



PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

OPERATOR EXPOSURE LEVEL TEST PROCEDURE FOR AUTOCOATER FLEXIBLE CANOPY

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| Client Name: | | | | |
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| Document Title: | Operator Exposure Level Test Procedure | | | |
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REVISION RECORD

| Issue No. | Date | Description of Revision | Page & Para. No. |
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OPERATOR EXPOSURE LEVEL TEST PROCEDURE FOR AUTOCOATER FLEXIBLE CANOPY

1. Description:

To perform a series of operating cycles in accordance with agreed operating procedure to test the operator exposure level recording during these operations by means of filter membrane capture and in accordance with the latest SMEPAC guide The external nominated Laboratory responsible for carrying out the testing of the OEL Samples will be:

M/S

2. Preparation:

2.1 Testing to be conducted within the General Assembly Area.

The area will be of dimensions to provide adequate access around all sides of the unit, typically 1m clearance for non-operational areas and 1.5m clearance for operational areas. There should be adequate space provided for storage of all materials to be used including inlet materials such as drums or kegs and outlet materials including any temporary discharge receivers.

2.2 Typically the enclosure in which the Containment Unit is kept and fan/filter system shall provide a stable environment.

2.3 The test material shall be Sodium Naproxen Tablets. The test material will be obtained from compression machine into the correct quantities, in the correct bags.

2.4 Before commencement of the test the Isolator must be checked that all items are fitted or provided to enable the test to be carried out without interruption or risk to the integrity of the test enclosure.

2.5 The appointed operator and test operative shall be provided with Clean Gown, Shoe covers, no. powder shedding gloves mask and head gear to prevent corruption of the test.

2.6 The following pump samples systems shall be calibrated and positioned at the pre-agreed locations:

- (1) Personal samples would be worn by the operator within the breathing zone (i.e. within 300 mm radius of the mouth and nose – typically on the right lapel for a right-handed person).
- (2) Background Static Sampler – adjacent to the strategic worst-risk points identified, e.g. Chamber front visor, waste port.
- (3) Continuous sampler – within the test enclosure positioned to provide the most representative results across the test period.

The pumps will only be turned on and the filter head caps removed when the test is ready to commence.

The specification of the filter membrane will be as recommended by Testing Laboratory and to be compatible with the OEL level to be tested against and is 25 mm PTFE, 0.2µ Type

The swabs used will be as recommended by

2.7 Each of the filter heads/swab shall be clearly identified with:-
ID no, position, run no.

2.8 Sampling Time

The run length will be a function of the target OEL (occupational exposure limit) and the analytical limit of detection for the surrogate material chosen for the project. Sufficient sample must be collected to demonstrate compliance with the OEL.

Results are best expressed as an average over the duration of the task, thus avoiding any problems associated with different time weighted average periods and relating the length of task for the surrogate to the actual duration of task on site.

In order to demonstrate compliance with the FDS and design criteria of 0.5 µg.m⁻³ The total Run length will need to be around 180 mins per run.



OPERATOR EXPOSURE LEVEL TEST PROCEDURE FOR AUTOCOATER FLEXIBLE CANOPY

Sampling is conducted at 2 litres per minute (l.min⁻¹) ± 0.1 l.min⁻¹.

Filter blanks to be analysed but these would be submitted 'blindly' for quality assurance purposes.

Sampling pump(s) utilised will be a SKC Model No.224-51TX, personal air sampler or equivalent

3. Surrogate Material:

- 3.1 Surrogate material Naproxen sodium tablets will not be introduced into the vicinity of the testing Isolator until immediately before the test and in a sealed container with cleaned external surfaces. Prevention of extraneous Naproxen Sodium contamination must be paramount to prevent adverse results invalidating the test.
- 3.2 It is recommended that disposable clothing, shoe covers, head gear, non-powder shedding gloves be worn when performing this task. Clothing should then be changed and all container external surfaces should be wiped clean to a suitable standard, prior to transfer of the surrogate to the test chamber.
- 3.3 Sufficient containers should be available to complete 3 protocol cycles without having to recycle the material out of the 'contaminated' Isolator.
- 3.4 Suitable surrogate is Naproxen Sodium tablets.

4. Pre-Test Checks and Tests:

- 4.1 Check that the visor gloves are correctly fitted to the glove ports with 'O'-rings fitted.
- 4.2 Check that the visor clamps are fully closed.
- 4.3 Check that the filter housing extract connection clamp is tightly fitted. Check that any additional clamps on the assembly are tightly fitted.
- 4.4 Check that the equipment's operating conditions against specification. Perform any necessary corrections and document them.
- 4.5 The test enclosure conditions shall be recorded before the start of the test and monitored throughout the duration of the test.
- 4.6 Before commencing the actual test a number of dry runs shall be carried out following the agreed standard operating procedure for the Isolator. (As devised by M/S)
- 4.7 The actual test shall not be started until all parties are satisfied that the operating procedure can be carried out without the risk of interruption or failure.
- 4.8 3 x 30 Kg tablets having surrogate (produced on Compression Machine) should be kept ready prior to commencement of the Pre-Operations background sample.
- 4.9 After the pre-trial background has run (at least 30 mins run time), Run 1 shall commence.



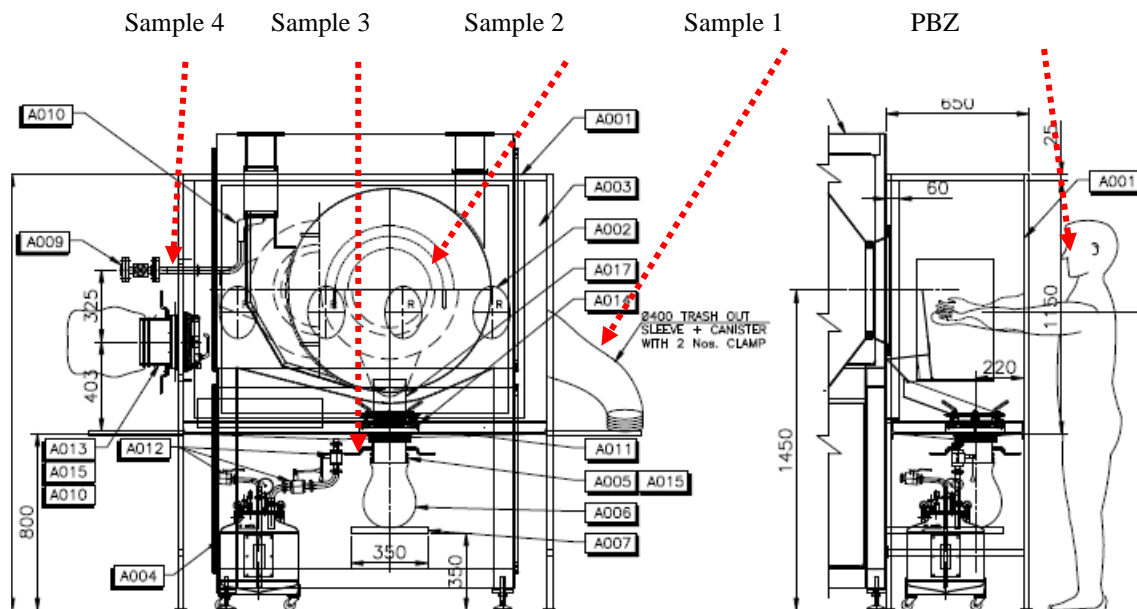
OPERATOR EXPOSURE LEVEL TEST PROCEDURE FOR AUTOCOATER FLEXIBLE CANOPY

5. Test Protocol & Record:

AIR SAMPLING:

- 5.1 Samplers will be uncapped and started and the start times and initial flow rates recorded.
- 5.2 After an elapsed time of 2 minutes, the operator will start the isolator (as appropriate) and when the isolator is determined to be in normal operating condition, the designated operator will start the operations
- 5.3 The operator will follow the process sequence as defined in FDS. For the purpose of this exercise, the surrogate tablets will be collected in the bag grommet attached to tablet collection glove box RTP's.
- 5.4 Contaminated waste in LDPE bag will be posted out and placed into the liner attached to RTP Passive in a waste bag.
- 5.5 Wait for 15 minutes and then stop sampling pumps and seal the sampling heads.
- 5.6 Record stop time and end flow rates.

Sampling Runs 2/3, will be identical to those described in 5.1 to 5.6 inclusive.



- PBZ– Personal sample on operator (Personal Air Sample).
- Sample 1 (Back Ground Static Sample) = On out feed sleeve
- Sample 2 (Back Ground Static Sample) = on front surface of Canopy at the Zip
- Sample 3 (Back Ground Static Sample) = directly adjacent to Unloading RTP at about 300 mm distance
- Sample 4 (Back Ground Static Sample) = On out feed sleeve
- SAMPLE 5 (Continuous Static sample)= on rear of isolator 1500mm from floor level.

Pre Trial = In front of Isolator at 2000 mm distance at 1500 mm height

Total samples =

Pre trial – 1 no. x 3 iterations = 3 nos.

Personal Air Sample (PBZ) – 1 no. x 3 Iterations = 3 nos.

Back ground Static Sample – 4 no. x 3 Iterations = 12 nos.

Continuous Static Samples – 1 no. x 3 Iterations = 3 nos.

The pre-trial background length should be a minimum of 30 minutes. Each of the 3 sampling runs should be approx. 180 minutes.



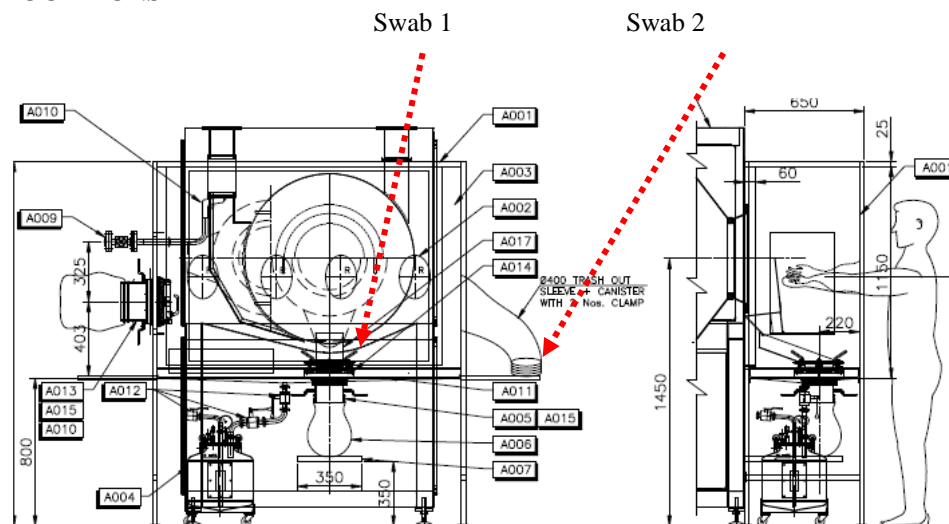
OPERATOR EXPOSURE LEVEL TEST PROCEDURE FOR AUTOCOATER FLEXIBLE CANOPY

Surface Swab sampling:

The surface contamination test will be performed in conjunction with the surrogate material particulate containment performance test. The purpose of the test is to determine the degree of surface contamination on any surfaces likely to be exposed to the general external environment.

e.g. surface of rapid transfer ports, area of glove change, door gasket etc.

SWAB LOCATIONS -



Sample 1 – Along the liner integration at Feed out sleeve

Sample 2 – Along the liner integration of Tablet collection grommet

In preparing the equipment the surface areas which are intended to be used for surface contamination swabbing should be identified and must be swabbed clean with 70% IPA prior to taking a baseline swab sample.

The swab samples at the different positions will be taken both before and after the completion of 3 iterations of Air sampling. Wearing appropriate impervious clean gloves and clean gown, mask and head gear as needed, carefully remove a new swab from its container. New gloves are required for each sample to prevent cross-contamination of the wipe sample.

Dip the swab into de-ionised water and shake excess water from the swab.

Grip the swab firmly, wipe the swab across the selected area.

Where feasible, this area should be 100 cm² (10 cm x 10 cm) and the swab should be drawn across in a zigzag fashion in both the horizontal and vertical plane.

Enough pressure should be applied to remove residues from the surface without tearing the swab material. The amount of pressure will vary and more pressure will be needed for uneven or indented surfaces than for smooth areas.

A good rule of thumb is to use the amount of pressure normally used to stick a stamp on an envelope.

Place the sample in a clean, labelled container and seal it. Change gloves to avoid cross-contamination.

Make a note of the exact location, date, surface condition and other relevant information for each sample. In particular, note the process conditions and whether these are typical of normal operating conditions at the time of sampling.

In certain areas it may not be possible to wipe a 100 cm² section, and in such cases as much of the identified area as possible should be swabbed. It is important that each of the sample locations before and after the test are similar and swabs taken in a repeatable way.

An estimate of the area of test should be recorded.



OPERATOR EXPOSURE LEVEL TEST PROCEDURE FOR AUTOCOATER FLEXIBLE CANOPY

Errors in the swab test method may arise during sampling and analysis, and good quality control must be adhered to at all times.

Unused swabs, which have been handled in the same way as sample swabs, should be analysed to correct for field errors and desorption efficiency.

Pre-requisites:-

Certain conditions have to be met before adopting this Protocol. These conditions have to be followed strictly in order to ensure reproducibility of results. The conditions are two-fold:

At the location of Isolator;

Written Standard Operating Procedure (SOP) for the specific Isolator should be in place.

A designated clean room should be made available to accommodate the Isolator and perform the sampling operations.

Suitable electrical points, trash bin, wash and drain facility, set-up table, adequate illumination and ventilation should be provided.

The Isolator should be subjected to the pressure hold test in the location where the Containment Performance Test is to be carried out. The result of the test should be satisfactory and must qualify for the limits specified in the FAT.

At client's/customer's site;

The Isolator must be installed and commissioned at the intended site of actual use.

The written Standard Operating Procedure (SOP) for the intended use by the client/customer must be in place.

All equipment and material (except the API's) required for the conduct of the SOP must be made available at the time of conducting the Containment Performance Test as per this protocol.

All operating personnel prescribed in the SOP must be trained and they must simulate the actions of the actual operations.

6. Requirements:

For successful conduct of this Protocol, certain requirements have to be stringently met and they have been categorized under sampling requirements and testing requirements.

6.1 Sampling requirements:

- a) Material
 - Naproxen sodium
 - DM water
 - Filter cassette with filter
 - Swab bottles
 - Poly bags for dispensing
- b) Equipment, Apparatus & Accessories
 - Air sampler ,Swabs, Calibrator, Rotameter
 - 500 ml Beakers
 - Marker
 - Sticker labels
 - Zip lock bags
 - Bag ties
 - Scissors
 - Latex gloves
- c) Personnel
 - Regular trained staff associated with the isolator

6.2 Testing requirements :

The sample testing will be done by
M/S



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7. Testing:

Limits –

Air sampling limit: In the breathing zone, the air sampling limit was pegged at 7.5 ng/filter (Based on 0.5 µg/m³/TWA) with LOQ of 0.02 µg (Target Concentration (µg) X Volume)
LOD = LOQ/[SAMPLE DURATION(min) X FLOW RATE (m³)]

For swabs the LOD is 0.025 µg with Limit of 5 µg/cm²

8. Storage, Shipment and Sample Analysis:

Upon completion of the test procedure the sample heads and material sample shall be passed to an accredited laboratory .The samples will be refrigerated to prevent bacterial growth due to the fact that swab is wet and therefore provides a nutrient for this growth. The samples will be shipped the same week that the sampling occurs.

9. SMEPAC Deviations:

The follow deviations from the SMEPAC guide should be noted.

| Potential Deviation | Comment |
|---|--|
| Section 4.3 – Test Enclosure Environmental Conditions – Temperature range: 25 ± 3 °C, Relative Humidity: 60 % ± 10 %, Positive Room Pressure: + 10 Pa (minimum) relative to adjacent space, Air Change Rate: 3-5/h. | Temperature is likely to be within the range specified. Relative Humidity is not specifically controlled and may or may not be within the range specified on the day of test. |
| Section 6.2.3 – Real-Time Aerosol Monitors – these should be used as fixed, static monitors to understand exposure patterns and identification of dust emission sources. | Most direct-reading light-scattering photometers are not substance-specific for the compound of interest, would not be calibrated specifically for the response to Naproxen Sodium and would only have a sensitivity of 1 µg.m-3. We do not propose to use this equipment. |

10. Results:

.....will be responsible for arranging the analysis with the laboratory and for producing the full test report including the results of the analysis.

11. Record:

Comments:

12. Conclusion:

| Design Value | Test Result | Complies (Yes/No) |
|---|-------------|-------------------|
| ≤ 0.5 µg/m ³ for 8 hour TWA Swab – ≤ 5 µg/cm ² | | |



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| PASS / FAIL | Name | Signed | Date |
|---|------|--------|------|
| On behalf of Consultants & Engineers Pvt. Ltd. | | | |
| On behalf of M/S | | | |

Abbreviations:

- FDS : Functional design Specifications
- TWA : Total Weighted Average
- LOD : Limit of Detection
- Pa : Pascal
- BP : British Pharmacopeia
- LDPE : Low Density Poly Ethylene
- RHS : Right Hand Side
- LHS : Left hand Side
- FAT : Factory acceptance Test
- API : Active Pharmaceutical Ingredient
- SMEPAC: Standardised Measurement of Equipment Particulate Airborne Concentration