SUMMARY RESULTS FOR THE FAT OEL TESTING OF A SOLOFLEX FLEXIBLE ISOLATOR (P151190) AT SOLO CONTAINMENT LTD, POYNTON, CHESHIRE – 04/FEB/16

Air sampling was carried out on the 04th February 2016 as part of a FAT (factory acceptance test) OEL (operator exposure level) containment test to assess the levels of operator exposure during normal operations while using a soloFLEX flexible isolator (P151190, Switzerland) at the Solo Containment Ltd. facilities in Unit 6 Rupert Park, London Road South, Poynton, Cheshire, England.

During the testing, tasks were carried out using lactose to mimic the activities that may foreseeably be performed during normal handling operations within the flexible isolator. The flexible isolator was located on the factory floor with the isolator exhaust air vented back into the flexible isolator area *via* the isolator's air handling unit (Serial No.: ED/1002, Year of Manufacture: 2014). The testing was, therefore, carried out under ambient pressure and temperature conditions.

It was reported that personal exposures should be less than (<) the target OEL of 0.1 $\mu g.m^{-3}$, as an 8-hour Time-Weighted Average (8h TWA). Where three repeat samples are taken, in accordance with the guidance BS EN 689:1996, it is desirable that personal exposures are controlled to 25% of this value or less i.e. $\leq 0.025\ \mu g.m^{-3}$, 8h TWA, in order to be confident that all future results will meet the target limit. Background airborne concentrations of the contaminant, over the sample duration, should ideally be below 10% of the target OEL (i.e. $\leq 0.01\ \mu g.m^{-3}$, 8h TWA).

A pre-trial background sample was taken in the test area before the start of each monitoring run, prior to the start of the personal sampling and before the lactose handling operations began. This was to assess the background airborne lactose concentrations in case of any excessive background levels that may affect the sampling results.

Four blank samples were also submitted for analysis. Each of the blank samples had no quantifiable amount of lactose detected (i.e. each of these filters had < 0.0025 µg of lactose on it).

Personal sampling results are expressed individually over the duration of the monitored operation and as an 8h TWA. Static and background results are shown over the sample duration only.

Results are reported to two significant figures. Sample volumes were calculated to three decimal places. $\mu g.m^{-3}$ = micrograms of lactose per cubic metre of air. Where the 'less than' symbol (<) has been used, there was no lactose detected above the analytical limit of quantification (LOQ) of 0.0025 µg (2.5 ng).

AIR SAMPLING RESULTS:

	Airborne concentration of lactose over task (µg.m^{-3})			
	RUN 1	RUN 2	RUN 3	RUN 4
PRE-TRIAL BACKGROUND	< 0.042	< 0.042	< 0.042	< 0.042
Run time (mins)	*30*	*30*	*30*	*30*
PERSONAL	0.021	< 0.029	< 0.032	< 0.046
POSITION 1	< 0.017	< 0.029	< 0.032	< 0.046
POSITION 2	< 0.017	< 0.029	< 0.032	< 0.046
POSITION 3	< 0.017	< 0.029	< 0.032	< 0.046
POSITION 4	< 0.017	0.12	< 0.032	< 0.046
POSITION 5	< 0.017	< 0.029	< 0.032	< 0.046
POSITION 6	< 0.017	< 0.029	< 0.032	< 0.046
Run time (mins)	*73*	*43*	*39*	*27*

	8h TWA Exposure (µg.m^{-3})			
	RUN 1	RUN 2	RUN 3	RUN 4
PERSONAL	**0.0032**	**< 0.0026**	**< 0.0026**	**< 0.0026**

For information, the sample positions used are described below:

- Pre-trial background = Static background sample in test area, approximately 2000 mm in front (centre) of isolator, approximately 1500 mm above floor level.
- Personal = Personal sample in breathing zone of operator, mounted within 300 mm of mouth/nose, on lapel of dominant hand (e.g. right hand side for a right handed operator).
- Position 1 = Static sample between main glove-ports on isolator's front panel.
- Position 2 = Static sample between main glove-ports on isolator's rear panel.
- Position 3 = Static sample adjacent to airlock outer zipped seal.
- Position 4 = Static sample adjacent to bag-out port spigot.
- Position 5 = Static sample adjacent to exhaust from isolator's air handling unit.
- Position 6 = Static background sample in test area, approximately 2000 mm in front (centre) of isolator at 1500 mm above floor level. (This is the same position as the pre-trial background samples).

The day before the monitoring exercise, the required lactose bags (3 x 250 g) were pre-dispensed and double bagged at a remote location from the isolator. Each bag was closed, cable tied and the outside of each bag wiped with water wetted wipes before being sealed in double bags and transferred to the isolator area.

Prior to the sampling runs, the required equipment (e.g. empty plastic bags, lidded plastic containers, cable ties, cable tie snips, scoop, wipes and alcohol spray) and lactose were placed in the airlock. At the start of Run 1, the airlock inner door was opened and the equipment plus lactose transferred into the main chamber. The airlock inner door was then zipped closed.

The process involved opening one of the lactose bags and weighing lactose (5 x 50 g) into each of five lidded containers using the scoop. Each container was re-lidded and the outside of each container wiped with an alcohol wetted wipe. The containers were then placed in plastic bags, the bags twisted and cable tied closed and the outside of the bags wiped with alcohol wetted wipes.

The scoop, balance plate, internal surfaces of the isolator main chamber and the isolator gloves were each wiped with alcohol wetted wipes. The used wipes and lactose bag were collected in a new plastic bag (waste). The waste bag was twisted and cable tied closed, the outside of the bag wiped with alcohol wetted wipes and left to one side in the isolator main chamber.

The bag-out port bung was opened and the bags containing the lactose containers were pushed into the continuous liner connected to the bag-out port spigot. The bag-out bung seal was sprayed with alcohol and the bung closed. The continuous liner was pulled from the bag-out port spigot, twisted, crimped (using the Heaton Green [HG] Liner Sealing Crimp), cut and the cut ends covered with the crimp covers. The cut liner containing the lactose containers was then placed below the isolator airlock. The bag-out bung was opened and the waste bag pushed into the continuous liner on the bag-out port spigot. The bag-out bung seal was sprayed with alcohol and the bung closed. The continuous liner was pulled from the bag-out port spigot, twisted, crimped, cut and the cut ends covered with the crimp covers. The cut liner containing the waste was placed to one side within the isolator area.

The cut liner section containing the filled lactose containers was transferred back into the isolator main chamber *via* the airlock. The liner was cut open and one of the bags with a lactose container removed. The outer bag was removed and the container opened. The contents of the container were poured into a new zip-lock plastic bag, the bag zip closed and the outside of the bag wiped with alcohol wetted wipes. The lactose bag was then double bagged, the outer bag twisted and cable tied closed. The bag-out port bung was opened and the lactose bag pushed into the continuous liner connected on the bag-out port spigot. The bag-out bung seal was sprayed with alcohol and the bung closed. The continuous liner was pulled from the bag-out port spigot, twisted, crimped (using the HG Crimps), cut and the cut ends covered with the crimp covers. The cut liner containing the lactose bag was then placed below the isolator airlock.

The process described above was followed 3 times to create sample runs 1, 2 and 3.

For information only, a fourth sample run (Run 4) was carried out in which:

- The bag-out port bung was not closed throughout the monitoring run.
- No wet wiping of any of the internal surfaces or lactose bags was carried out.
- A spillage of part of the lactose (50 g) was simulated by pouring the material onto the base of the isolator main chamber.
- The isolator gloves were used to pick-up some of the lactose from the isolator base and transfer the material to one of the lidded plastic containers.

A representative from Solo Containment (Arnie Maguire) undertook the role of the operator for each of the monitoring runs and was fitted with a personal sampler. During the testing the operator was gowned wearing a laboratory coat.

Pre-trial background samples

There was no detectable level of lactose found in any of the pre-trial background samples taken in the isolator area before the start of each monitoring run (i.e. each filter had < 0.0025 µg of lactose on it) giving rise to the measured airborne concentrations of < 0.042 $\mu g.m^{-3}$ for each of the pre-trial background samples.

Personal samples

A detectable level of lactose was found on one of the four personal samples with measured concentrations over the duration of the sampling runs of 0.021 $\mu g.m^{-3}$, < 0.029 $\mu g.m^{-3}$, < 0.032 $\mu g.m^{-3}$ and < 0.046 $\mu g.m^{-3}$, for Runs 1 to 4 respectively. No observations were made during Run 1 that would indicate any reason for detecting lactose on this personal sample. The difference in the measured concentrations for Runs 2 to 4 is due only to the time over which these samples were run.

The 8h TWA exposures were calculated to be 0.0032 $\mu g.m^{-3}$ for Run 1 and < 0.0026 $\mu g.m^{-3}$ for Runs 2 to 4. These results assume that the activity monitored is performed only once per shift, that no further exposure would occur over the remainder of the shift and that the shift length is no longer than 8 hours. These results indicate that the target OEL of < 0.1 $\mu g.m^{-3}$, 8h TWA is likely to be met.

Although guidance (BS EN 689:1996) states that statistical analyses of personal exposure results should be undertaken, as three of the four results are below the analytical LOQ, any statistical analyses is unlikely to be valid. Also, as all of the 8h TWA results were significantly below the desirable 25% of the target OEL (i.e. $\leq$ 0.025 $\mu g.m^{-3}$, 8h TWA), it can be regarded that the target OEL is unlikely to be exceeded on a future occasion.

Background or static samples

A detectable level of lactose was found on only one of the static samples over the four sampling runs. Ideally airborne concentrations for background or static samples, over the duration of the task, should be below 10% of the target OEL (i.e. $\leq$ 0.01 $\mu g.m^{-3}$).

On Runs 1, 3 and 4, no detectable level lactose was found in any of the background or static samples (i.e. these filters had < 0.0025 µg of lactose on them).

For Run 2, lactose was detected only at position 4 (adjacent to the bag-out port spigot) with a measured airborne concentration of 0.12 $\mu g.m^{-3}$ (120% of the target OEL). No observations were made during this sampling run that would indicate any reason for detecting lactose on this static sample. No lactose was detected in the personal sample for this run indicating that this result had no influence on the personal exposure of the operator. Additionally no lactose was detected in the samples at the same position on Runs 1, 3 and 4 or in any of the other static samples collected during this run. It is, therefore, thought that this result is an anomaly that cannot be readily explained.

It should be considered that static sampling results should not be directly compared with the target OEL, as exposure limits are set for personal exposures and a fixed (non-personal) sampling location may not give a result that is representative of this. Also, the dust in the work environment is not uniformly distributed. Static samples are used essentially to indicate the main areas of dust emission. These samples are used primarily as a tool to aid diagnosis, if and when, on the odd occasion, the personal exposure target is not met.

Conclusion

The personal sampling results obtained from the surrogate containment testing to measure airborne levels of lactose during use of the soloFLEX flexible isolator (P151190, Switzerland) indicate that the target OEL of < 0.1 $\mu g.m^{-3}$, 8h TWA, is likely to be met.

It is recommended that the containment testing is repeated as part of a Site Acceptance Test (SAT), once the soloFLEX flexible isolator is installed on the client's site. It is further recommended that consideration be given to monitoring personal exposure to the actual active pharmaceutical ingredients (APIs) or intermediates. The surrogate material should ideally match the API(s) closely in terms of particle size distribution, bulk density, etc. but will inevitably behave in a slightly different fashion to that of APIs or intermediates in actual use.

It is also recommended that these conclusions be kept under review, particularly if there is reason to suspect that they may no longer be valid due to significant changes in working procedures from the tasks simulated, or due to modifications to the equipment.