PROTOCOL

FOR

CLEAN EQUIPMENT

HOLD TIME STUDY VALIDATION

(ONCOLOGY BLOCK)

PRODUCT NAME	
BATCH No:	

 PHARMA DEVILS	PROTOCOL FOR CLEAN EQUIPMENT HOLD TIME STUDY VALIDATION (ONCOLOGY BLOCK)	PROTOCOL No.:

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1.0 PRE-APPROVAL:

Signing of approval page of this document indicates the Clean equipment Hold Time Study approach described in this document. If any modification approach becomes necessary, a revision through change control shall be prepared, checked and approved. This document cannot be executed unless approved.

Prepared By	Department	Designation	Sign & Date

Reviewed By	Department	Designation	Sign & Date

Approved By	Department	Designation	Sign & Date

2.0 OBJECTIVE:

The objective of this protocol is to generate back up data to demonstrate the clean equipment hold time after cleaning and effectiveness of established cleaning procedures after completion of hold time.

3.0 SCOPE:

This protocol is applicable to perform to establish the clean equipment hold and evaluate the effectiveness of established cleaning procedures after completion of hold time.

4.0 RESPONSIBILITY:

Department/ Function	Responsibility
Validation group	Preparation of study protocol and review of study report.
Quality Control	Review of the protocol, and sampling as per the sampling plan provided in the protocol and analysis of the samples collected and sharing of analytical results to QA for report compilation.
Production	Review the protocol/ report.
QA	Review & Approval of study protocol/ report and execution of the study protocol, by collecting the samples as per the protocol.

5.0 PRE-REQUSITE:

5.1 Ensure the training is completed to all the executors involved in the study.

5.2 Ensure that the Validation or Calibration status of the equipments involved in the study.

6.0 SAFETY PRECAUTIONS:

6.1 Safety aspects while operation of equipment and process shall be ensured.

7.0 CLEANING PROCEDURE:

As per the standard cleaning procedures (SOP).

8.0 LEAN EQUIPMENT HOLD TIME STRATEGY:

Following are the lines to be performed for clean hold time study

S.No.	Line	Type of presentation	Rationale
1.	1	Vial	As the process equipments are similar for all the products

9.0 PROCESS DESCRIPTION:

9.1 Facility is having the adequately commissioned and qualified lines to manufacture liquid sterile drug products in vials containers. The bulk product is manufactured in compounding area C-grade and filling takes place in B-grade area. In this having a common compounding process flow, manufacturing of batch take place in a manufacturing vessel followed by the primary filtration into a Filtration vessel and filling with the secondary filtration into a filling area.

10.0 VALIDATION REQUIREMENTS & OBSERVATIONS:

10.1 **Procedure:**

- After completion of the batch processing performing the cleaning the equipment with the established cleaning procedures.
- After completion of cleaning process of respective equipment, the cleaned equipment shall be visually verified for cleanliness and shall be rinsed with defined quantities.
- The samples shall be collected after the cleaning, from Manufacturing vessel, Filtration vessel, buffer tank, filling pump & nozzle.
- Carryout the swab sample & rinse sample for all the locations as mentioned in point no 10.3 & 10.5.
- After performing the sampling, hold the equipments for next 36hours.
- Perform the swab sampling at an interval of 0, 16, 24, 30 & 36hours.
- At the 36hours after performing the swab sampling, take the rinse sample and sent it for QC.
- The rinse samples shall be tested for Conductivity, pH, BET & Bioburden.
- The swab sample shall be tested for Bioburden.
- Initial swab & rinse results [0^{th} hour] and final swab & rinse [36^{th} hour] shall be compared.
- A summary & conclusion shall be drawn based on the outcome of the study.

10.2 **Sampling procedure for rinse sample:**

- Perform visual inspection of the cleaned equipments and ensure that the equipment is visually clean before sample collection.

Equipment	Volume of WFI for rinsing
Manufacturing Vessel	5 % of vessel working capacity
Filtration Vessel	5 % of vessel working capacity
Buffer Tank	1.0 L
Filling Pump	1.0 L
Filling manifold	1.0 L
Nozzle	1.0 L

- Collect the rinse samples and send it for testing pH, conductivity, bioburden & BET

Test	Sample quantity
pH	100mL
Conductivity	50mL
Bioburden	100 mL
BET	20mL

10.3 **Sampling Locations & Test for rinse sample:**

S.No.	Name of Equipment	Rinse Quantity	Sampling location	Sample ID No.	Test
1	Manufacturing Vessel	*	Outlet of the vessel		pH
					Conductivity
					Bioburden
					BET
2	Filtration Vessel	*	Outlet of the vessel		pH
					Conductivity
					Bioburden
					BET
3	Filling Nozzles	1 L	Outlet of the		pH

S.No.	Name of Equipment	Rinse Quantity	Sampling location	Sample ID No.	Test
			nozzle		Conductivity
					Bioburden
					BET
4	Buffer Tank	1 L	Outlet of the buffer tank		pH
					Conductivity
					Bioburden
					BET
5	Filling pump	1 L	Outlet of the pump		pH
					Conductivity
					Bioburden
					BET

*** - 5 % of vessel working capacity**

Note: pH & conductivity results are only for information purpose.

10.4 **Sampling procedure for swab sample:**

- This method allows collection of the samples directly from the cleaned equipment/system surfaces.
- Immediately after wetting the swab stick, swab the specific equipment surface area as per Figure.1 The surface area to be swabbed is 25 cm2 as per Figure.2 and if the area is less than the specified surface whole surface to be swabbed.

Figure – 1[A template for surface sampling]

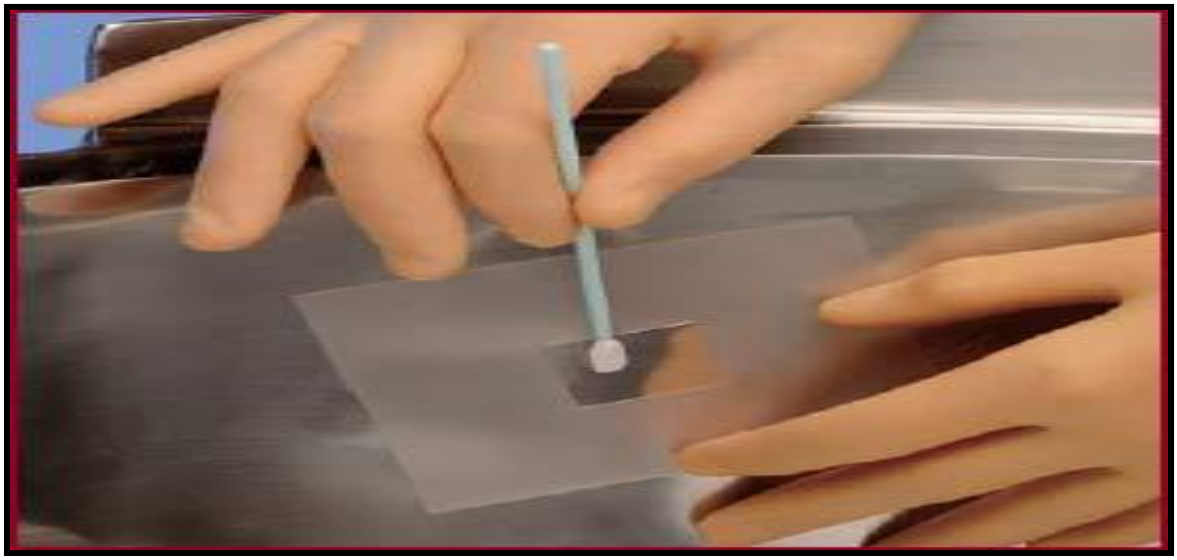
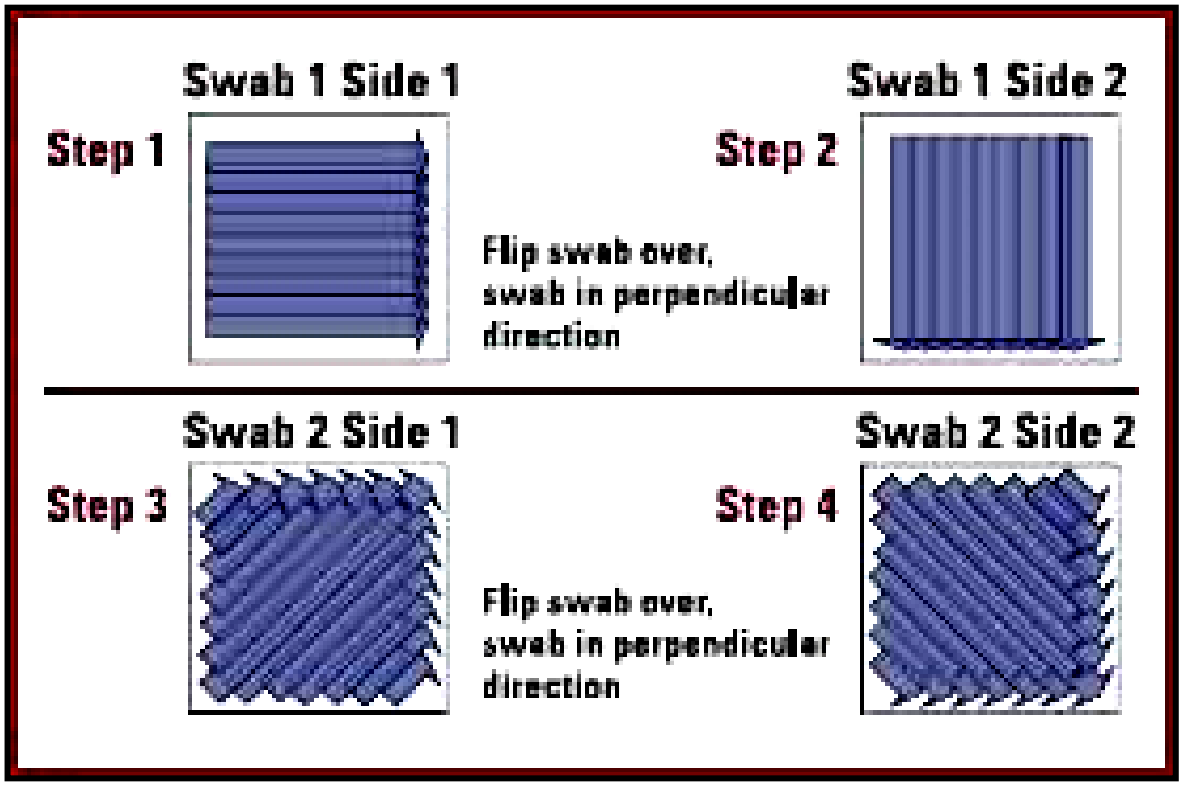


Figure – 2



- Incase of surface area where swab sampling for 25 cm^2 is not possible following approach shall be followed; Swab the surface such that it will cover the maximum possible accessible area.
- Test the swab sample for the bio-burden as per respective SOP.

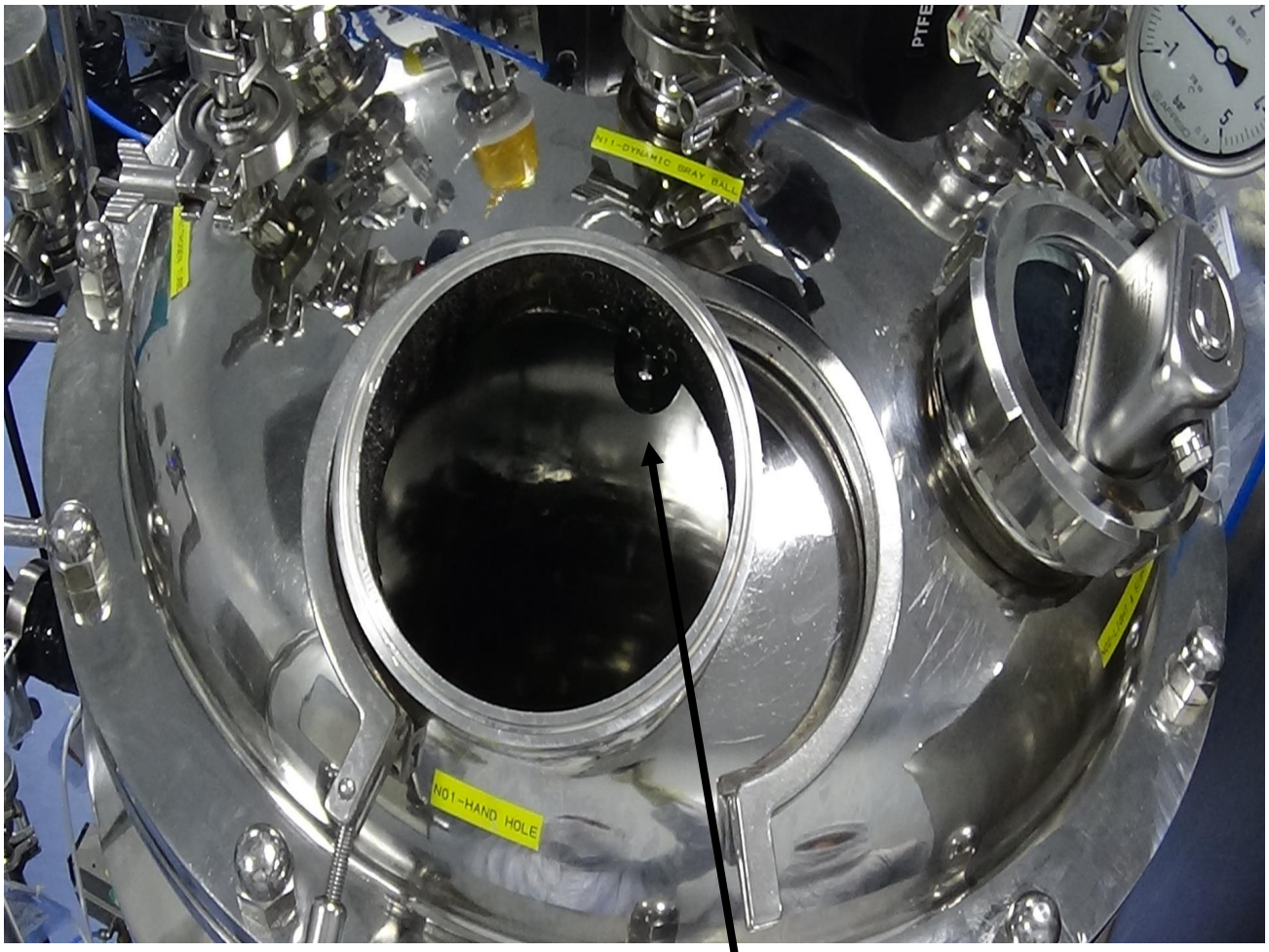
10.5 **Sampling Locations for swab sample:**

S.No.	Name of Equipment	Sampling Location	Sample ID No.	Snap No.
1.	**Manufacturing Vessel**	Inner surface of vessel		01
		Inside walls of material adding port		02
		Inside of Sampling valve		03
		Outlet of the vessel		04
2.	**Filtration Vessel**	Inner surface of vessel		05
		Inside walls of material adding port		06
		Inside of Sampling valve		07
		Outlet of the vessel		08
3.	**Buffer Tank**	Inner surface of the buffer tank		09
		Outlet of the buffer tank		10
4.	**Filling Pumps**	Inner surface of pump		11
5.	**Filling Nozzles**	Outlet of the Nozzle		12

10.6 **Snapshot of the above locations is listed below for reference:**

- **MANUFACTURING VESSEL:**

Snap No-01 (Inner Surface of Vessel)

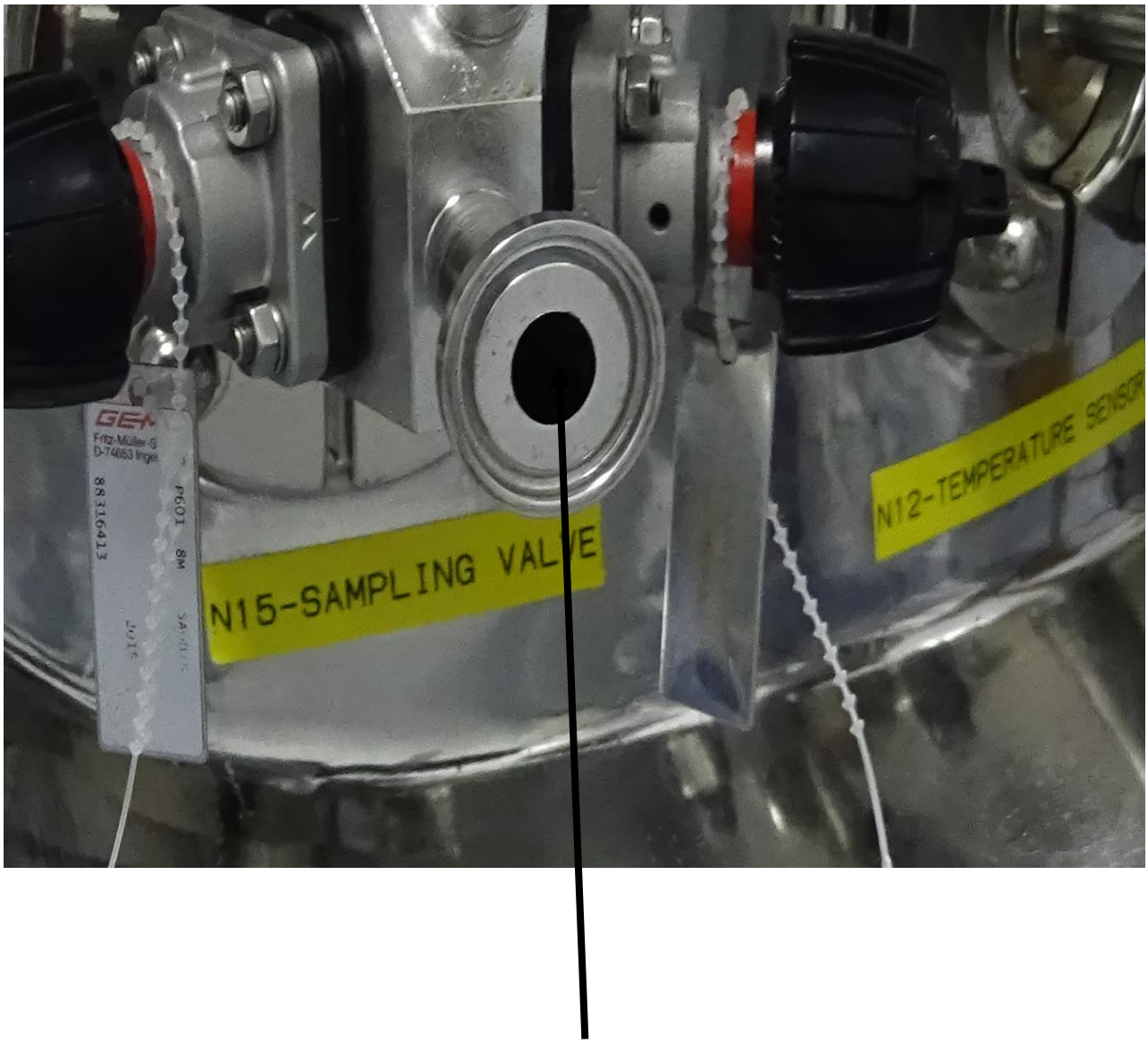


Sampling Location

Snap No-02 (Inside walls of material adding port):

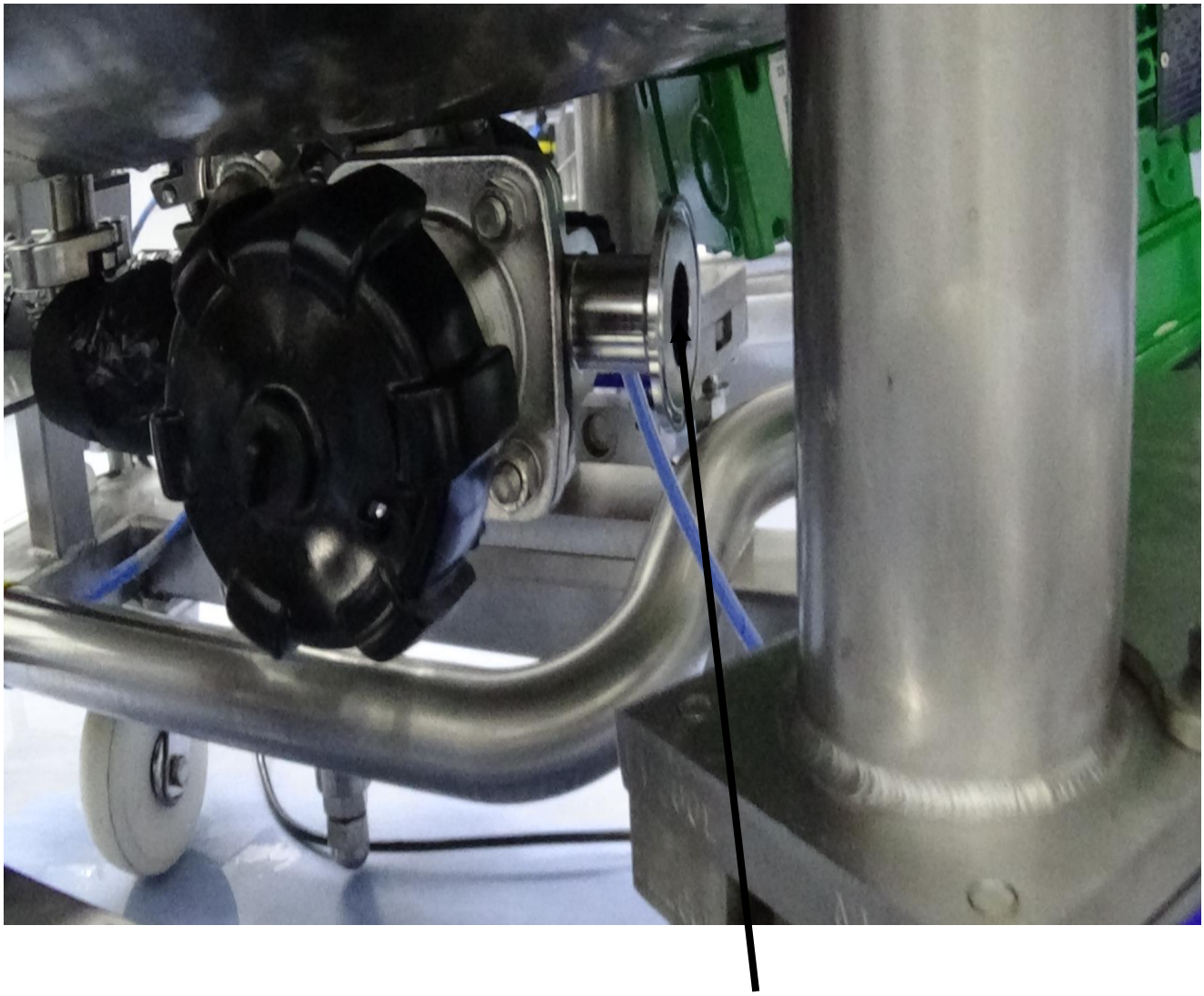
Sampling Location

Snap No-03 (Sampling valve):



Sampling Location

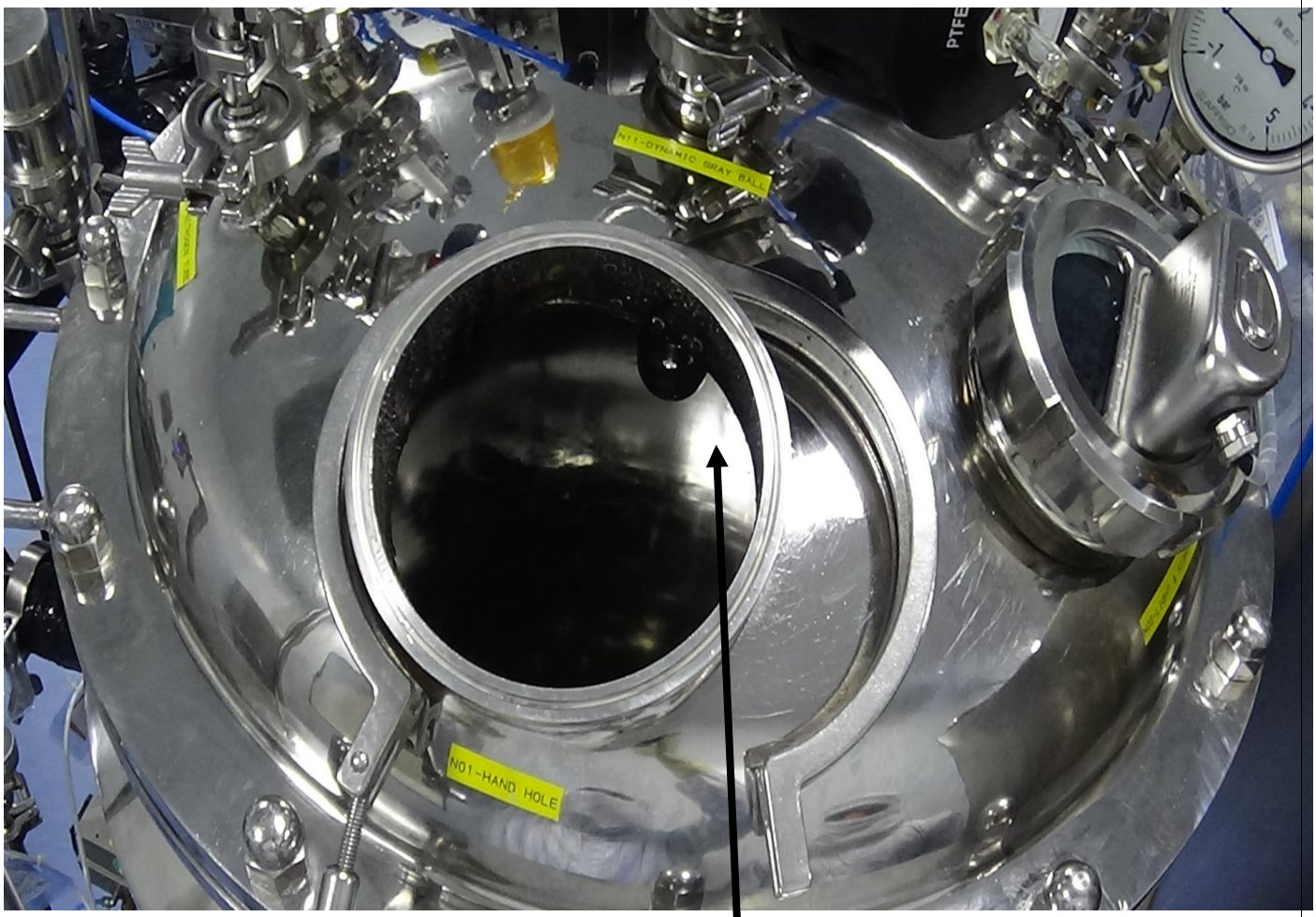
Snap No-04 (Outlet of the vessel)



Sampling Location

- **FILTRATION VESSEL:**

Snap No-05 (Inner Surface of Vessel)

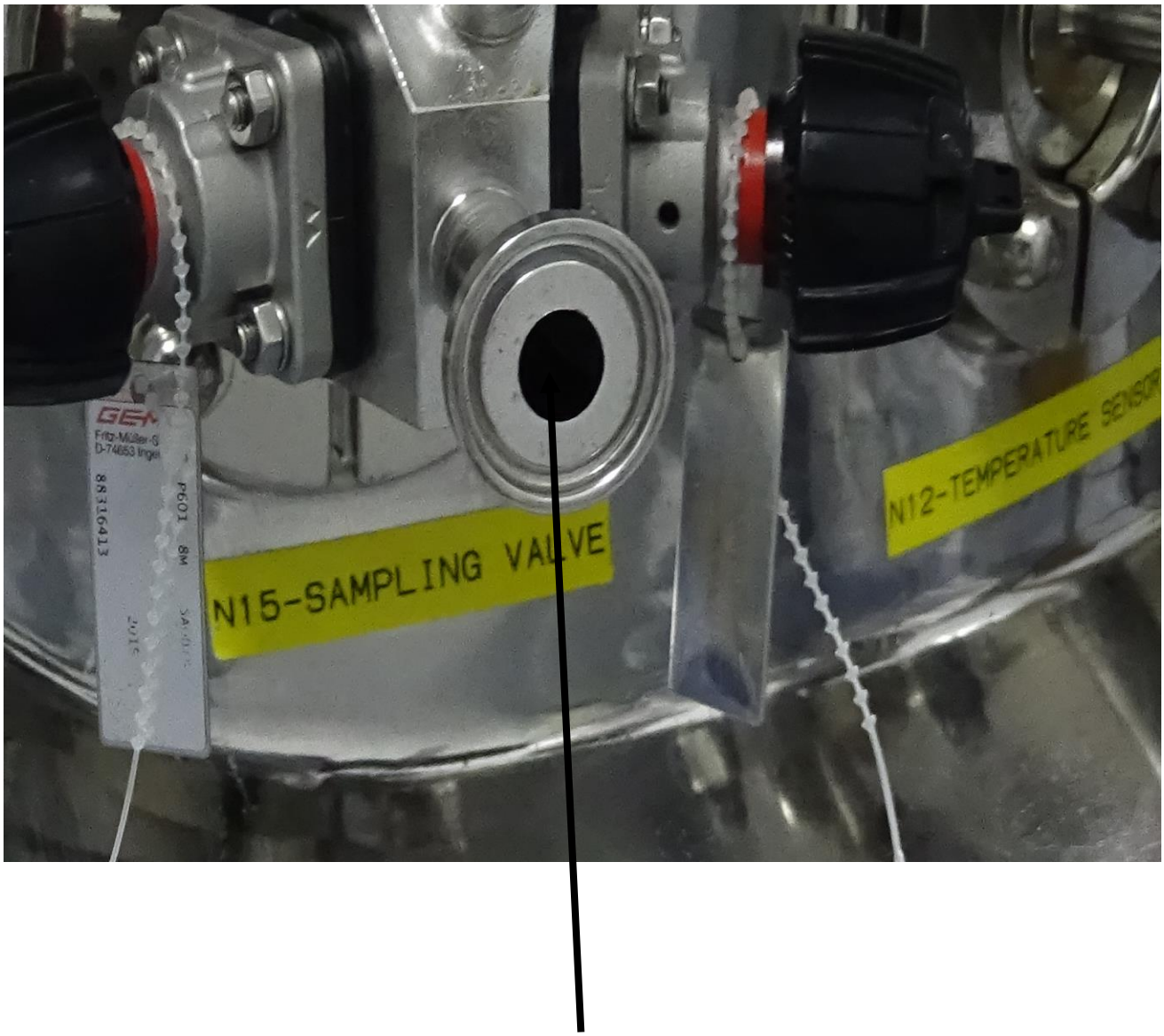


Sampling Location

Snap No-06 (Inside walls of material adding port)

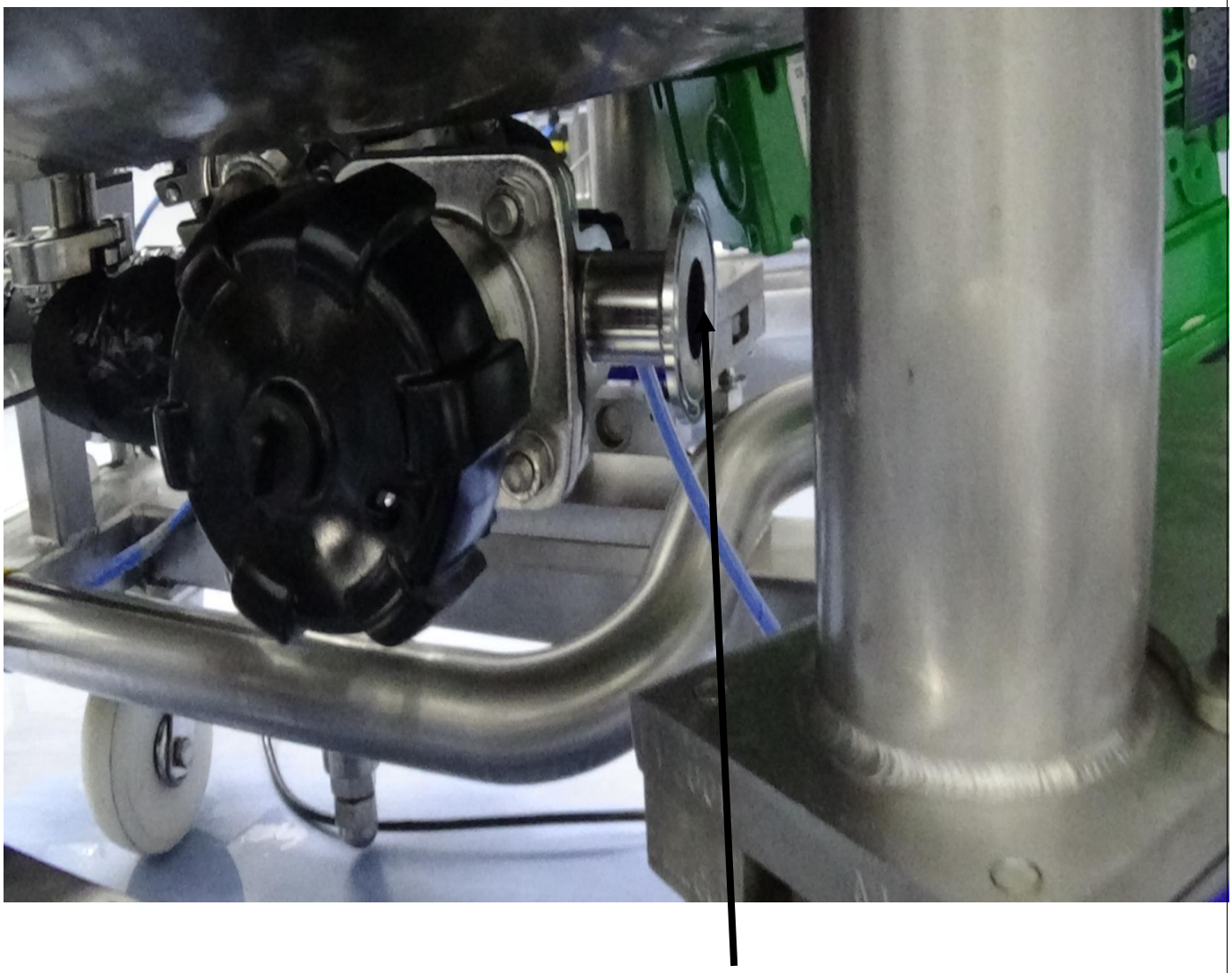
Sampling Location

Snap No-07 (Sampling valve)



Sampling Location

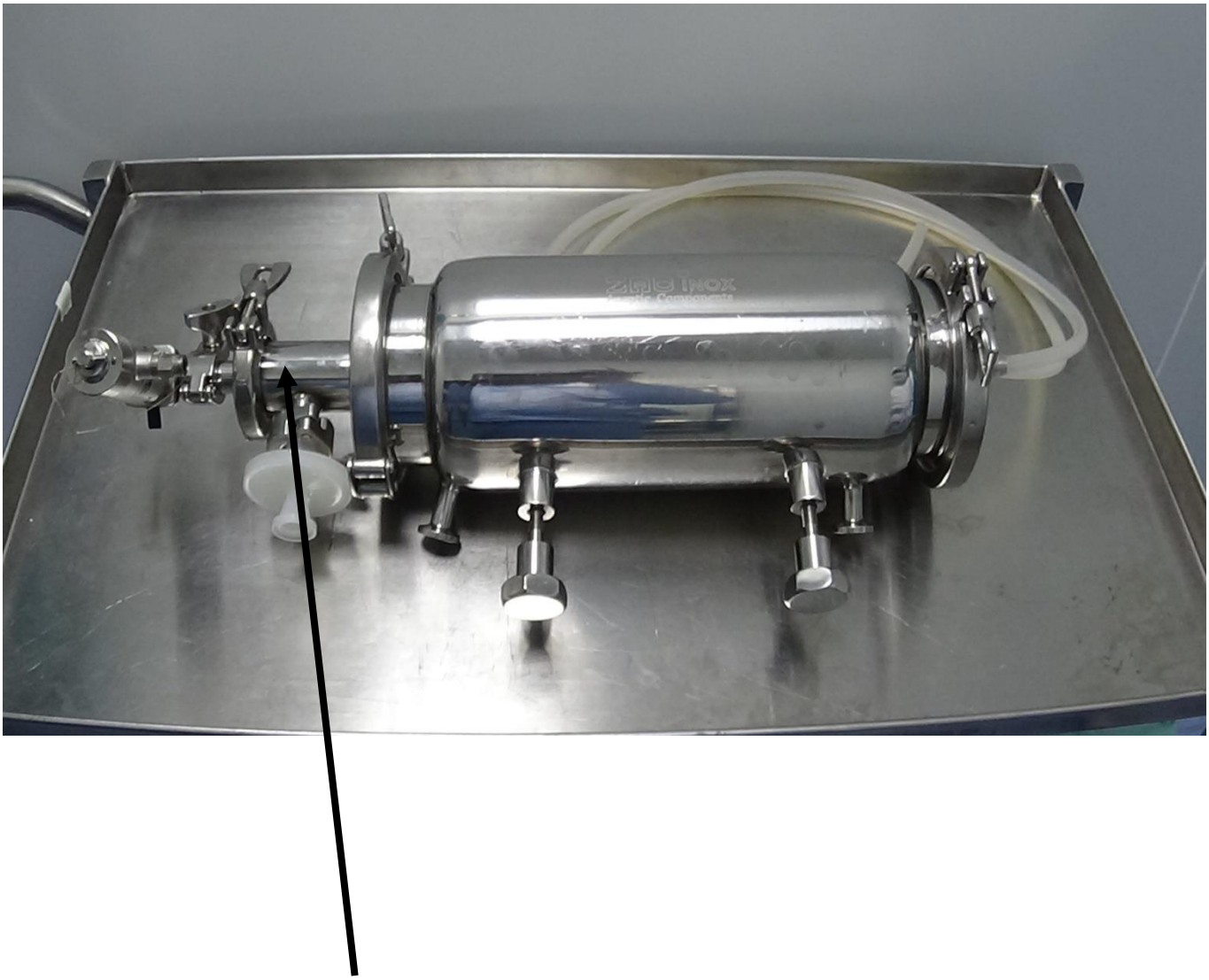
Snap No-08 (Outlet of the vessel)



Sampling Location

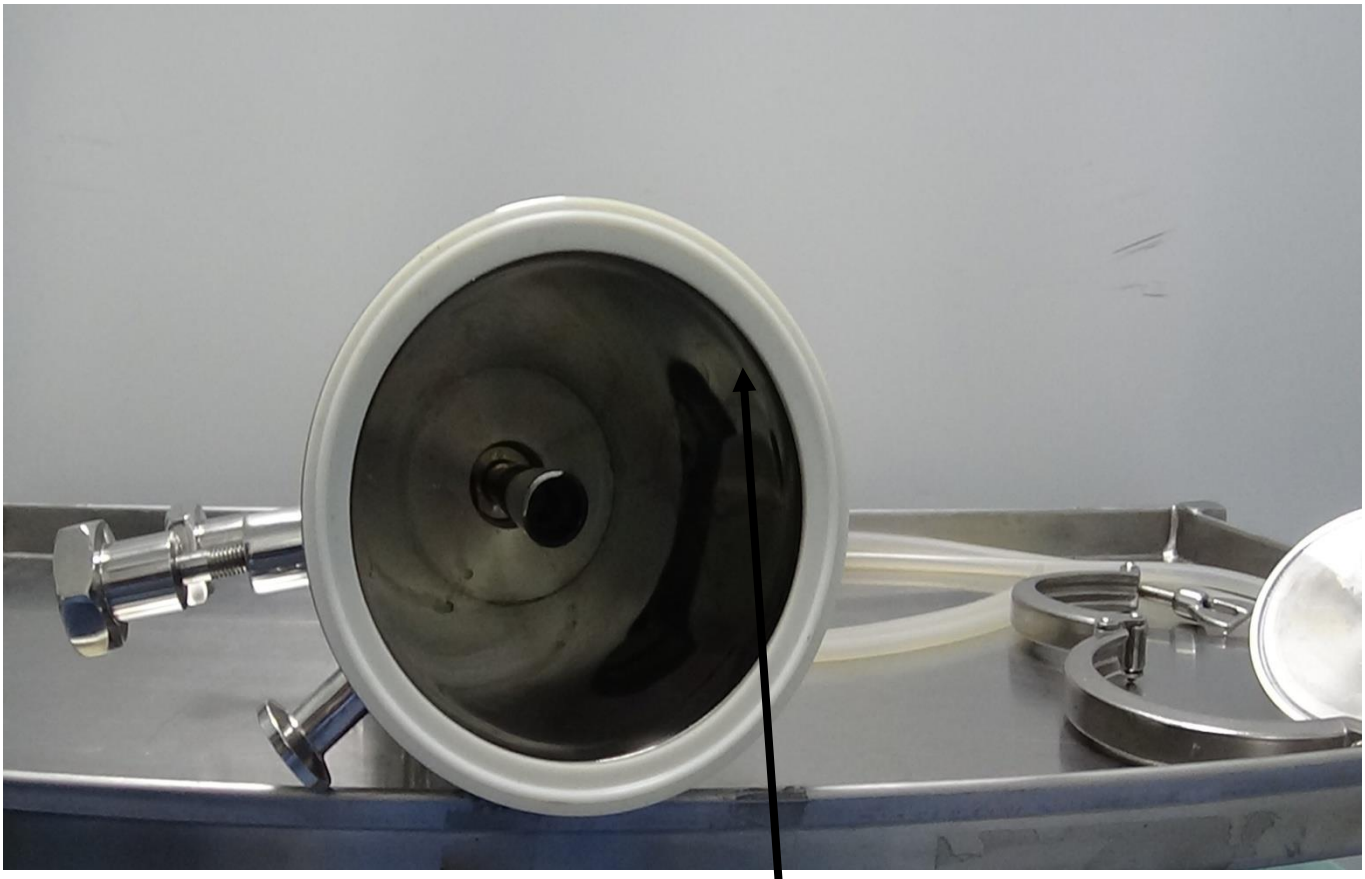
- **BUFFER TANK:**

Snap No-09 (Inlet of the vessel)



Sampling Location

Snap No-10 (Outlet of the vessel)



Sampling Location

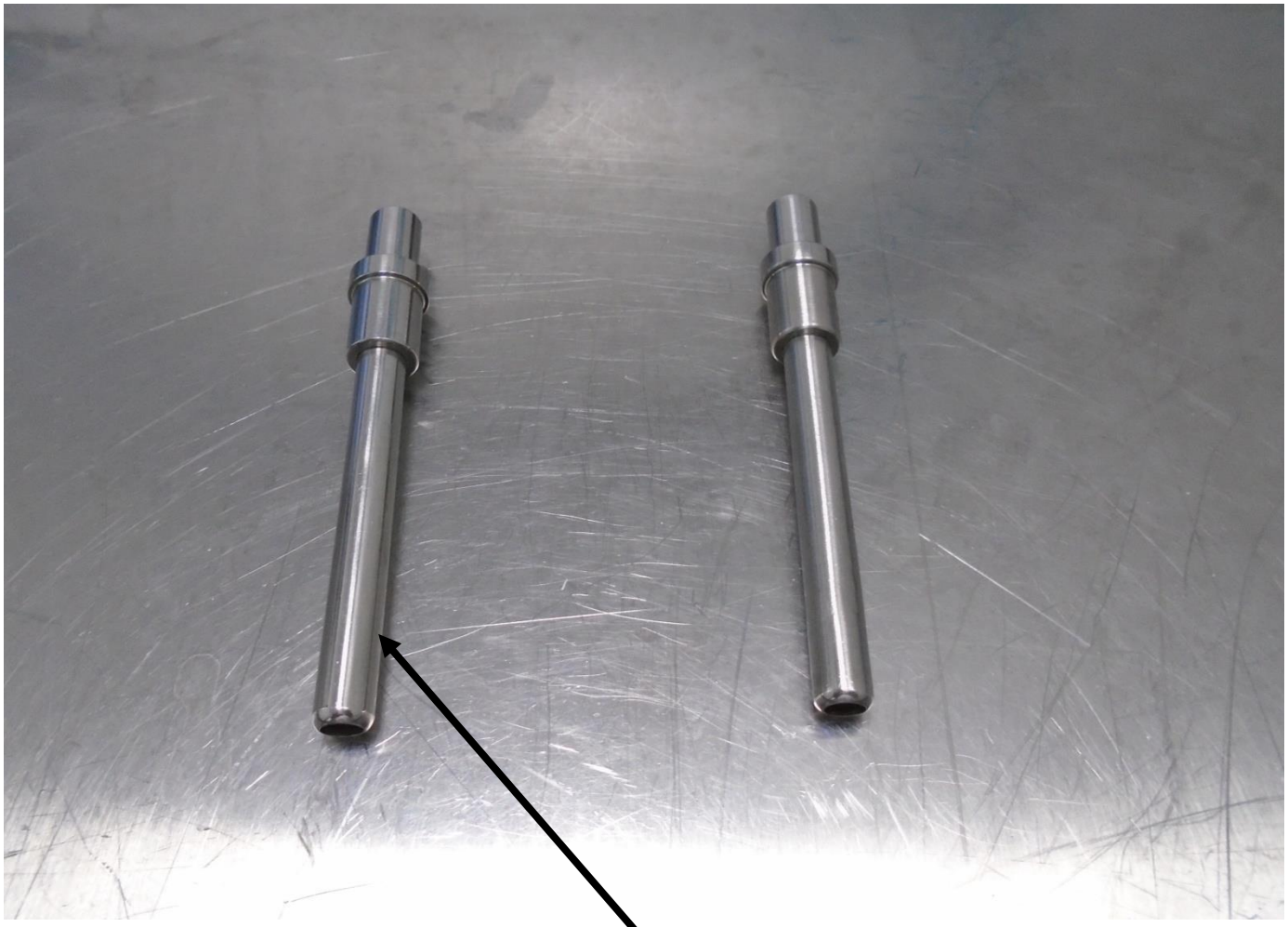
- **FILLING PUMPS:**

Snap No-11 (Inner surface of pump)

Sampling Location

- **FILLING NOZZLE:**

Snap No-12 (Outlet of the Nozzle)



11.0 ACCEPTANCE CRITERIA:

- After respective cleaning procedure, all the product contact parts should be visually clean.
- The limits for rinse and swab sample tested for following tests are mentioned in the below table:

Test		Acceptance criteria
pH		5.0-7.0
Conductivity		NMT 1.3 µs/cm^2
Bioburden	**Rinse Sample**	10 CFU / 100 mL
	Swab Sample	10 CFU / Swab
BET		NMT 0.125 EU / mL

12.0 DEVIATION AND CORRECTIVE ACTION REPORT:

Record the deviations occurred during the execution of program and their justifications, corrective & preventive actions taken shall be recorded in Annexure-1

13.0 SUMMARY & CONCLUSION;

13.1 Results shall be documented in the test data sheets provided as ANNEXURE-1 to the protocol.

13.2 Based on the observations recorded, evaluation of the results shall be carried out.

13.3 After completion of the test, a detailed summary report (ANNEXURE-2) shall be prepared insisting on the process performed and results obtained.

13.4 On the basis of the results and evaluation, a summary report shall be prepared. The summary report shall signify a conclusion to confirm the successful qualification of the procedure.

13.5 Any modification in the method required before initiating revalidation shall be included in the report.

13.6 The summary report shall be attached with the protocol along with the test data reports.

14.0 ABBREVIATIONS:

Abbreviation	Description
CIP	Clean In Place
DOC	Document
QA	Quality Assurance
QC	Quality Control
SOP	Standard Operating Procedure
No.	Number
LAF	Laminar Air Flow
CM^2	Square Centimeter

15.0 REFERENCES:

NA

16.0 ANNEXURES:

S.No.	Name of ANNEXURE	ANNEXURE No.
1	Record of Observations of Protocol for Clean Equipment Hold Time Study Validation	Annexure-1
2	Summary Report of Protocol for Clean Equipment Hold Time Study Validation	Annexure-2