APPENDIX B: Sample Risk Assessment for Cepheid GeneXpert Tests

RISK MATRIX - ISO 14971	SEVERITY OF HARM				
PROBABILITY OF HARM	**Negligible**	**Minor**	**Serious**	**Critical**	**Catastrophic**
Frequent	3	3	2	1	1
Probable	4	3	2	2	1
Occasional	5	4	4	3	2
Remote	6	5	5	4	3
Improbable	6	6	5	4	4

LEGEND	
Unacceptable	**1, 2, 3**
Acceptable	**4, 5, 6**

	Possible Source of Error	Potential Failure	Phase	Severity	Probability	Risk Index Before	Manufacturer Features to Minimize Risks	Possible Laboratory Solutions to Minimize Risk	Risk Index After	Documentation
1. SPECIMEN										
1.1	Test is performed in incorrect patient population	Inaccurate result	Pre-analytical				Package insert and training	Establish training for specimen collectors Establish sample rejection criteria		
1.2	Wrong specimen type collected	No result or inaccurate result	Pre-analytical				Package insert and training	Establish training for specimen collectors Establish sample rejection criteria		
1.3	Wrong collection device used	No result or inaccurate result	Pre-analytical				Package insert and training; Manufacture recommends appropriate collection device	Establish sample rejection criteria		
1.4	Specimen not collected correctly	No result or inaccurate result	Pre-analytical				Package insert and specimen collection guides (available for some tests)	Establish training for specimen collectors Follow manufacturer's instructions		

Based on the IQCP Interpretive Guidelines from CMS - 8/2013. This document is for illustrative purposes only and is not intended to be a complete IQCP.
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Possible Source of Error		Potential Failure	Phase	Severity	Probability	Risk Index Before	Manufacturer Features to Minimize Risks	Possible Laboratory Solutions to Minimize Risk	Risk Index After	Documentation
1.5	Improper specimen storage or transit	No result or inaccurate result	Pre-analytical				Package Insert	Establish training for specimen collectors on proper shipping and handling Follow manufacturer's instructions		
1.6	Target/Analyte recovery low	Potential false negative result	Analytical				Extraction is automated Specimen Processing Control	Repeat test according to retest procedure Adhere to proper specimen collection		
1.7	Specimen volume insufficient for retest	No result	Analytical				Package insert and training	Collect additional specimen per labeling (as applicable)		
2. TESTING PERSONNEL										
2.1	Cartridge knocked over/ dropped after reagents added	No result	Pre-analytical				Training	Training Annual competency assessment		
2.2	Wrong cartridge used for test	No result or inaccurate result	Pre-analytical				Package insert and training	Verify cartridge matches test ordered		
2.3	Incorrect assay selection from menu	Alternate/ unexpected result	Pre-analytical				Package insert and training	Establish training for operators		
2.4	Incorrect barcode label placement on cartridge	Mechanical failure No result	Pre-analytical or analytical				Training	Remove or reposition label Retest with new cartridge if applicable		
2.5	Too much specimen added to cartridge	No result or inaccurate result	Analytical				Package insert, training and Internal Controls	Review test result Follow instructions for retesting procedure		

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2.6	Too little specimen added to cartridge	No result or inaccurate result Potential false negative	Analytical				Package insert, training and cartridge preparation cards	Adhere to package insert procedure		
2.7	Sample omitted	Potential false negative	Analytical				Package insert, training and cartridge preparation cards	Visually inspect cartridge to ensure sample addition		
2.8	Specimen added to wrong place in cartridge	No result or inaccurate result	Analytical				Package insert, training and cartridge preparation cards	Follow manufacturer's instructions Establish annual competency assessment		
2.9	Incorrect result read/ reported by operator	Inaccurate result	Post-analytical				Easy to read test result print out Ability to connect to LIS	Use LIS		
3. REAGENTS										
3.1	Improper cartridge and reagent storage or shipping conditions	No result or inaccurate result	Pre-analytical				Internal controls and Probe Check Control	Monitor storage/ shipping temperatures when possible Implement QA processes to monitor appropriate shipping and/or storage conditions Test new lot/shipment with external controls		
3.2	Reagents added incorrectly/omitted	No result or inaccurate result	Pre-analytical				Internal controls, on-board reagents, training, cartridge preparation cards	Visually verify presence of on-board reagents Follow manufacturer's instructions		

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3.3	Cartridge or reagent defects	No result or inaccurate result	Pre-analytical				Appropriate packaging considerations Training Internal controls	Visually inspect for source of defects Follow manufacturer's instructions; retest		
3.4	Reagents not reconstituted properly	No result	Analytical				Internal controls	Follow manufacturer's instruction; retest		
3.5	Inhibition of PCR	No result	Analytical				Internal controls; package insert	Follow manufacturer's instructions; retest Establish specimen collection training		
3.6	Expired reagents	No result or inaccurate result	Analytical				System will not allow cartridge to be run if expired Extended product shelf life	Visually verify expiration date; discard expired cartridges immediately		
4. ENVIRONMENT										
4.1	Ambient temperature not optimal	No result	Analytical				Fans	Follow manufacturer's maintenance procedure		
4.2	Specimen contaminated with target/analyte carry-over	Potential False Positive	Analytical				None	Change gloves when handling different specimens Process samples individually		
4.3	Work area contaminated with target/analyte	Potential False Positive	Post-analytical				Closed test system	Follow manufacturer's maintenance procedure		

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5. TEST SYSTEM										
5.1	Untrained personnel access system	No result or inaccurate result	Pre-analytical or analytical				Ability to create unique user log-in and timed operator lockout	Define user IDs Establish training for operators		
5.2	Pressure too high or too low	No result	Analytical				System checks and internal controls	Follow manufacturer's maintenance procedure		
5.3	Cartridge not inserted correctly into instrument	No result	Analytical				Module door will not shut	Adjust appropriately and restart		
5.4	Test stopped and restarted by operator	No result	Analytical				System software will not retest duplicate cartridge serial number	Repeat test with new cartridge		
5.5	PCR contamination within system	Potential False Positive	Analytical				Closed test system Cleaning procedure detailed in operators manual	Establish training for operators Change gloves frequently and appropriately Discard used cartridges Follow manufacturer's maintenance procedure		
5.6	Air bubbles in reaction tube	No result	Analytical				Internal and probe check controls	Follow proper specimen addition procedure Contact facilities to confirm clean and uninterrupted power Contact manufacturer to report observation as appropriate		

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5.7	Power failure	No result	Analytical				Built-in fuse	Connect system to UPS Contact manufacturer if power failures do not resolve		
5.8	Thermocycler temperature out of range	No result	Analytical				System control check status: system control checks temperature, optics and mechanical integrity of each cartridge XpertCheck	Follow manufacturer's maintenance procedure		
5.9	Optical signal error	No result	Analytical				System control check status: system control checks temperature, optics and mechanical integrity of each cartridge XpertCheck	Follow manufacturer's maintenance procedure		
5.10	Incorrect result communicated to laboratory LIS - automated data transfer	No result or inaccurate result	Post-analytical				None	Verify host test communication settings in GeneXpert and LIS		

For more information about conducting risk assessment in a laboratory, please see:
CLSI. Laboratory Documents: Laboratory Control Based on Risk Management; Approved Guideline—First Edition. CLSI document EP-23-A1. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.

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