 06-30-2025
See PRA statement on page 6.

FDA USE ONLY

Triage unit sequence #

FDA Rec. Date

For VOLUNTARY reporting of adverse events, product problems and product use/medication errors

Note: For date prompts of "dd-mmm-yyyy" please use 2-digit day, 3-letter month abbreviation, and 4-digit year; for example, 01-Jan-1900.

A. PATIENT INFORMATION

1. **Patient Identifier** *(In confidence)*

2. Age
☐ Year(s) ☐ Week(s)
☐ Month(s) ☐ Day(s)

or Date of Birth *(e.g., 01-Jan-1900)*

3a. **Sex:** Enter the patient's sex at birth *(the sex that a person has or was assigned to at birth).*
☐ Male ☐ Undifferentiated
☐ Female ☐ Decline to answer

3b. **Gender:** Enter the patient's current gender *(how the patient thinks of themself).*
☐ Cisgender man/boy (gender corresponds with birth sex)
☐ Cisgender woman/girl (gender corresponds with birth sex)
☐ Transgender man/trans man/female-to-male (FTM)
☐ Transgender woman/trans woman/male-to-female (MTF)
☐ Other gender category; please specify:
☐ Decline to answer

4. **Weight**
☐ lb
☐ kg

5. **Ethnicity** *(Check one)*
☐ Hispanic/Latino
☐ Not Hispanic/Latino

6. **Race** *(check all that apply)*
☐ American Indian/Alaska Native
☐ Asian
☐ Black or African American
☐ Native Hawaiian/Other Pacific Islander
☐ White

B. ADVERSE EVENT, PRODUCT PROBLEM

1. **Type of Report** *(check all that apply)*
☐ Adverse Event
☐ Product Use/Medication Error
☐ Product Problem *(e.g., defects/malfunctions)*
☐ Problem with Different Manufacturer of Same Medicine

2. **Outcome Attributed to Adverse Event** *(check all that apply)*
☐ Death – Date of death *(e.g., 01-Jan-1900)*:
☐ Life-threatening
☐ Hospitalization (initial or prolonged)
☐ Other Serious or Important Medical Events
☐ Required Intervention to Prevent Permanent Impairment/Damage
☐ Disability or Permanent Damage
☐ Congenital Anomaly/Birth Defects

3. **Date of Event** *(e.g., 01-Jan-1900)*

4. **Date of this Report** *(e.g., 01-Jan-1900)*

5. **Describe Event, Problem or Product Use/Medication Error**

Characters Remaining (max. 4,000):

https://www.fda.gov/media/76299/download

- Mandatory reporters
  - FDA Form 3500A
    - Manufacturers
    - User Facilities
    - Importers
- Voluntary reporters
  - Medwatch Form 3500
    - Healthcare professionals
    - Patients
    - Consumers

EVENT INVESTIGATION

- Manufacturers must demonstrate a ***reasonable attempt*** to follow up and obtain relevant required information
- Document and justify why certain information could not be obtained
- Includes:
  - Obtaining suspect device and evaluating/testing it
  - Going to the facility to evaluate the device
  - Follow-up discussions with the user facility, clinician or patient
  - Evaluating labeling & IFUs
  - Reviewing manufacturing documentation
  - Testing devices from same lot/batch
  - Trending similar complaints

INVESTIGATION RESULTS

- Results of investigation summarized in MDRs
  - Narrative text
  - Manufacturer evaluation codes
- May submit supplemental MDRs
  - If investigation is not complete by reporting deadlines
  - If corrections are needed to previous submissions after additional information is obtained
- FDA may request additional information regarding event investigation

ADDITIONAL INFORMATION (AI) LETTERS

21 CFR 803.15: AI letters are used to collect additional or clarify information in an MDR

1) We will notify you in writing if we require additional information and will tell you what information we need. We will require additional information if we determine that protection of the public health requires additional or clarifying information for medical device reports submitted to us and in cases when the additional information is beyond the scope of FDA reporting forms or is not readily accessible to us.
2) In any request, we will state the reason or purpose for the request, specify the due date for submitting information and clearly identify the reported event(s) related to our request.

In Addition to Filing MDRs…

- Device manufacturers must conduct a complete investigation of each event (21 CFR 820.198)
- Develop, maintain and implement written MDR procedure (21 CFR 803.17)
- Establish and maintain MDR event files/records (21 CFR 803.18)
- Specific requirements are dependent on submitter:
  - User Facilities – 21 CFR 803 Subpart C
  - Importers – 21 CFR 803 Subpart D
  - Manufacturers – 21 CFR 803 Subpart E
- Have a system in place that ensures access to information that facilitates timely follow-up/inspection by FDA!

LIMITATIONS OF MDR DATA

- Under-reporting
  - Users unfamiliar/unaware
  - Fear of unintended consequences
  - Confusion about HIPPA privacy and reporting
  - Malfunction/injury may not be clinically apparent

- Incomplete information in reports
  - Not obtainable from user end
  - Devices not returned or made available for manufacturer evaluation

- Causality not confirmed
  - Cannot determine link between device use/malfunction and negative clinical outcomes

Lack of MDRs ≠ Lack of problems

CONSIDERATIONS FOR OPTN…

- Both the Centers for Medicare and Medicaid Services (CMS) and the Organ Procurement and Transplantation Network (OPTN) require transplant programs to maintain quality assurance and performance improvement (QAPI) programs directed toward clinical and nonclinical transplant activities.

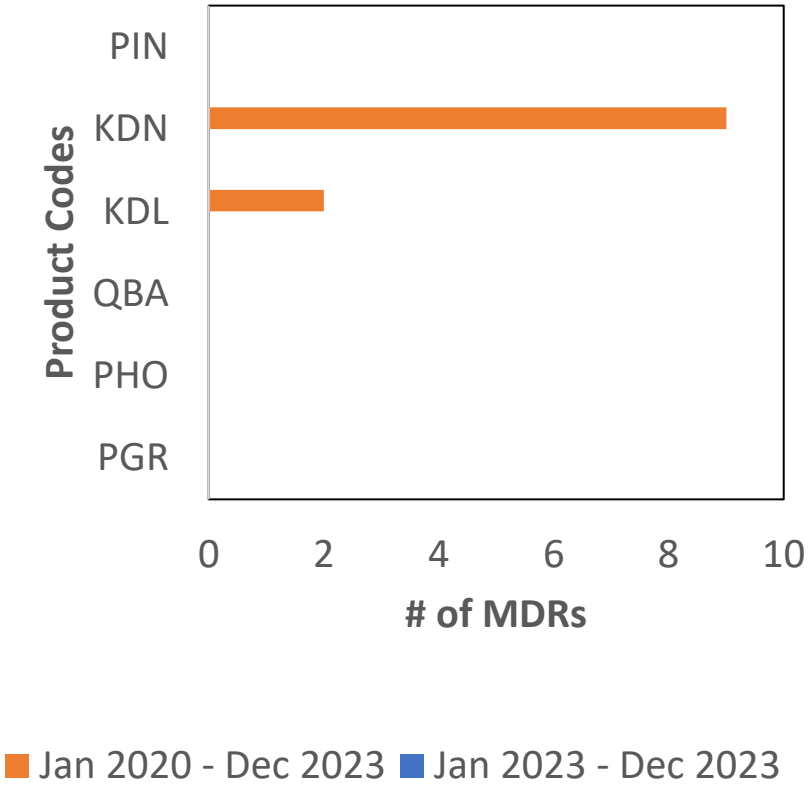
- Transplant program QAPI requirements mandate *review of adverse events*, including patient deaths and graft losses, with the intent to change practice through the implementation of better care processes.

Mathur AK et. Al., *Mayo Clin Proc Innov Qual Outcomes* (2019): https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6713855/

MDRs RECEIVED Since JAN 2020

For Product Codes:

Product Code	Regulatory Pathway	Description*
PGR	PMA	NORMOTHERMIC DONOR HEART PRESERVATION SYSTEM FOR TRANSPLANTATION
PHO	PMA	NORMOTHERMIC PRESERVATION SYSTEM FOR TRANSPLANTATION OF INITIALLY UNACCEPTABLE DONOR LUNGS
QBA	PMA	NORMOTHERMIC MACHINE PERFUSION SYSTEM FOR THE PRESERVATION OF STANDARD CRITERIA DONOR LUNGS PRIOR TO TRANSPLANTATION
KDL	510(k)	SET, PERFUSION, KIDNEY, DISPOSABLE
KDN	510(k)	SYSTEM, PERFUSION, KIDNEY
PIN	Enforcement Discretion	KIDNEY PERFUSION KIT



https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm

CONSIDERATIONS FOR OPTN…

- Patient safety issues from debriefings and incident reports – related to Medical Device Equipment:
  - Failure/Malfunction
  - User Error
  - Poor Presentation/Packaging/Labeling
  - Lack of Availability
  - Unclean/Unsterile
  - Dislodgement/Misconnection

McElroy LM et. Al., *Surgery* (2014): https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4254469/

Recommendations to OPTN When Reporting MDRs

- Do so in a timely manner
- Always report back to the manufacturer (or to FDA if the manufacturer is unknown) if you find any defects in the device that caused or attributed to an adverse event.
- In your text narratives, emphasize how the event (graft failure, low organ quality, etc.) may be related to the specific device
- For events related to graft failure or graft loss, you may consider using the words “serious injury” in your complaint to the manufacturer so they may be able to pay attention to the complaint and evaluate whether it is reportable as an MDR.
- When in doubt regarding whether to report an event or not, err on the side of reporting and allow FDA to evaluate whether this is a reportable event.

DISCUSSION

- What are the challenges you commonly face with transplant devices with regards to safety or device malfunctions?

- What are the challenges associated with determining whether an adverse event is related to the medical device used?

- What recommendations do you have for improving MDR reporting of transplant devices?

THANK YOU!

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