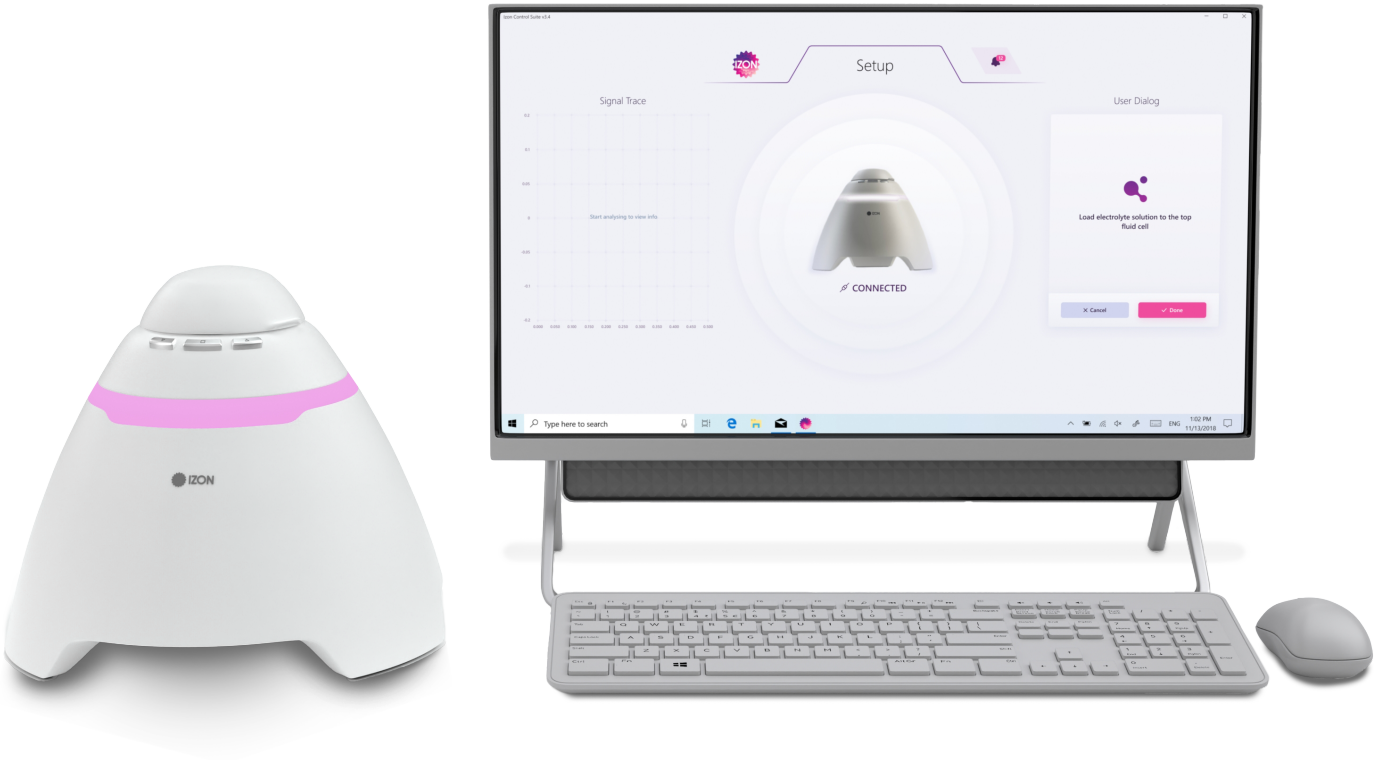
EX1-IQ-001 SOP AND VERIFICATION OF INSTALLATION QUALIFICATION FOR THE EXOID



IZON

CONTENTS

1 SCOPE

1.1 PURPOSE

This document provides and verifies the steps and information required to perform an Installation Qualification (IQ) for the Exoid. Following this protocol will verify that this installation has been completed successfully and where applicable, meets the requirements in 21 CFR Part 11 software regulations. Sections marked with an asterisk (*) do not need to be completed if 21 CFR Part 11 compliance is NOT required. This document should be executed any time an IQ is performed for an Exoid. This document should be completed and signed by an Executor (typically an Izon staff member) and a Reviewer (a customer QA representative).

This document relates to equipment that is supplied by Izon Science Limited. The information contained within this protocol is proprietary information and is the property of Izon Science Limited. This information may not be copied or disclosed in whole or in part by any third party / parties without the prior written consent of the company.

1.2 OBJECTIVES

To ensure that:

- All goods are received.
- To guide the user through correct installation of both the hardware and the software.
- The electrolyte is correctly prepared.
- The functionality of the instrument is verified.

2 REQUIRED MATERIALS AND DOCUMENTS

2.1 MATERIALS

The following materials are required to perform the entire IQ protocol and are not provided by Izon:

- Computer (must meet minimum specifications as described in Section 8)
- Calibrated micropipettes - 1 µL to 1 mL
- A vortex mixer
- Compressed nitrogen for drying. Alternatively, clean compressed air spray is also acceptable
- Lint-free tissue for drying
- Standing racks for tubes (optional)
- Refrigerator
- Deionised water
- Clean glass bottle
- 50 mL Falcon tubes
- Powder-free disposable gloves

2.2 DOCUMENTS

Confirm that the documents and drawings required to complete the IQ procedure are present and satisfactory (S) or unsatisfactory (US); and where they will be stored as a hard copy. Compare the drawings in EX1-IQ-002 to 003 Exoid IQ Procedure Reference Drawings, highlighting any areas which may be incorrect.

Documents Storage Location	Title	Initial	Date
	Executor		
	Reviewer		

Document Code	Document Code	Doc status S/US	Initial	Date
EX1-IQ-001	Verification of Installation Qualification Protocol for the Exoid			
EX1-IQ-002 to 003	Exoid IQ Procedure Reference Drawings			

2.3 DOCUMENTATION ACCEPTABILITY VERIFICATION

Acceptance Criteria	All listed documentation must be stored in a secure known location. The scope of the documentation must be sufficient to ensure that the equipment can be installed, maintained and operated in accordance with cGMP requirements and vendor recommendations. All drawings reflect the as-built condition of the equipment and/or installation.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

3 IDENTIFICATION OF PERSONNEL PERFORMING IQ

Enter the details of the people involved with this Installation Qualification. The training records for all Izon Science personnel are held on file and can be inspected at the QA department.

Date of IQ		
Executor (Izon Staff)	Name	
	Position	
	Signature	
Reviewer (Customer QA Rep)	Name	
	Position	
	Signature	

4 SYSTEM DESCRIPTION

Description of Equipment Use

The instrument operation of Izon's nanoparticle analysis system is based on the Coulter principle applied at the nanoscale. A tunable nanopore is connected to the base Exoid instrument via a fluid cell. An automatic pressure system (APS) provides pressure and vacuum control to the instrument as well as displaying the applied system pressure in real time. The Exoid is then connected to a computer via a USB cable and interfaces with Izon's Exoid Control Suite software (ECS). Calibration particles are used as benchmarks for all nanoparticle measurements and allow the system to be used in the scientific industry to determine particle size, concentration and charge of many samples.

Description of Equipment Functionality

The equipment setup consists of a fluid cell, which has an upper fluid cell and a lower fluid cell; these upper and lower fluid cells contain either an Ag/AgCl paste or sintered electrode and are separated by a tunable nanopore. In the Exoid, a motorised mechanical actuator system controls the stretch applied to the nanopore, thus affecting the size of the nanopore opening. A bias voltage is applied across the electrodes in the upper and lower fluid cells.

Particles flow through the nanopore via convection and/or electrophoresis. The presence of a nanoparticle in the pore produces a resistive or conductive pulse in the background ionic current. This current pulse is detected by the inbuilt system electronics, and a real-time display of pulses is presented by the software. The software analyses the pulses and correlates them to particle characteristics.

5 VERIFICATION OF SHIPMENT

Bill of Goods

Attach the Purchase Order and Packing Slip/Invoice as appendices to this document to provide a source of comparison for shipped goods.

Document	Attached (Y/N)	Customer PO number or Izon SO Number	Signature	Initial	Date
Purchase Order					
Packing Slip (SO) or Invoice					

Shipment Details

Indicate whether the specified materials were included in the instrument shipment if applicable and whether the materials were received in good visible condition. Initial and date when completed. At this stage any particles included in the shipment should be removed and stored in an appropriate location at 4-8°C, this includes the two training kit particles found inside the Izon Training Kit.

System Component	Included in shipment?	In good visible condition? (If no, describe)	Initial	Date
Exoid Base Instrument				
Fluid Cell				
Reference Cell				
24 V Power Supply and Cable				
USB to USB C Cable				
Nanopores		See subsequent pages.	-	-
Calibration Particles		See subsequent pages.	-	-
qEV Columns		See subsequent pages.	-	-

Nanopores

For any Nanopores included in the purchase order, fill out the table below:

Nanopore Size (e.g. NP250)	Quantity	In good visible condition? (If no, describe)	Initial	Date

Calibration Particles

For any Calibration Particles included in the purchase order, fill out the table below. Calibration Particles must be stored at 4-8°C when not in use.

Calibration particle size	Batch ID	In good visible condition? (If no, describe)	Initial	Date

qEV Columns

For any qEV columns included in the purchase order, fill out the table below. qEV Columns must be stored at room temperature before use; refer to the qEV user manual for post-use storage instructions.

qEV size	Gel type	Quantity	In good visible condition? (If no, describe)	Initial	Date

Acceptance Criteria	Materials were received as specified and in good visible condition.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

6 HARDWARE SETUP

Refer to drawing document EX1-DR-002 to 003 Exoid IQ Procedure Reference Drawings for part terminology.

Exoid Base Instrument

When handling the Exoid, make sure to hold it by the body and NOT a moving part like the lid.

- Place the Exoid onto a stable and level laboratory bench.
- Make sure the power supply box is positioned away from fluids, in a location where it can be quickly and easily disconnected from the mains power. DO NOT cover.
- Ensure that the buttons near the top of the Exoid are facing the user.
- Connect the power lead to the 24 V power supply.
- Make sure the power is off at the wall and on the instrument before plugging the power lead into a earth grounded protected wall socket and connecting the cable from the 24 V power supply to the rear of the instrument.

7 PREPARING THE SOLUTIONS

Use the Izon Reagent Kit to prepare the following solutions:

7.1 MEASUREMENT ELECTROLYTE (ME)

Make up a fresh batch of ME weekly and filter 15 mL daily with a 0.22 µm syringe filter before use.

Step	Requirement	Complete?
a	Rinse a clean glass bottle with deionised (DI) water. DI water should be high quality with resistivity of approximately 18 MΩcm-1. Water should be filtered with a 0.22 µm syringe filter.	
b	Completely dissolve one PBS tablet in 200 mL of DI water.	
c	Add 600 µL of Wetting Solution Concentrate to the PBS solution and swirl gently to mix.	
d	Seal container and label, along with the date. Store at 4-8°C. Always allow solutions to warm up to room temperature before use.	

7.2 WETTING SOLUTION

Make up a fresh batch of Wetting Solution weekly and filter daily with a 0.22 µm syringe filter before use.

Step	Requirement	Complete?
a	Add 9.9 mL of ME to a 15 mL Falcon tube.	
b	Add 100 µL of Wetting Solution Concentrate.	
c	Label, along with the date, and store at 4-8°C.	

Reagent Kit (S/N)	
Total Volume of Measurement Electrolyte prepared (mL)	

Acceptance Criteria	Solutions are filtered into the Falcon tubes through a 0.22 µm filter.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

8 CALIBRATION PARTICLE PREPARATION

Background Information

Particle size and concentration are converted from a blockade magnitude (nA) and blockade rate (blockades per minute) into a diameter (nm) and concentration (particles per mL) using calibration particles of known diameter and concentration. Different calibration particles are used depending on the nanopore size selected. For this IQ procedure, particle details are as follows:

Catalogue Number	Analysis Range (nm)	Izon Calibration Particle	Target Particle Conc (/mL)
NP250	110-630	CPC200/400 or TKP200/Sol S	$2.0x10^9$

Calibration particles are supplied in concentrated form and should be diluted in the same electrolyte as the sample particles, to achieve the target concentration shown above.

Required Techniques

The SOP executor must have understanding and experience with Forward Pipetting Technique. Forward pipetting should be used in ALL sample preparation. For more information on pipetting techniques, please visit https://support.izon.com/pipetting-techniques

Great care should be taken during particle preparation – any errors in the dilution process will relate directly to an error in calculated particle concentration. Below are some tips for particle preparation:

- All particles must be diluted immediately before use. Forward pipetting should be used for sample preparation to give the most accurate dilutions and to avoid wastage.
- Take care to mix fluids homogeneously before and after dilution (larger particles will tend to sediment and can be seen on the bottom of the vial prior to mixing).
- Avoid transferring excess calibration particles on the outside of the pipette tip.
- Incorrect pipetting technique or using a non-calibrated pipette will affect the final concentration of the prepared sample.
- Use tips that are clean and do not have filters in them

Particle Preparation Checklist

Complete the following checklist to verify that calibration particles have been correctly prepared:

Step	Requirement			Complete?
a	Measurement Electrolyte has been freshly filtered through a 0.22 µm filter.			
b	Pipettes are all calibrated (if not, ensure that they are used at exactly the same settings for preparing the different samples).			
c	Pipette exactly 500 µL of filtered electrolyte into two 1.5 mL Eppendorf tubes and label each vial as "TS" and "CAL". Write the dilution factor of 1:51.			
d	Prepare calibration particles: – Vortex Training Particles (TKP-200) on medium speed for 15 seconds. Ensure no sediment can be seen. – Pipette exactly 10 µL of Training Particles into the vials labelled "CAL" – If using CPC200s use a 1:501 dilution			
e	Prepare sample particles: – Vortex Solution S (Training Sample) on medium speed for 15 seconds. Ensure no sediment can be seen. Pipette exactly 10 µL of Solution S into the vials labelled "TS" – If using CPC400s use a 1:501 dilution			
f	Vortex the diluted particle vials "CAL" and "TS" on medium speed for 15 seconds.			
g	Record the details of TKP200 and Sol S:			
	Particle Details	Mean Diameter (nm)	Concentration (Particles/mL)	
	TKP200 or CPC200			
	Solution S or CPC400			

Particle Preparation Verification

When Particle Preparation is complete, fill in the following sign-off box:

Task	Name	Signature	Date
Executed			
Reviewed			

9 SITE ACCEPTANCE TEST

9.1 COMPUTER SPECIFICATION REQUIREMENTS

In order to allow for a smooth user experience, the computer used to run the Izon ECS must adhere to the following minimum requirements:

Computer Description		Minimum Requirement	Requirement Met?
Serial Number		NA	-
Manufacturer		NA	-
Model Number		NA	-
Operating System		Windows 10 (64-bit). The Professional Edition is recommended.	
RAM		16GB RAM	
CPU		i7 processor	
GPU		Dedicated graphics processor and memory (1 GB). On board graphics is NOT ACCEPTABLE.	
Hard Drive Size		Hard drive with at least 50 GB free space.	
Number of USB Ports		At least one free USB port	
Location of Computer		NA	-

CAUTION Installation done on any other edition of the Operating System e.g. Windows Home Edition is an automatic FAIL. The entire installation MUST BE done on a system specified as above.

Acceptance Criteria	The computer meets the minimum requirements.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

9.2 INSTALLATION OF THE EXOID DATA SUITE (IDS)

CAUTION If this is a non-Part 11 compliant system, download the two software packages from: support.izon.com/how-can-i-get-the-latest-exoid-control-suite-software-release
DO NOT complete sections coloured pink and marked with an asterisk.

If this is a Part 11 compliant system, please contact Izon Support for the appropriate software. DO NOT use the non-part 11 compliant software downloads from the support portal. Make sure to complete sections coloured pink and marked with an asterisk.

Step	Requirement	Complete?
a	Depending on the requirements of the installation (part 11 compliance required, or not) follow the appropriate instruction above to obtain the software packages.	
b	Run the installer.	
c	A Wizard window will appear. The Wizard will guide you through the installation of the software.	
d	Click "Finish" once complete, do not restart the computer at this stage.	

9.3 INSTALLATION OF THE EXOID CONTROL SUITE (ECS)

Step	Requirement	Complete?
a	Run the installer.	
b	A Wizard window will appear. The Wizard will guide you through the installation of the software.	
c	Click "Finish" once complete. Restart the computer at this stage.	
d*	Assign Windows user groups to the appropriate users using the Administrator account. This validation protocol will require one Administrator, one user assigned to the Izon Manager group, and one user assigned to the Izon User group.	

Acceptance Criteria	The computer has been restarted after the install of both softwares, and they launch successfully.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

9.4 INSTALLATION OF THE EXOID SYSTEM

Step	Requirement	Complete?
a	Make sure the power switch on the Exoid is set to the off position, as indicated in the Exoid quick start guide BEFORE connecting the power cable to the instrument.	
b	Using the USB to USB C cable, connect the Exoid system to the computer. The computer should automatically go through the process of installing the device drivers. – If using a laptop, ensure that the power cable of the laptop is connected, and the power is turned on. – Upon completion, a confirmation popup will be displayed in the taskbar.	
c	Turn the instrument on using the power switch on the rear.	
d	Open the Exoid Control Suite software.	
e	The Exoid lighting will activate indicating a successful instrument installation, and the Exoid graphic in the software will display "Connected" below. (This may take up to a minute).	

Acceptance Criteria	The Exoid lighting activates and the instrument status is "Connected."	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

9.5 VERIFICATION OF FUNCTIONALITY

System Details

Computer Used	
ECS Version	
IDS Version	
Exoid Instrument Serial Number	
Measurement Electrolyte	
Nanopore Serial Number (NP250)	

Preparing the System

Step	Requirement	Complete?
a	Enter the investigation details, the investigation ID should be "Test File 1." The nanopore ID is located on the long arm of the nanopore. Select the correct nanopore type and electrolyte from the dropdown menus and select done.	
b	Prepare the Fluid Cell – Pipette 75 µL of filtered electrolyte into the lower fluid cell via the side access channels. Once the electrolyte extends across the fluid cell, remove and discard the fluid. – Leave the surface wet.	

Nanopore Setup

Step	Requirement	Complete?
a	Enter Nanopore Setup.	
b	Load a nanopore onto the system when prompted to do so. A correctly loaded nanopore is one where the serial number is facing upwards, and all arms are fitted snugly onto the stretcher teeth. Click done.	
c	The nanopore type should already be populated, click done.	
d	Nanopore serial number should already be populated, click done.	
e	Device moves to setup position of 47 mm stretch.	
f	Load wetting solution into the lower and upper fluid cells following the on-screen instructions, click done.	
g	Manually wet the nanopore following the on-screen instructions. Click done once wetting has been successfully completed.	
h	Once manual wetting is complete, the user will be prompted to perform a soak process. This should proceed without issue and display confirmation that the wetting process has completed. Click done.	
i	Follow the on screen instructions to exchange wetting solution for measurement electrolyte in the top and bottom fluid cells. This will involve de-stretching and re-stretching the nanopore.	
j	Check there are no bubbles in the lower fluid cell when prompted by the on-screen instructions.	
k	Select no for "is your sample biological."	
l	The system will establish a stable baseline current and perform a nanopore characterisation.	
m	Replace the electrolyte in the upper fluid cell with "CAL", click OK to begin calibrated nanopore characterisation.	
n	Successful calibration will be marked with a display message announcing what particle range is resolvable with the nanopore. Ensure this range covers 200 nm and 350 nm.	
o	Select OK and the software will return to the home screen.	

Acceptance Criteria	The baseline current is >20 nA with RMS noise <10 pA, and the nanopore is capable of measuring particles that are 200 nm and 350 nm in size.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

10 COMMISSIONING OF EQUIPMENT

Computer Specification Requirements

Successful completion of Section 9 constitutes the commissioning of equipment for release for the Operations Qualification. Section 9 is deemed complete when section results are in-line with Acceptance Criteria, as defined in each section.

When Site Acceptance Test verification is complete, fill in the following sign-off box:

Task	Name	Signature	Initial	Date	Pass / Fail
Executed					
Reviewed					

11 SYSTEM FUTURE MAINTENANCE

Rationale

It is required to verify that once this equipment is qualified it will be maintained to a standard that will not compromise its validated status (21 CFR Part 820.70).

11.1 CLEANING AND STERILISATION PROCEDURE

The Exoid is not designed for a wash-down environment. If working with materials that may constitute a biohazard, the instrument should be used inside an approved hood.

Component	Cleaning Task	Frequency	Sterilisation
Nanopore	DI water rinse of wetted parts.	After removal from base instrument.	70% ethanol - short term exposure.
Upper fluid cell	DI water rinse of wetted parts.	Between experiments, plus before fitting and after removal from base instrument.	70% ethanol - short term exposure.
Lower fluid cell	DI water rinse of wetted parts. 70% ethanol gentle wipe of connection pins.	Before fitting and after removal from base instrument.	70% ethanol - short term exposure.
Base Instrument	External wipe ONLY.	Only when contaminated. The Exoid system has NO ingress protection rating.	70% ethanol - short term exposure.
APS Nozzle	Remove and rinse or soak.	Once a week or when fluid is visible inside nozzle.	70% ethanol - short term exposure.
APS Tubing	Remove and rinse or soak.	When fluid is visible inside tubing	70% ethanol - short term exposure.

Components should be completely dried with compressed gas (preferable) or lint-free tissue before re-fitting to the system.

Complete drying is extremely important for the lower fluid cell. It is critical that no liquid enters the pin holes in the fitting for the lower fluid cell as it may cause major functional issues. Any liquid contact should be remedied immediately after occurrence by blow drying extremely well with compressed air.

11.2 PREVENTATIVE MAINTENANCE SCHEDULE

With the exception of regular cleaning after use the equipment does not require preventative maintenance by the user. Equipment can be returned to Izon for servicing or repair as required, at a cost.

11.3 PARTS REPLACEMENT SCHEDULE

System parts may be replaced as follows (refer to system assembly drawings). Contact Izon Support to diagnose system malfunction issues and to identify the root of the problem.

Drawing Ref.	Part Title	Replacement Schedule
EX1-IQ-003	Base Instrument	When malfunctioning.
	VCA PCB	When malfunctioning.
	APS Subassembly	When malfunctioning.
	PU Tube 2.5mm ID 4mm OD	When degraded (no longer airtight).
	Nozzle seal 3x1mm N70	When degraded (no longer airtight).
EX1-IQ-002	Fluid Cell Assembly	When malfunctioning.
	O Ring MR007x1	When degraded (no longer fluid tight).
QN1-IQ-902	Nanopore Assembly	As needed.

11.4 CALIBRATION SCHEDULE

Equipment Requiring Calibration	Frequency
Exoid stretch mechanism	Automatic each time the instrument is started up.
Automated Pressure System	Automatic each time the instrument is started up.
Nanopore	Immediately before or after the sample measurement is collected. Calibration is made using Izon calibration particles.
Micropipettes	Refer to recommendation made by supplier; this is typically performed annually.

Acceptance Criteria	Maintenance schedules are sufficiently rigorous to ensure the system's validation status is not compromised over time.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

12 SECURITY OF BACK-UP SOFTWARE

Rationale

If the operation of the equipment is controlled by the software, it is required in this protocol to verify that the backup copy of this software is available and that it is stored in a weather and fire proof area, remote to its area of use, and that access to it is controlled.

Test Method

Locate backup software and confirm storage and access conditions.

Acceptance Criteria	A backup software program must be stored in a secure weather and fire-proof area remote to area of use. Access to this software must be restricted to authorised personnel and documented.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

13 CONCLUSION/ COMPLETION OF IQ

List any discrepancies between anticipated/accepted and actual results of the previously described sections. Describe any corrective actions that are required to certify execution of the IQ.

Protocol Section	Further Action Required	Are there GMP implications?	Corrective Action Number

Circle the appropriate answer from the bold words below:

According to the information collected and reviewed as a result of this IQ process, it is our opinion that the required work **has / has not** been completed and satisfactory results **have / have not** been obtained, with the exception of those related to the following items on which corrective action is required:

Number of items requiring Corrective Action:

This IQ cannot be approved or permission to proceed to Operation Qualification execution given, if any of the outstanding Corrective Actions (CA) could compromise the company's cGMP procedures or standards.

- The number of outstanding CAs is: _____
- Do these CAs have cGMP implications: **YES/NO**

IF YES THEN THIS DOCUMENT CANNOT BE SIGNED OFF AS COMPLETED.

Signing this block below confirms that all variations and failures listed within this IQ have been accounted for in the IQ Report. This IQ has therefore been completed.

Installation Qualification Completion

Name	Title	Signature	Date

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