Software in the World of In Vitro Diagnostics

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What Is Software

- Firmware
- Stand-alone software applications (incl. algorithms)
- Dedicated hardware/software for medical devices
- Software in accessories to medical devices
- Data management systems
- Web based applications

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Review Of Software

Why?

- Software is integral to the operation and safety of medical devices.
- Software is part of medical devices, therefore regulated.

Where?

- PMAs, 510(k)s, HDEs

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Regulated, Not Reviewed

- HIS
- LIS (Unless uses new algorithms)
- LAS (Unless takes over instrument functions like bar code reading)
- HIS and LIS Still subject to MDR reporting and recalls

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Software Guidance

- Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089593.pdf)
- Level of concern – section 3.1
- Software Description - section 3.2
- Device Hazard Analysis - section 3.3
- Software Requirements Specification (SRS) - section 3.4
- Architecture Design Chart - section 3.5
- Design Specification - section 3.6
- Traceability Analysis - section 3.7
- Development - section 3.8
- Validation, Verification and Testing - section 3.9
- Revision Level History - section 3.10
- Unresolved Anomalies (Bugs) - section 3.11
- Release Version Number - section 3.12

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Software Guidance

SOFTWARE DOCUMENTATION	MINOR CONCERN	MODERATE CONCERN	MAJOR CONCERN
Level of Concern	Required for all.		
Software Description	Required for all.		
Device Hazard Analysis	Required for all.		
Software Requirements Specification (SRS)	Summary SRS.	The complete SRS document.	
Architecture Design Chart	No documentation is necessary.	Detailed depiction of functional units and software modules.	
Software Design Specification (SDS)	No documentation is necessary.	Software design specification document.	

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Software Guidance

SOFTWARE DOCUMENTATION	MINOR CONCERN	MODERATE CONCERN	MAJOR CONCERN
Traceability Analysis	Required for all.		
Software Development Environment Description	No documentation is necessary.	Summary Software Development Environment Description	Full Software Development Environment Description
Verification and Validation Documentation	Software functional test plan, pass / fail criteria, and results.	Description of V&V activities with System level test protocols and results.	V&V activities with Unit and System level test protocols and results.
Revision Level History	Required for all.		
Unresolved Anomalies (Bugs or Defects)	No documentation is necessary.	List of remaining software anomalies.	

Common Issues: Level Of Concern

- Level of concern defines documentation submitted, and *does not* indicate what is required by a quality system.
- Software guidance should be used to determine the device's level of concern.
- Most IVDs are moderate level of concern.

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Common Issues: Documentation

- All functions of the device should have:
  - Requirements (SRS)
  - Design (SDS)
  - Hazard analysis identification/mitigation
  - Functionality verified
  - Its use in the device validated
- The traceability analysis should describe these relationships.

Requirement	Design	Hazard	Verification	Validation
Requirements Section V.V	Design Section W.W	Hazard Section X.X	Verification Section Y.Y	Validation Section Z.Z

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Common Issues: Hazard Analysis

- Hazard analysis should include all potential hazards identified in standards, those unique to device use, AND address possible software errors/failures.

- Software failures
  - Systematic in nature
  - Probability of occurrence cannot be determined

Therefore, the software portion of the Hazard Analysis should focus on the SEVERITY of the harm that could result from the software failure.

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Common Issues: Hazard Analysis

Identification of hazardous event	Severity of hazard	Cause of hazard	Method of control (design, protective measures, labeling)	Corrective measures taken	Verification that the method of control was implemented correctly
1. Incorrect result	Major	Thermal cycling temperatures too high.	Design	Software Requirement -Assay specifications are not able to be modified by end user.	Verification and Validation document 1.2, page 52.

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Common Issues: Unresolved Anomalies (Bugs)

- List ALL unresolved software anomalies.
- For each anomaly, indicate the: problem, impact, plans for correction.
- Communicate unresolved bugs to customers.

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Off The Shelf Software

- Off-The-Shelf Software Use in Medical Devices (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM073779.pdf)
- Examples
  - Networks
  - Microsoft operating systems
  - Databases, spreadsheets

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Off The Shelf Software

Minor Level of Concern
Hazard Analysis
Basic Documentation

Moderate Level of Concern
Minor Level PLUS:
Hazard Mitigations
Describe and Justify Residual Risks

Major Level of Concern
Moderate Level PLUS:
Special Documentation (includes audit of OTS developer, V&V performed by developer and device manufacturer, continued maintenance plans should developer terminate support)

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Wireless

- What if your software has wireless capability?
- This feature should still be documented like any other required feature of the device.
- Draft Guidance for Industry and FDA Staff - Radio-Frequency Wireless Technology in Medical Devices (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077272.pdf)

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Should You Send Code?

- No.
- The review of software is based on the *results* (design, functionality, safety) of the software's code.

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Guidance List

- Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089593.pdf)
- Off-The-Shelf Software Use in Medical Devices (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM073779.pdf)
- Guidance for Industry - Cybersecurity for Networked Medical Devices Containing Off-the-Shelf (OTS) Software (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077823.pdf)
- Draft Guidance for Industry and FDA Staff - Radio-Frequency Wireless Technology in Medical Devices (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077272.pdf)

Combined RUO/IVD Functionality

Conditions to be met (molecular diagnostic instruments):

- RUO functions do not interfere with cleared/approved functions or functions under review in a way that results in the device being less safe and effective than the predicate or that causes the device to have different questions of safety and effectiveness than the predicate.
  - How separation is managed
  - Risk/Hazard analysis addressing co-existence (mitigations and testing)
- Labeling for the clinical intended use is separate from labeling for the RUO intended use.
- You must not promote the device's RUO functionality as cleared or approved for clinical use.

Combined RUO/IVD Functionality

You Can:

- Promote instrument as cleared/approved for use with assays that are cleared/approved for use on that instrument/system
- Promote instrument for RUO uses without claiming or implying that RUO uses are cleared/approved
- Provide RUO labeling separately from IVD labeling

You Cannot:

- Combine promotional claims (i.e., “you can use this for MRSA and for developing LDTs”)
- Combine labeling (i.e., user’s manual, brochures, etc.)
- Claim cleared status for RUO functions
- Claim blanket clearance or approval for the instrument implying instrument clearance for any assay other than those cleared or approved

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Questions?

- Ask away!