Managing an LDT/IVD Quality System

A Review of Regulatory Considerations, Reporting Requirements, and Future Directions

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October 20, 2022

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Agenda

- PGDx Quality System Background
- Reporting Systems (IVD and CLIA)
- Regulatory Considerations Impacting LDT Process
- Conclusions/Recommendations

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PGDx Quality System Background

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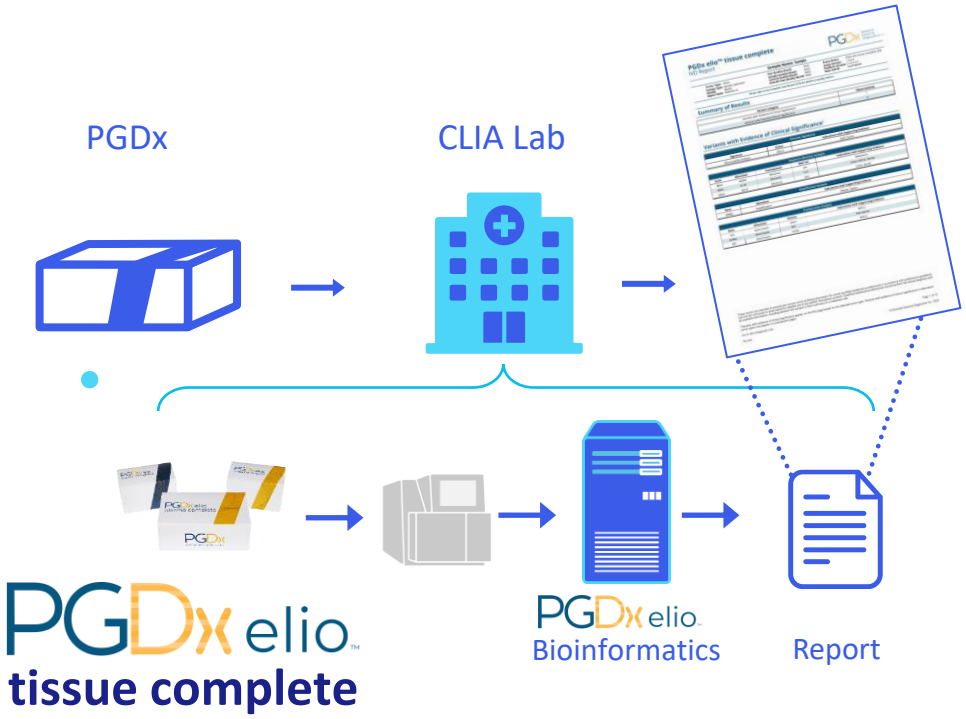
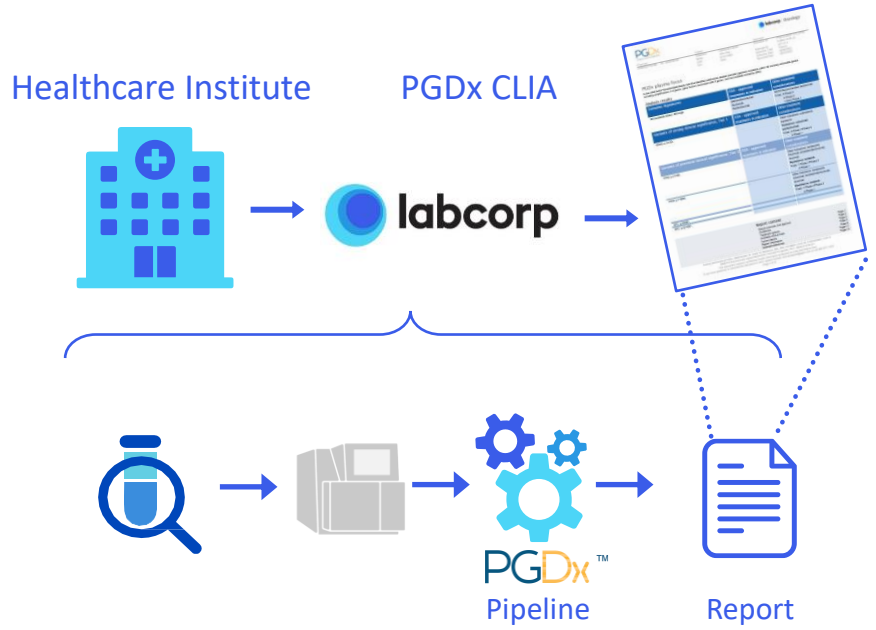
Enabling Both Kitted and IVD Strategies

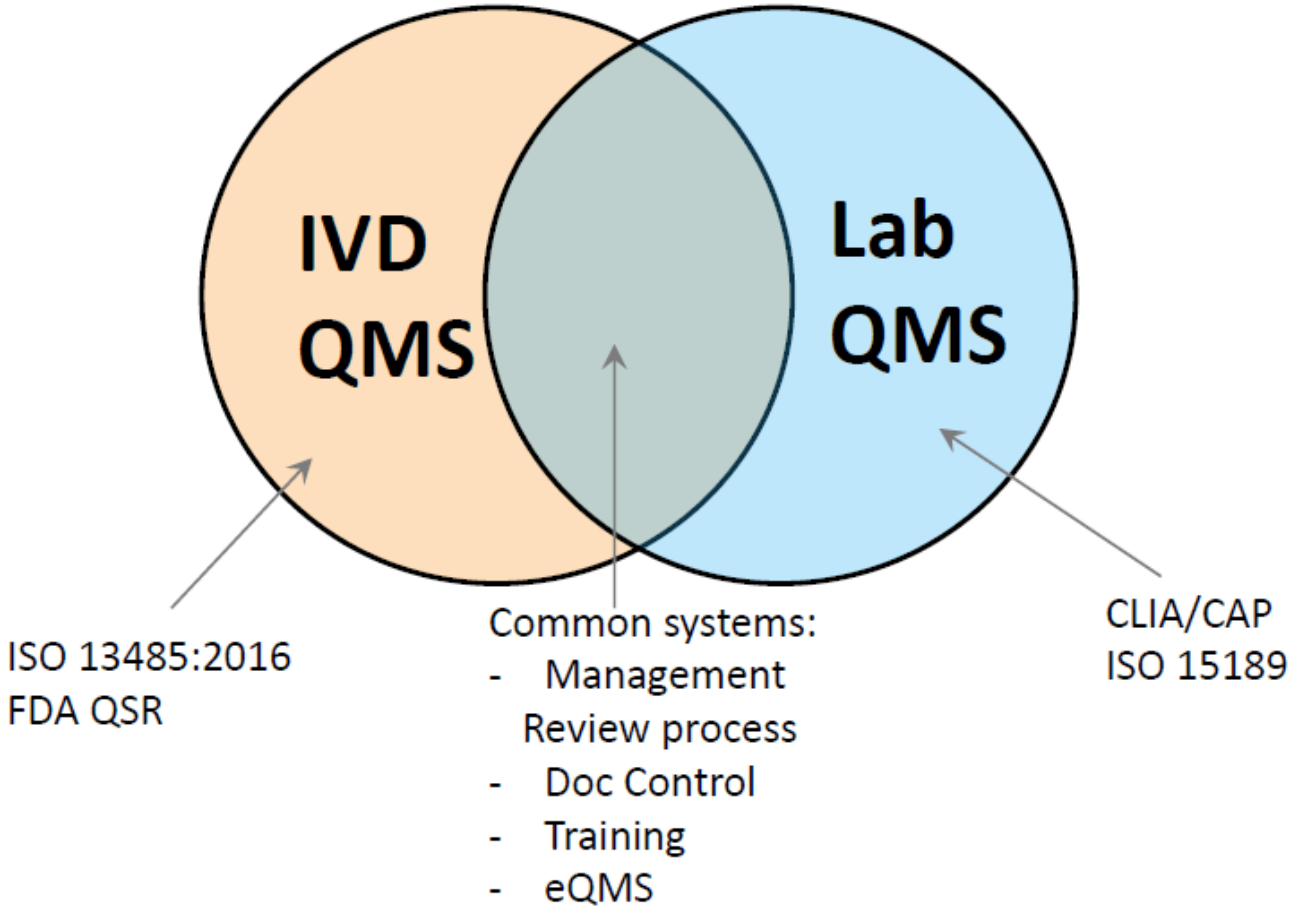
Decentralized/Kitted Testing
(processed at in-house testing institution)



Centralized Testing
(processed at PGDx-Labcorp site in Baltimore)



PGDx Quality System Overview



Providing Solutions Across the Drug Development Continuum

PGDx CAP/CLIA Lab

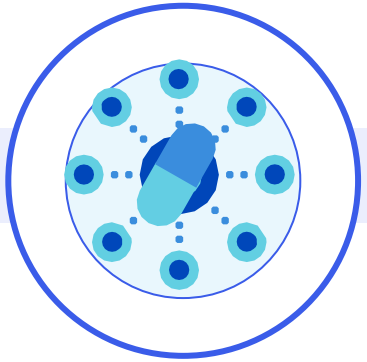
Research and Discovery Support

Define biomarkers of response

Single Site Trial Enrollment/Clinical Testing

Rx/Dx hypothesis testing

External CAP/CLIA Labs



Clinical Trial Assay Support

Global CRO footprint for registrational trials

Global CDx Commercialization

Global Patient Access

PGDx elio tissue complete

PGDx elio tissue complete

Kitted Product (IVD/CE-IVD)

- 500 + genes including TMB & MSI biomarkers to align with CDx & NCCN guideline targets
- FDA cleared and CE-IVD marked
- US FDA and IVDR Reporting Requirements

Clinical Lab and Investigational Product

- Offered in Baltimore CAP/CLIA Laboratory
- Has supported IDE studies
- Adverse Events/Annual IDE Reports/CAP Reporting

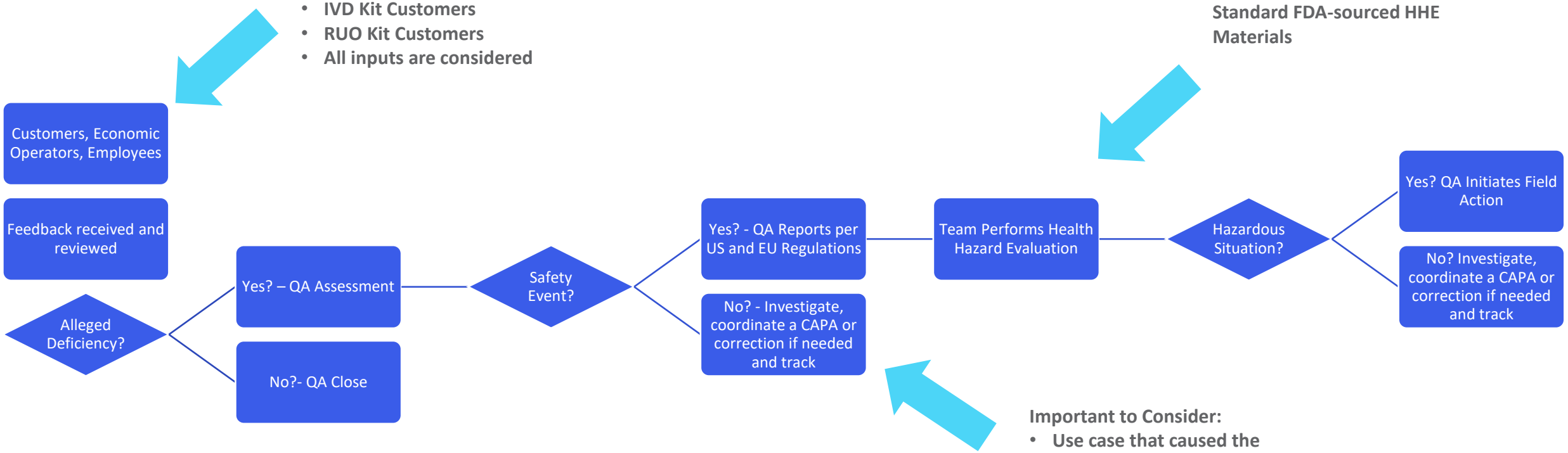
Research Tool

- Server containing a bioinformatic pipeline for analysis
- Raw data is available for research studies

Risk Assessments Consider All Product Lines

Customers include:
- **Baltimore CLIA Lab**
- **IVD Kit Customers**
- **RUO Kit Customers**
- **All inputs are considered**

Standard FDA-sourced HHE Materials



Important to Consider:
- **Use case that caused the complaint**
- **If complaint could impact the IVD Product, even if complaint sourced from RUO customers**

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Regulatory Considerations Impacting LDT Process

Regulatory Considerations Impacting LDT Process

US Regulatory Considerations

- QMSR
- VALID????

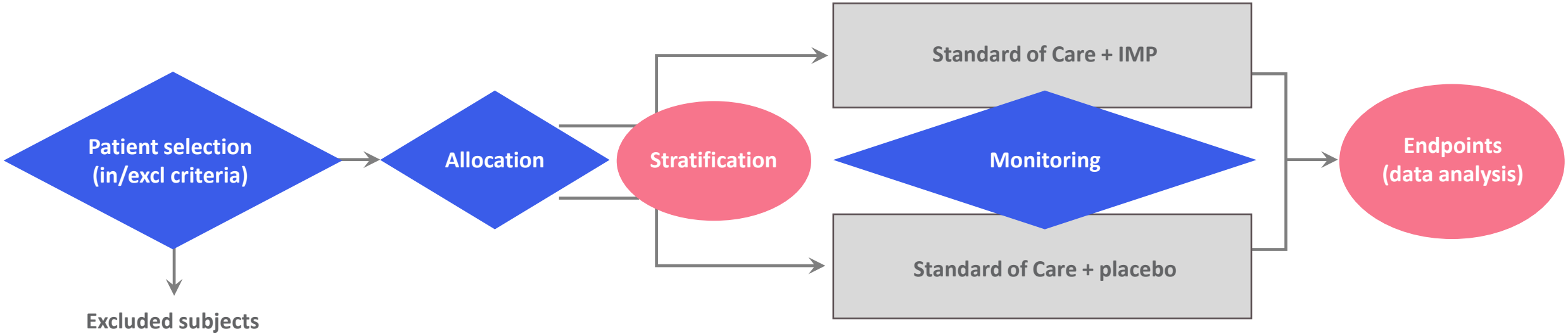
Clinical Trial Regulation (CTR) in Europe

- CE marked distributed assays that can be deployed to enable global trials including Europe

IVDR

- Everyone's favorite Regulatory Topic!
- US LDTs in scope because of distance sales provisions

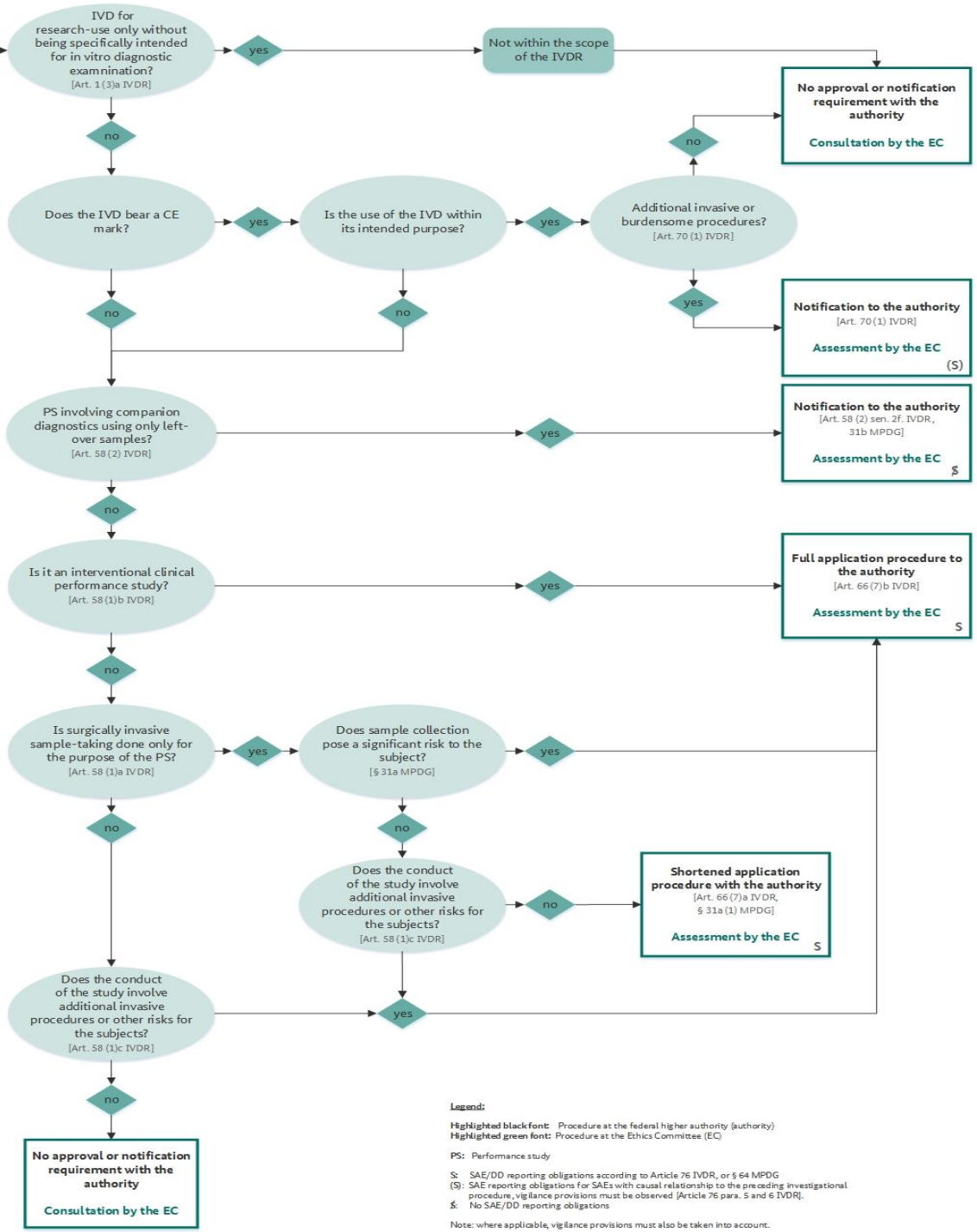
Enable Global Clinical Trials



Activities in blue diamonds will likely be considered IVDs (medical management decisions for subjects within a trial)

MDCG 2022-10
Q&A on the interface between Regulation (EU) 536/2014 on clinical trials for medicinal products for human use (CTR) and Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR)

CTR Decision Tree



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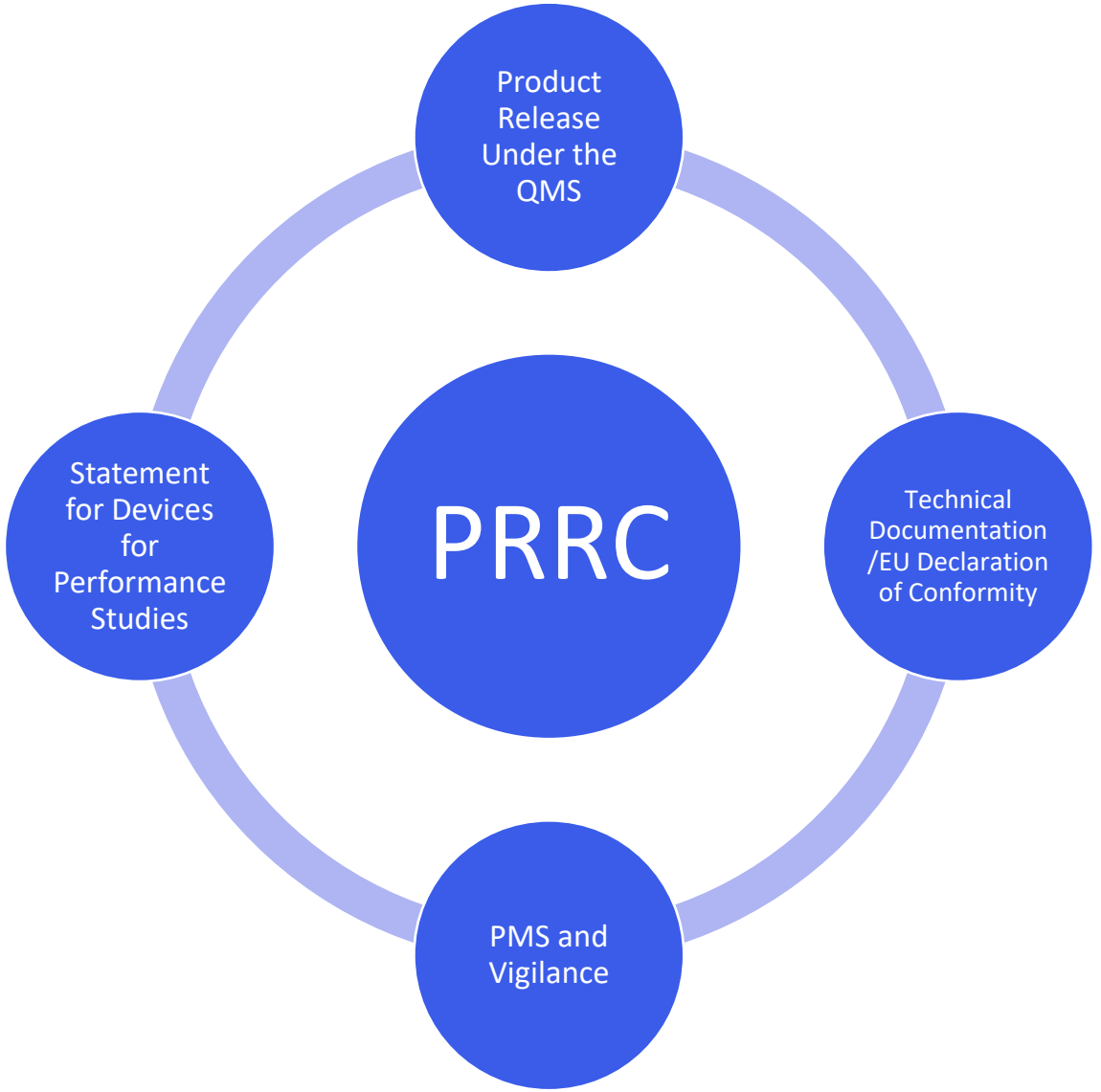
EU Reporting Expectations Have Evolved

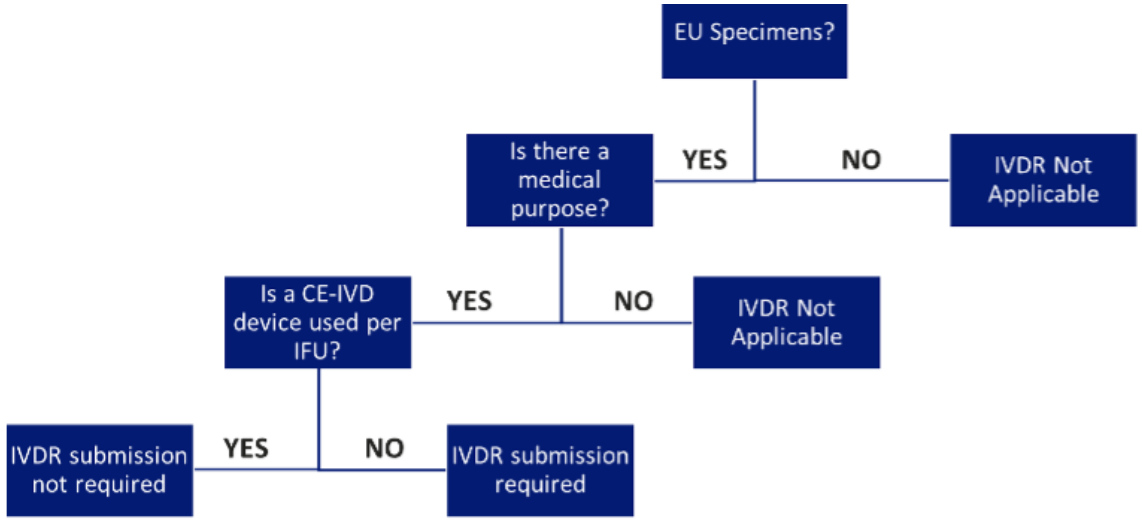
CDx IVDs are now defined and considered Class C

	EU MDR	EU IVDR
Post-market surveillance report (PMSR)	Required for Class I manufacturers - updated when necessary	Required for Class A and Class B manufacturers - updated when necessary
Periodic safety update report (PSUR)	Required for Class IIa, Class IIb, and Class III manufacturers - updated at least annually	Required for Class C and Class D manufacturers - updated at least annually
Post-market follow-up	Post-market clinical follow-up (PMCF) report	Post-market performance follow-up (PMPF) report
Vigilance reporting	Serious threat to public health: No later than 2 days	Serious threat to public health: No later than 2 days
	Death or serious deterioration of health: No later than 10 days	Death or serious deterioration of health: No later than 10 days
	Serious incident: No later than 15 days	Serious incident: No later than 15 days



Impact of IVDR on LDTs in the US

LDTs in the US are Not Exempt



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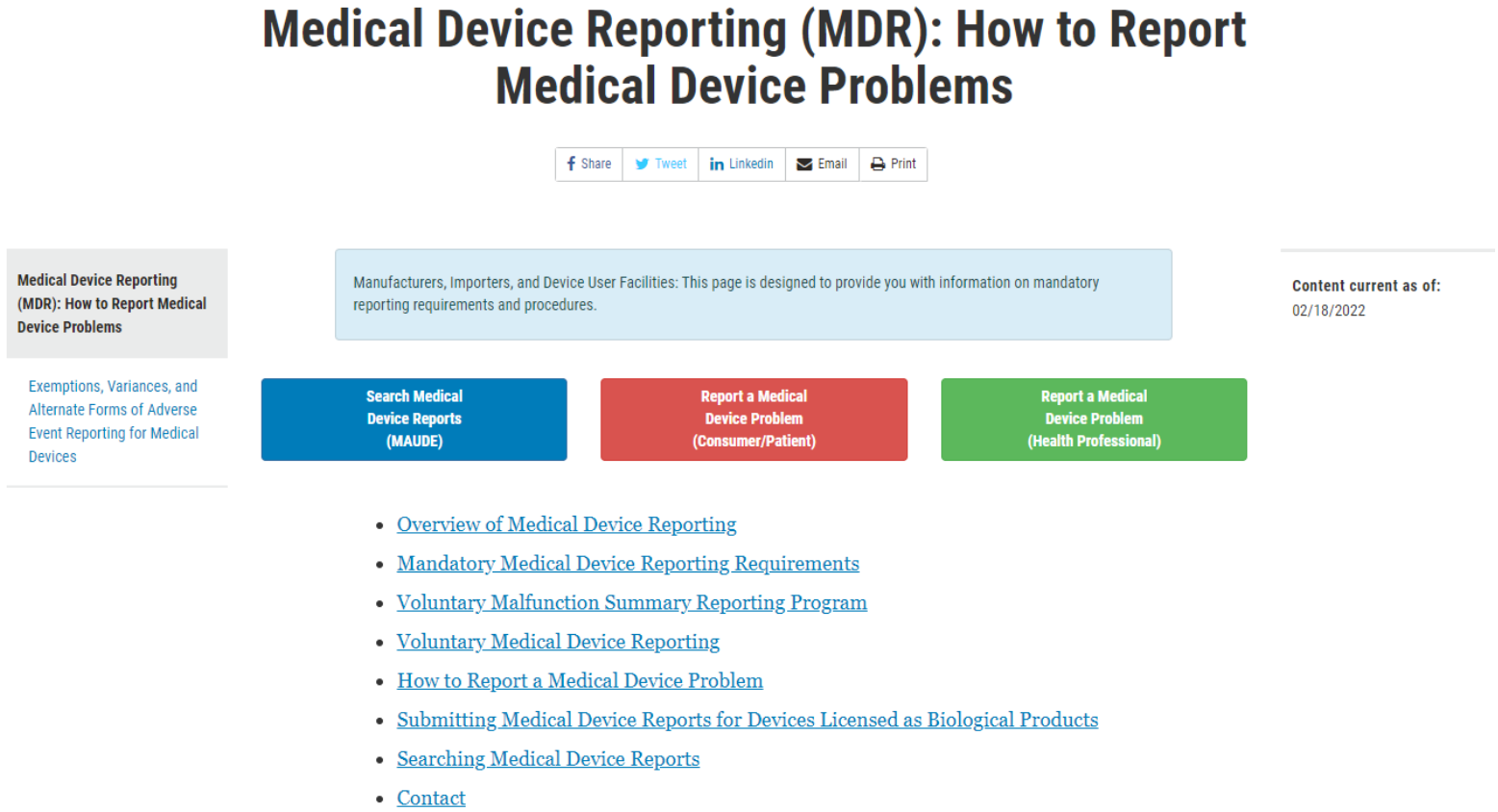
Reporting Systems (IVD and CLIA)

US Medical Device Reporting



Medical Device Reporting (MDR): How to Report Medical Device Problems

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Medical Device Reporting (MDR): How to Report Medical Device Problems

Exemptions, Variances, and Alternate Forms of Adverse Event Reporting for Medical Devices

Manufacturers, Importers, and Device User Facilities: This page is designed to provide you with information on mandatory reporting requirements and procedures.

Content current as of:
02/18/2022

Search Medical Device Reports (MAUDE)

Report a Medical Device Problem (Consumer/Patient)

Report a Medical Device Problem (Health Professional)

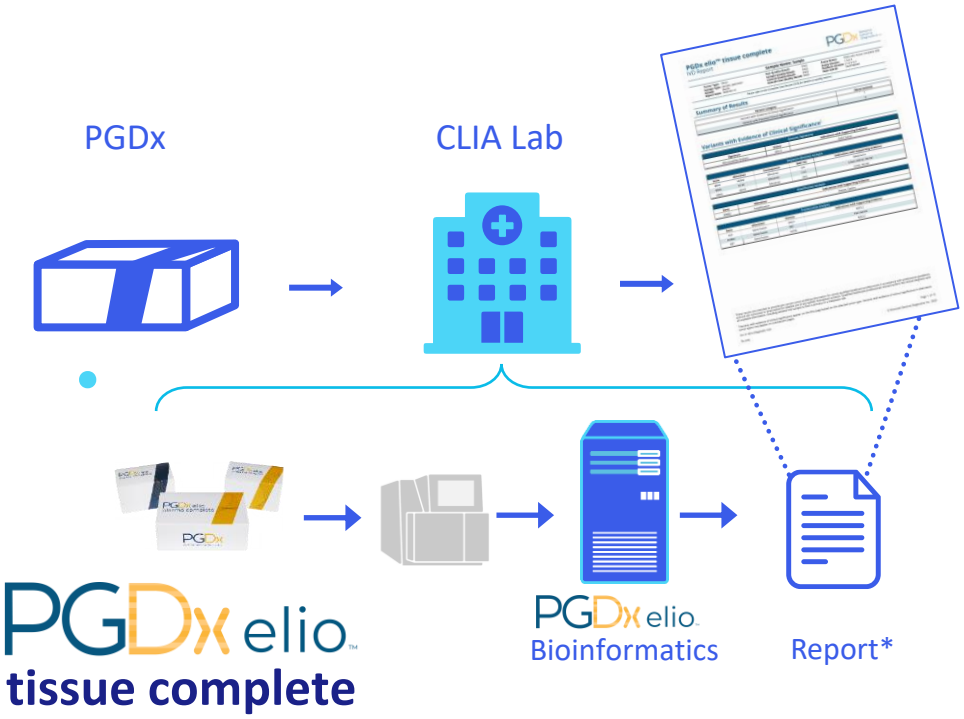
- Overview of Medical Device Reporting
- Mandatory Medical Device Reporting Requirements
- Voluntary Malfunction Summary Reporting Program
- Voluntary Medical Device Reporting
- How to Report a Medical Device Problem
- Submitting Medical Device Reports for Devices Licensed as Biological Products
- Searching Medical Device Reports
- Contact

https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems

Reporting Requirements

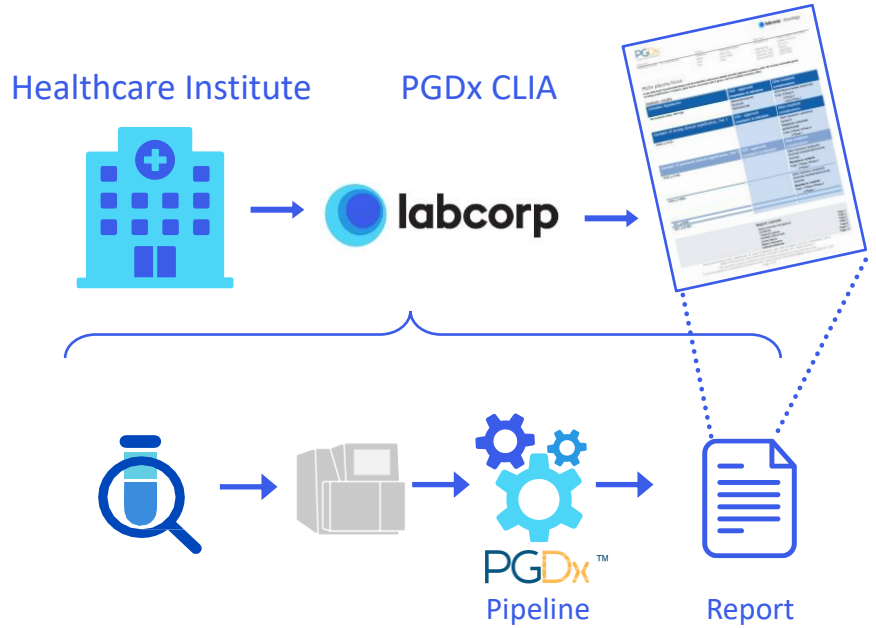
Decentralized/Kitted Testing

Reporting requirements as a Manufacturer



Centralized Testing

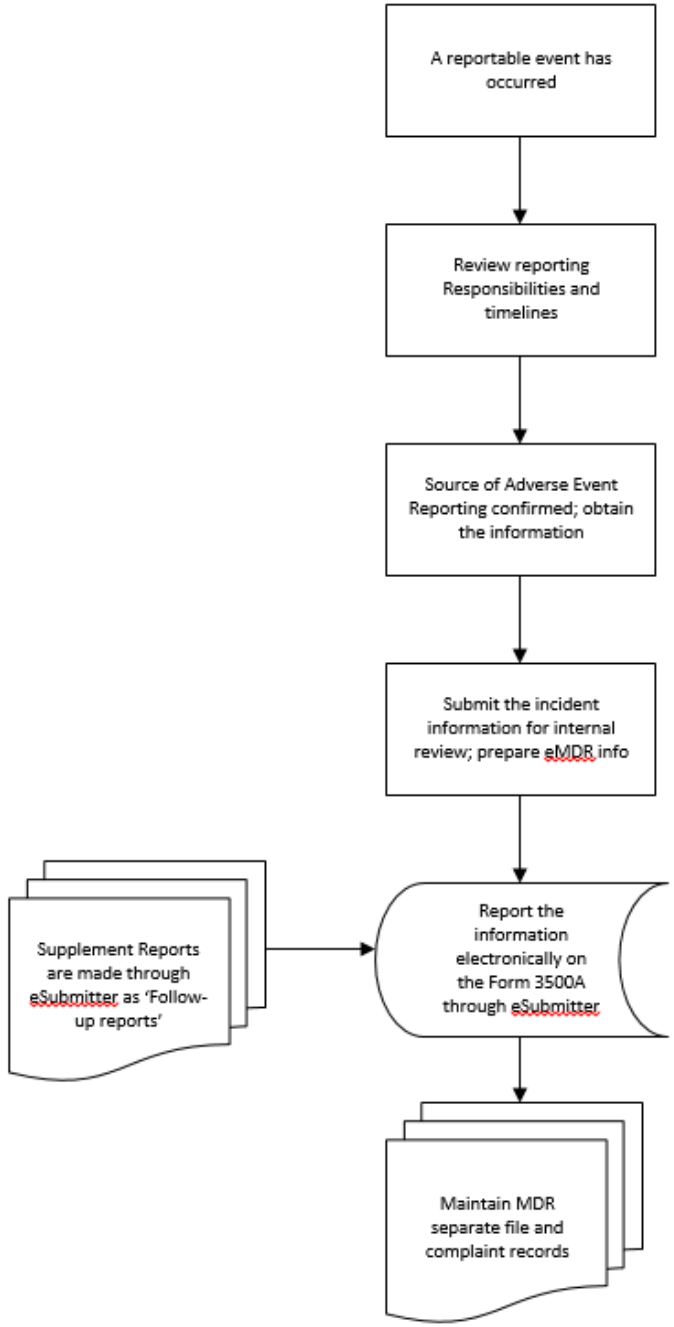
Reporting Requirements as a Device User Facility



IVD Manufacturer Reporting Process

- **Manufacturers:** Manufacturers are required to report to the FDA when they learn that any of their devices may have caused or contributed to a death or serious injury. (Key terms are defined in 21 CFR 803.3.) Instructions are available for completing the required 3500A form. Manufacturers must also report to the FDA when they become aware that their device has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems

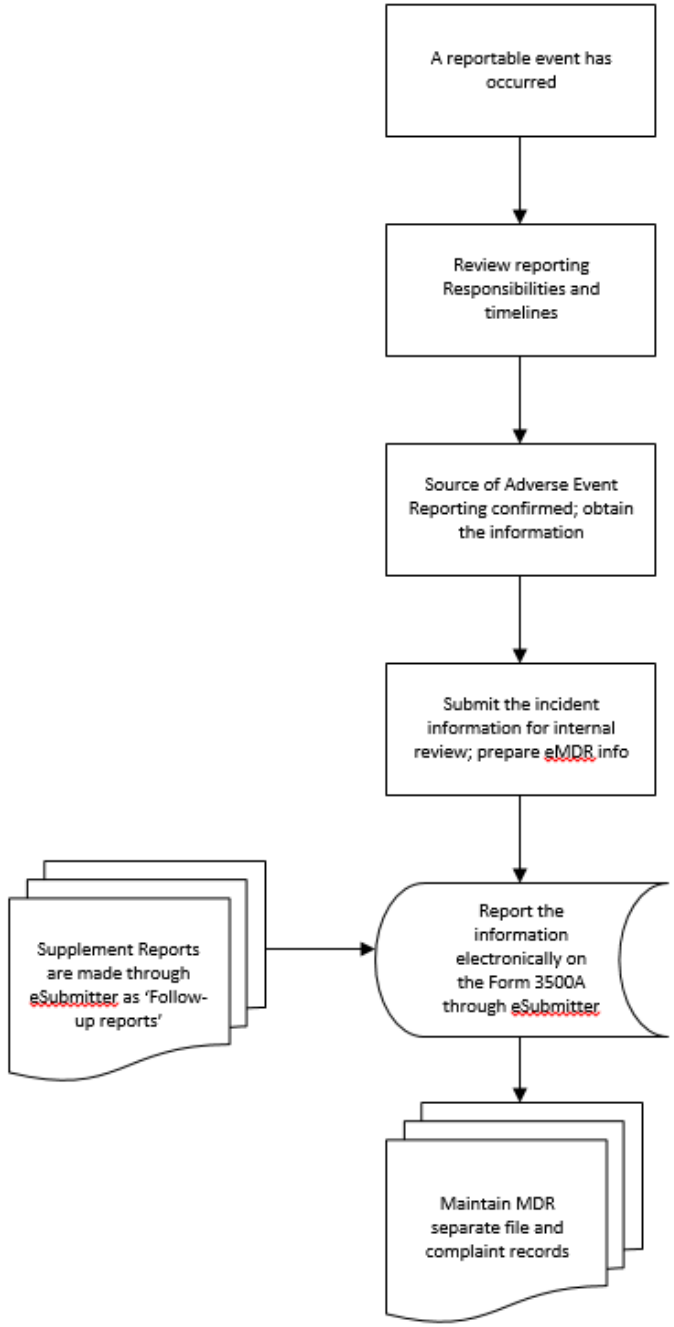


CAP/CLIA Reporting Process

- Device User Facilities: A "device user facility" is a hospital, ambulatory surgical facility, nursing home, outpatient diagnostic facility, or outpatient treatment facility, which is not a physician's office. User facilities must report a suspected medical device-related death to both the FDA and the manufacturer. User facilities must report a medical device-related serious injury to the manufacturer, or to the FDA if the medical device manufacturer is unknown.

Additional Considerations for:

- **CAP Adverse Media Reporting**
- **Any necessary clinical trial reporting**
- **Reporting to manufacturers of IVDs used in laboratory**



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Conclusions/ Recommendations

Conclusions/Recommendations

- Expectations for LDTs have changed for Europe (Design Control and CE Marking)
- CE Marking Needed for Many Clinical Trial Assays
- Make Reporting Processes As Efficient As Possible

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Thank You!

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