



Software in the World of In Vitro Diagnostics

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U.S. Department of Health and Human Services

Food and Drug Administration





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

■ ■ ■ *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

■■■ *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



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

■ ■ ■ *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.	



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.



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



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.



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.



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.



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



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)

■ ■ ■ *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>)

■ ■ ■ *Should You Send Code?*

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



Combined Non-approved/Approved Functionality

Conditions to be met (molecular diagnostic instruments):

- Sponsor demonstrates that non-approved functions do not interfere with approved functions by providing sufficient information to establish that the approved functions are not affected by the coexistence of non-approved functions on the same instrument.
 - How separation is managed/made clear to user
 - Risk/Hazard analysis addressing co-existence (mitigations and testing)
- Labeling for the approved functions is separate from labeling for the non-approved functions.
- Sponsor must not promote the device's non-approved functionality as approved for clinical use.



Combined Non-approved/Approved Functionality

Sponsor may generally:

- Promote instrument as approved for use with assays that are approved for use on that instrument/system.
- Promote instrument for non-approved uses without claiming or implying that non-approved uses are approved.
- Provide information about non-approved functions separately from approved labeling.



Combined Non-approved/Approved Functionality

Sponsor generally should not:

- Combine non-approved/approved promotional claims (i.e., “you can use this for MRSA and for basic research”).
- Combine labeling describing approved functions (i.e., user’s manual, brochures, etc.) with information about non-approved functions.
- Claim or imply approved status for non-approved functions.
- Claim or imply that the instrument is approved for any assay other than those specifically FDA-approved.



Guidance List

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- 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
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Questions?

- Ask away!