QN1-IQ-002 SOP AND VERIFICATION OF INSTALLATION QUALIFICATION FOR THE qNANO

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CONTENTS

1 / SCOPE

PURPOSE

This document provides and verifies the steps and information required to perform an Installation Qualification (IQ) for the qNano. The successful completion of this protocol will verify that this installation is compliant with the Company Quality Standard (ISO 13485) and 21 CFR Part 11 software regulations. This document should be executed any time an IQ is performed for a qNano. This document should be completed and signed by an Executor (typically an Izon staff member) and a Reviewer (a customer QA representative).

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

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
- 70% Ethanol
- 50 mL Falcon tubes
- Powder-free disposable gloves
- Water bath

DOCUMENTS

Confirm that the documents and drawings required to complete the IQ procedure are present and satisfactory (S) or unsatisfactory (US); and that the documents are located on the USB drive supplied with the instrument and where they will be stored as a hard copy. Compare the drawings in QN1-IQ-901 to 906 qNano 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
QN1-IQ-002	Verification of Installation Qualification Protocol for the qNano			
QN1-IQ-901 to 906	qNano IQ Procedure Reference Drawings			

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 vender 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, Ltd. 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 qNano instrument via a fluid cell. A variable pressure module (VPM) provides pressure and vacuum control to the instrument. The Pressure Reading Module (PM2) measures the applied system pressure in real-time. The qNano is then connected to a computer via a USB cable and interfaces with Izon's Control Suite Software (CSS). 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 Ag/AgCl electrodes and are separated by a tunable nanopore. In the qNano, a 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 Ag/AgCl 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 analyzes 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
qNano Base Instrument				
Pressure Reading Module				
VPM				
Fluid Cell				
Izon Training Kit				
Digital Callipers				
12 V Power Supply				
USB to USB Mini 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. While they are shipped at ambient temperature, qEV Columns must be stored at 4-8°C when not in use for longevity purposes.

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 QN1-DR-901 to 906 qNano IQ Procedure Reference Drawings for part terminology.

qNANO BASE INSTRUMENT

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

- Place the qNano onto the recessed area of the VPM base plate.
- Remove the fluid cell unit from the qNano by removing the fluid cell cap, before gently pulling the lower fluid cell up while holding onto the base.
- If the lower fluid cell is not connected to the qNano via an SMA cable, then screw the lower fluid cell into the SMA connector inside the top of the qNano.
- Push the lower fluid cell back into the base instrument until it clicks into place.

VPM

- With a knurled collar fitted onto the piece of plain tubing, push the tube firmly onto the barbed fitting located on the top of the VPM and tighten the knurled collar into position by hand. DO NOT use tools to tighten the collar.
- Push another knurled collar onto the same piece of tubing and connect the other end to the barbed fitting on the side on the PM2. Again, tighten the knurled collar by hand.
- Take the tubing with the nozzle on the end and, with a knurled collar fitted, push the tubing onto the barb located on the top of the PM2. Direct the nozzle end of the tubing away from the working area around the fluid cell, so that it does not get in the way when disconnected, and hand tighten the collar.

7 / PREPARING THE SOLUTIONS

Use the Izon Reagent kit to prepare the following solutions:

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.	

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)	
Volume of 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 / SITE ACCEPTANCE TEST

COMPUTER SPECIFICATION REQUIREMENTS

In order to allow for a smooth user experience, the computer used to run the Izon CSS must adhere to the MINIMUM requirements outlined in the table below.

Computer Description		Minimum Requirement	Requirement Met?
Serial Number		NA	-
Manufacturer		NA	-
Model Number		NA	
Operating System		Windows (7 onwards) Professional Edition (64-bit) Operating System.	
RAM		8GB RAM	
CPU		i7 processor	
GPU		Dedicated graphics processor and memory (1 GB). Intel HD Graphics 620 or higher on an i7 processor is acceptable.	
Hard Drive Size		Hard drive with at least 50 GB free space.	
Number of USB Ports		At least one USB port	
Location of Computer		NA	-

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		

INSTALLATION OF THE CONTROL SUITE SOFTWARE (CSS)

Step	Requirement	Complete?
a	Insert the Izon USB drive into the computer.	
b	Run the file "Install.exe".	
c	A Wizard window will appear. The Wizard will guide you through the installation of the software.	
d	Click "Finish" once complete.	
e	Initially, the Izon splash screen will be displayed, this will be followed by the full software window and Administrator Login window. The customer QA representative should set up the login details for administrator access. THESE DETAILS CANNOT BE CHANGED AT A LATER DATE. If the Welcome screen appears, the software has installed successfully.	

Acceptance Criteria	The software opens and the welcome screen is displayed.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

INSTALLATION OF THE qNANO SYSTEM

Step	Requirement	Complete?
a	Connect the power cable to the power supply by plugging the DC power supply into an earthed power socket, turn the power on at the wall before plugging the power lead into the appropriate socket on the PM2.	
b	The power indicator light beside the power socket on the PM2 will turn on.	
c	Using the USB to mini USB cable, connect the qNano system to the computer. The computer will automatically go through the process of installing the device software. – 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.	
d	Open the Control Suite Software and enter the appropriate details in the Login window.	
e	Click on the Classic Capture tab. The home screen will be replaced by a Signal Trace window.	
f	Turn the voltage on by clicking the “Turn On” icon in the upper ribbon. A yellow line will be visible at 0±1 nA in the signal trace window. The yellow line in the signal trace window indicates successful installation of the base instrument.	

Acceptance Criteria	There is a yellow line in the signal trace window of 0±1 nA	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

VERIFICATION OF FUNCTIONALITY

System Details

Computer Used	
CSS Version	
Base Instrument Serial Number	
Fluid Cell Serial Number	
Measurement Electrolyte	
Nanopore Serial Number (NP250)	

Preparing the System

Step	Requirement	Complete?
a	Open Izon Control Suite Software and enter login details	
b	Click on the Classic Capture tab. The Signal Trace window will appear.	
c	Prepare the Fluid Cell – Pipette 75 µL of the 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.	
d	Fit and calibrate nanopore stretch – Fit the nanopore to the qNano with the serial number upwards. – Decrease the stretch mechanism so that it is easy to pull all four arms of the the nanopore over the teeth. – Use the digital calliper to measure the stretch across the outside of the teeth.	
e	When the callipers read approximately 45 mm (±0.l mm) enter the stretch value (e.g 44.95) into the Applied Stretch box and press enter or click “Calibrate”.	

Wetting the Nanopore

Step	Requirement	Complete?
a	Stretch nanopore to 47 mm and load 75 µl of wetting solution in the lower fluid cell.	
b	Re-fit the upper fluid cell and re-place the fluid cell cap.	
c	Load 35 µL of wetting solution into the upper fluid cell and apply >0.1 V after clicking "Turn On"	
d	Ensure that the VPM is in standard pressure mode (no red visible under the knob on the top of the VPM). Check that the pressure "PRE" scale is set to zero.	
e	Connect the PM2 nozzle to the upper fluid cell	
f	Close the vent valve and apply a maximum pressure (20 mbar) for at least 4-5 minutes.	
g	After 4-5 mins. take the pressure off by opening the vent valve and disconnecting the PM2 nozzle. Verify that the aperture is wetted by checking for a stable baseline current.	
h	If not. first effectively apply a pressure using the Izon PAD up to 10x (NB remove the shielding cap to complete this step). If there is still no current. click the fluid cell cap by gently pushing down on the nanopore arms and twisting it around.	
i	Take off and dry the upper fluid cell. Remove the wetting solution from the bottom fluid cell.	

Establishing a Baseline Current with ME

Step	Requirement	Complete?
a	Add 75 µL of ME to the lower fluid cell ensuring that no bubbles are trapped beneath the central nanopore as well as spilling fluid outside of the channels. If air bubbles are present. remove the fluid and replace with a fresh aliquot.	
b	Re-fit the upper fluid cell and cap and pipette 35 µL of ME into the upper fluid cell.	
c	A yellow line (baseline current) greater than 20 nA with RMS noise of ~10 pA should be visible. Signal trace largely horizontal (guideline <1% drift per minute). If baseline current is not visible, repeat the Wetting Procedure.	
d	Once there is a stable current. proceed to the next stage of instrument preparation. If the baseline current is greater than 20 nA with RMS noise less than 10 pA, the system is ready for use.	

Acceptance Criteria	The baseline current is >20 nA with RMS noise <10 pA.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

9 / COMMISSIONING OF EQUIPMENT

COMPUTER SPECIFICATION REQUIREMENTS

Successful completion of Section 8 constitutes the commissioning of equipment for release for the Operations Qualification. Section 8 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					

10 / VERIFICATION

The following tests in accordance with 21 CFR are **not applicable** to the qNano but are included in this document to verify that the customer agrees that they are not needed.

Test	Required by 21 CFR Part #	Rationale	Verified?
Electrical Conformance Verification	Part 820.70	It is required to verify that all electrical equipment is installed in accordance with cGMP requirements and follows good electrical practices and procedures.	
Sensor Calibration Verification	Part 211.65	It is required to verify that all sensors used on and with this equipment are calibrated and that calibration certificates are available to verify this.	
Critical Area Material Verification	-	It is required in this protocol to verify that all product contact parts are manufactured from material appropriate to the environment.	
Verification of Lubricants	Part 178.3570 Part 178.3620 Part 211.65 Part 174.5 Part 174.6	The FDA has issued guidance documents for the selection of lubricants that are to be used in the pharmaceutical industry, it is required in this protocol to verify that the lubricants to be used in the maintenance and use of this equipment conform to these requirements.	
Analog Address Verification	-	It is required in this protocol to verify that all analog addresses are as specified in the system drawing and or specification.	
Digital I/0 Verification	-	It is required in this protocol to verify that all digital addresses are as specified in the system drawing and or specification.	

Acceptance Criteria	The customer agrees that the above tests are not applicable to the qNano.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

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).

CLEANING AND STERILIZATION PROCEDURE

The qNano 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	Sterilization
Nanopore	DI water rinse of wetted parts.	Before fitting and 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.	Before fitting and after removal from base instrument.	70% ethanol - short term exposure.
Base Instrument	External wipe ONLY.	Only when contaminated. The qNano system has NO ingress protection rating.	70% ethanol - short term exposure.
VPM Nozzle	Remove and rinse or soak.	Once a week or when fluid is visible inside nozzle.	70% ethanol - short term exposure.
VPM 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.

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.

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
QN1-IQ-904	Base Instrument Subassembly	When malfunctioning.
	SMA Cable	When malfunctioning.
	Enigma PCB	When malfunctioning.
QN1-IQ-903	Fluid Cell Assembly	When malfunctioning.
	O Ring MR007x1	When degraded (no longer fluid tight).
QN1-IQ-905	VPM Subassembly	When malfunctioning.
	Seal - Vent Valve Size 010 N70	When degraded (no longer airtight).
	PU Tube 2.5mm ID 4mm OD	When degraded (no longer airtight).
	Nozzle seal 3x1mm N70	When degraded (no longer airtight).
QN1-IQ-902	Nanopore Assembly	As needed.

CALIBRATION SCHEDULE

Equipment Requiring Calibration	Frequency
qNano stretch mechanism	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 bolded 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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