EX1-OQ-001 SOP AND VERIFICATION OF OPERATIONAL QUALIFICATION FOR THE EXOID

IZON

CONTENTS

1 SCOPE

1.1 PURPOSE

This Operational Qualification (OQ) for the Exoid defines the responsibilities and the procedures that must be complied with to ensure that the OQ of this equipment is successfully completed. It also outlines the materials and tasks required to perform the OQ procedure.

Prior to this procedure being carried out the Installation Qualification for the Exoid must have already been performed.

The successful completion of this protocol verifies that the operational performance of this equipment complies with the relevant guidelines and rules contained within the Company Quality Standard (ISO 13485) and 21 CFR part 11 software regulations where relevant. Sections marked with an asterisk (*) do not need to be completed if 21 CFR Part 11 compliance is NOT required.

1.2 OBJECTIVES

To ensure that:

- The equipment functionality is in accordance with requirements of the Functional Specification.
- The equipment operates in a manner safe to operational staff.
- The equipment operates in manner safe to the product.
- That there are documented procedures covering all aspects of the use of this equipment.

2 REQUIRED MATERIALS AND DOCUMENTS

2.1 MATERIALS

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

- Computer (must meet minimum specifications) with Exoid Control Suite Software and Izon Data Suite installed and verified.
- Calibrated micropipettes - 1 µL to 1 mL
- A vortex mixer
- Filtered deionised water (for cleaning)
- Compressed nitrogen for drying. Alternatively, clean compressed air spray is also acceptable
- Lint-free tissue for drying
- Standing racks for tubes (optional)
- Powder-free disposable gloves
- Refrigerator

2.2 DOCUMENTS

Confirm that these documents required to complete the OQ procedure are present. They will be stored in the same location as outlined for the documents in EX1-IQ-001.

Document Reference	Document Title	Present?	Initial	Date
EX1-IQ-001	Verification of IQ Protocol for the Exoid (COMPLETED)			
EX1-OQ-001	Standard Protocol and Verification of OQ for the Exoid			
EX1-OQ-002*	21 CFR Part 11 Software Regulation Guidelines for the Exoid			

2.3 DOCUMENTATION ACCEPTABILITY VERIFICATION

If the documents meet the Acceptance Criteria, fill out below

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.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

3 IDENTIFICATION OF PERSONNEL PERFORMING OQ

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

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

4 PARTICLE SIZE AND CONCENTRATION ANALYSIS

4.1 RECORD A CALIBRATION FILE

Complete the following checklist to verify that the calibration file has been correctly recorded:

Step	Requirement	Complete?
a	Select "Start Analysis" and select "Size and concentration."	
b	A baseline (magenta line) current with <10 RMS noise is visible in the "Signal Trace" area.	
c	Use the slider bar to select a stretch that will allow a target analysis size range that encapsulates 200 nm and 350 nm particles.	
d	Select yes for "Would you like to run a calibration at this stage?"	
e	Enter the calibration particle details: • Calibration ID: TKP200 (unless using alternative particles) • Size: As specified on stock vial • Raw Concentration: As specified on stock vial • Dilution: 51 (unless using alternative particles)	
f	Click done to proceed.	
g	When the system is "Ready to (pre)calibrate," change the applied voltage so that the current is approximately 80-140 nA.	
h	Change the applied pressure to be at least 300 Pa. Aim for a particle rate of 500-1500 particles/min.	
i	Record the below values: • Nanopore Stretch (mm): • Voltage (V): • Average Baseline Current (nA): • Average RMS Noise (pA):	
j	Start analysis, the system will automatically apply three pressure steps and take recordings for each one. The ECS will automatically require 500 blockades to be measured before proceeding. Confirm this is correct.	
k	Calibration completes successfully. Click done.	
l	Clean the system following the on-screen instructions. Pore is cleaned successfully.	

4.2 RECORD A SAMPLE FILE

Complete the following checklist to verify that a sample file has been correctly recorded and calibrated:

Step	Requirement	Complete?
a	Enter the sample details. Sample name is "TS" and dilution should be 51 (unless using alternative particles).	
b	Replace the liquid in the upper fluid cell with 35 µL of the diluted Training Sample "TS" by following the on screen instructions.	
c	Ensure that the baseline current and RMS noise levels have not changed significantly (within 5%) from the calibration particles' run. • Nanopore Stretch (mm): • Voltage (V): • Average Baseline Current (nA): • Average RMS Noise (pA):	
d	Refer to the Relative Particle Size plot. The blockades should be visible. If not, refresh the sample in the upper cell.	
e	Choose a Maximum Blockade Count from the dropdown menu.	
f	Start analysis, the system will automatically apply three pressure steps and take recordings for each one. The ECS will require the number of blockades selected in the previous step to be measured before proceeding. Confirm this is correct.	
g	Sample recording completes successfully. Click done.	

4.3 PROCESS DATA

Complete the following checklist to verify that all recorded files have been correctly processed and calibrated:

Step	Requirement	Complete?
a	Open the IDS.	
b	Open the data files by selecting Open Data Files and navigating to the appropriate folder within the "Exoid Data" folder.	
c*	For Part 11 compliant systems the "Exoid Data" folder must be a controlled location, regulated by company IT policy, it can be found in the Windows File explorer on the default system drive (usually C:).	
d	Process the files.	
e	Use the three sample files and the three calibration files to perform a "Multi-Point Concentration" calibration. All "TS" files now display size in nm in the data plots and reports.	
f	Review the measurement. In order for sample particle size and concentration to be correctly calculated using calibration particles: • The settings (stretch and voltage) must not be changed between both recordings. • Baseline current between calibration and sample recording should be within 5%. • Both calibration and sample particles must have a blockade magnitude sufficiently larger than the RMS noise. • A linear rate plot is achieved.	
g	Confirm calculated size meets acceptance criteria: Given Mean Diameter (GMD) x 0.1 = Allowable Deviation (AD) _____ x 0.1 = _____ GMD – AD < Calibrated Mean Diameter < GMD + AD _____ < _____ < _____	
h	Confirm calculated concentration meets acceptance criteria: Given Concentration (GC) x 0.25 = Allowable Deviation (AD) _____ x 0.25 = _____ GC – AD < Calibrated Concentration < GC + AD _____ < _____ < _____	

Acceptance Criteria	• Solution S (Training Sample), "TS" particle size distribution histogram shows an approximate normal distribution. • The calibrated MEAN diameter of Training Sample particles is within ±10% of the value shown on the label. • The calibrated Solution S (Training Sample), "TS" particle concentration is within ±25% of the value shown on the label.	
Result satisfies AC? (Y/N)		Executor Initial/Date: Reviewer Initial/Date:
Notes		

5 NANOPORE CLEANING

At the end of an experiment it is critical to wash out the pore before removal of the pore from the Exoid instrument. Removal of the pore with electrolyte and salts within it will shorten its lifespan. Salt crystals will form within the pore often rendering it impossible to wet or with reduced resolving capability when next used.

Complete the following checklist to verify that the cleaning protocol has been performed correctly:

Step	Requirement	Complete?
a	Clean the system following the on-screen instructions. Pore is cleaned successfully and current is <5 nA.	
b	The cleaning process completes.	
c	Take nanopore off, wash with DI water, and dry.	
d	Rinse the fluid cells with DI water and dry with a lint-free tissue followed by compressed gas.	

Acceptance Criteria	The baseline current drops to <5 nA.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

6 21 CFR PART 11 SOFTWARE REGULATION*

CAUTION This section is not required for a non Part 11 installation, skip this section unless you require a Part 11 compliant system.

Work through and approve EX1-OQ-002 21 CFR Part 11 Software Regulation Guidelines for the Exoid.

Acceptance Criteria	The Exoid Control Suite and Izon Data Suite softwares pass the tests laid out in EX1-OQ-002.	
Result satisfies AC? (Y/N)		Executor Initial/Date:
		Reviewer Initial/Date:
Notes		

7 CONCLUSION / COMPLETION OF OQ

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 OQ.

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 OQ process, it is our opinion that the required work **has been / has not been** completed and satisfactory results **have been / 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 **OQ** cannot be approved 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 OQ have been accounted for in the OQ Report. This OQ has therefore been completed.

7.1 OPERATIONAL QUALIFICATION COMPLETION

Name	Title	Signature	Date

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