

CONTROLLED QUALIFICATION RECORD · GMP ANNEX 1 (2022) · GRADE A / B

Aseptic Filling Suite F7

Technical qualification report — performance qualification of filling line 2, lyophiliser LY-40 and automated inspection

Document	TQR-F7-26-014	Revision	C
Site	Corvenne Sterile Operations, Building F7		
Product family	Ostravex 40 mg/mL vials 2R–20R; Pelvane RTU syringes		
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Reviewed by	Ana Prieto-Kalnins, Process Engineering	Status	Approved
Approved by	Dr. Ilse Marrow-Quint, Head of Quality	Pages	12

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Revision history

Rev.	Date	Change	Author
A	02 Jun 2026	First issue for the qualification	T. Eberveld
B			ieto-Kalnins
C		DV-F7-0419, final approval	rrow-Quint

1. Executive summary

The second filling line in Building F7 meets every acceptance criterion of the qualification protocol, with two deviations closed before the final batch.

Three consecutive process-simulation runs and three commercial-scale batches were executed between May and August 2026. Every media-filled unit was incubated and inspected; none showed growth. The isolator leak rate, glove integrity and bio-decontamination cycle were demonstrated at the worst-case conditions defined in the risk assessment[1]. The board recommends release of the line for routine commercial manufacture, subject to the monitoring commitments listed in section 5 on page 8.

1.1 Key findings

1. Sterility assurance

1.1 All 34 560 media-filled units were negative after 14 days of incubation.

1.2 Interventions: 27 inherent and 9 corrective interventions were simulated, each at least three times.

a) maximum intervention duration 6 min 40 s;

1 Risk assessment RA-F7-0091, revision 4, approved 11 March 2026. The worst cases were selected by a cross-functional team using a failure-mode scoring of severity, occurrence and detectability.

b) glove-port interventions performed by 11 operators.

2. Process performance

2.1 Fill-weight Cpk of 1.71 across 10 needles (target ≥ 1.33).

2.2 Stopper placement defects below 50 ppm at 400 units per minute.

3. Environmental control

3.1 No Grade A excursions; two Grade B alert-level counts, both investigated.

1.2 Open commitments

- Extend the glove-integrity test interval only after 12 months of trend data.
  - Owner: Microbiology — due Q3 2027.
- Re-map the lyophiliser after any shelf-fluid service.
  - Trigger: maintenance order class M3 or higher.
    - Mapping uses 15 probes in the empty chamber.
- Add the new vial format 20R to the next process simulation.

1.3 Release decision

Key figures

34 560
units media-filled, zero positives

1.71
fill-weight Cpk, 10 needles

0.62 %
automated-inspection reject rate

Every vial passes the automated inspection machine, which images each container in eight positions. The rejection rate during the three PQ batches averaged 0.62 %, of which 0.11 % were cosmetic defects and none were critical particulate findings. The rejection figures were reconciled against the manual re-inspection of a 2 000-unit sample, which confirmed the machine's sensitivity[2].

The freeze-dryer cycle was challenged at the minimum and maximum shelf loads. Product temperature, measured by wireless probes at the edge and centre of the shelves, stayed at least 3 °C below the collapse temperature for the whole primary drying phase.

The board noted that the line clearance procedure and the stopper bowl cleaning frequency should be re-evaluated after the first six months of routine operation. The decision was recorded in minutes QB-F7-26-07 and is reproduced, with signatures, in the controlled archive.

2. Site and process overview

2.1 Building and utilities

Building F7 at the Corvenne campus of Halvorsen-Vire Biologics houses two isolator-based aseptic filling lines, a forty-square-metre freeze-dryer suite and a Grade C preparation

3 Surface finish Ra ≤ 0.5 µm, electropolished, passivated with citric acid after installation.

area with its own water-for-injection loop. The building was commissioned in three phases between 2023 and 2026; this report closes the performance-qualification phase for Line 2 and records the evidence reviewed by the qualification board. Clean utilities are generated in a dedicated plant room on the ground floor and distributed through orbitally welded 316L stainless-steel loops[3].

Unidirectional airflow over the open-product zone was measured at 0.45 m/s ±20 % at working height on a 300 mm grid. Smoke studies were recorded from six camera positions and reviewed frame by frame; no reverse flow towards the stopper bowl was observed during interventions.



Figure 1: Grade C corridor with pass-through hatches (photograph cropped 10 % each side).

The water-for-injection loop runs at 80 °C with a minimum return velocity of 1.2 m/s. Sampling points are numbered clockwise from the generator; the isometric view of the skid is shown in Figure 8 on page 11.

Viable monitoring used settle plates, contact plates on gloves and active air samplers at fourteen locations. Non-viable particles were counted continuously at three points in the Grade A zone, with the alarm limits set at 80 % of the regulatory action level for particles of 0.5 µm and 5.0 µm.

Pressure cascades of 15 Pa between adjacent grades were held during door-opening tests, and the recovery time from Grade B in-operation to at-rest conditions was 11 minutes, inside the 15 to 20 minute guidance.

2.2 Process flow

1 · Tub decontamination. Electron-beam tunnel, 25 kGy surface dose, three nests per minute.

2 · Debagging. Automated peel of the Tyvek lid inside the transfer isolator.

3 · Filling. Ready-to-use tubs enter through an electron-beam tunnel, are debagged in the transfer isolator and presented to the filling module on a servo-driven nest gripper. Ten peristaltic heads dose the product with a target accuracy of ±0.5 %, after which a star-wheel places the stoppers and the nests move to the lyophiliser loading system without leaving Grade A air.

4 · Stoppering. Star-wheel placement of lyophilisation stoppers, half-seated for drying.

5 · Lyophilisation. Automatic loading at −45 °C shelf temperature, 72-hour cycle.

6 · Capping. Crimping in Grade A air supply; residual seal force measured on every 50th vial.

7 · Inspection. Eight-camera automated inspection, then 100 % leak testing by headspace analysis.

The relationship between the steps, with the transfer points that break Grade A continuity, is drawn in Figure 6 (chapter 6).

3. Filling line and isolator

3.1 Glove ports and interventions



***Figure 2**: Glove port on the filling isolator — crop to the middle band (20 % top, 18 % bottom).*



Bio-decontamination of the isolator uses vaporised hydrogen peroxide at a nominal 900 ppm for 34 minutes. Biological indicators carrying 10^6 spores of the reference organism were placed at 48 worst-case locations, including the glove fingertips and the underside of the stopper chute. Each glove is tested before and after the campaign with a pressure-decay tester; a loss of more than 2 Pa per minute fails the glove and triggers an impact assessment on the batches filled since the last passing test.

Interventions were classified as inherent (part of the normal process, such as weight checks and stopper replenishment) or corrective (jam clearance, needle replacement). The photograph at left is printed in greyscale mode with an orange border; it floats beside the text.

I. inherent — weight checks, stopper replenishment, environmental sampling;
II. corrective — jam clearance, needle replacement, broken-vial removal;
III. prohibited — any action that places the operator above open containers.

Ready-to-use tubs enter through an electron-beam tunnel, are debagged in the transfer isolator and presented to the filling module on a servo-driven nest gripper. Ten peristaltic heads dose the product with a target accuracy of ±0.5 %, after which a star-wheel places the stoppers and the nests move to the lyophiliser loading system without leaving Grade A air.

3.2 Operator notes (linked frames)

The two framed columns below are a single linked text chain: text that overflows the left frame continues in the right frame.

Shift A, 14 July — Needle 7 showed a 0.8 % low drift after the second hour; the dosing pump auto-compensated within two cycles. No manual correction was needed.

Shift B, 14 July — Stopper bowl replenished four times. The vibratory feeder was set to level 6 after two short jams at the transfer rail; both cleared through glove port 4.

Shift A, 15 July — Settle plate at location A-07 exposed for 4 hours 10 minutes and replaced on schedule. Air sampler A-03 calibration verified at start of shift.

Shift B, 15 July — Planned corrective intervention: replacement of needle 3. Time from glove insertion to restart was 5 minutes 52 seconds.

3.3 Filling accuracy



***Figure 3**: Filling needles (left, shadow bottom-left) and peristaltic head (right, cropped 10 %, contrast +25 %).*

Fill weights were checked by in-process control on every needle every ten minutes, giving 4 210 checks per batch. The process capability figures are listed in Table .

4. Labelling and typography specimen

Labels, cartons and electronic batch-record screens use a controlled set of typefaces. This chapter documents the faces and the character effects available to the artwork team.

4.1 Approved typefaces

Source	Face	Specimen	Use
Windows	Segoe UI Light	Ostravex 40 mg/mL — 0123456789	Screen labels, light
Windows	Segoe UI Semibold	**Ostravex 40 mg/mL — 0123456789**	Screen headings
Windows	Segoe UI Black	**Ostravex 40 mg/mL — 0123456789**	Hazard pictogram text
Windows	Bahnschrift Light Condensed	Ostravex 40 mg/mL — 0123456789	Narrow carton panels
Windows	Bahnschrift SemiBold SemiCon-den	Ostravex 40 mg/mL — 0123456789	Shipper labels
Windows	Cambria	***Ostravex 40 mg/mL — 0123456789***	Leaflet headings
Windows	Georgia	*Ostravex 40 mg/mL — 0123456789*	Patient leaflet body
Windows	Consolas	`Ostravex 40 mg/mL — 0123456789`	Batch code 26F7-0412-B
Windows	Franklin Gothic Demi Cond	**Ostravex 40 mg/mL — 0123456789**	Pallet signage
Windows	Sitka Small	Ostravex 40 mg/mL — 0123456789	Small-print legibility
Windows	Gabriola	Ostravex 40 mg/mL — 0123456789	Ceremonial certificate
LibreOffice	Linux Libertine G	Ostravex 40 mg/mL — 0123456789	Body text of this report
LibreOffice	Linux Biolinum G	**Ostravex 40 mg/mL — 0123456789**	Report lead paragraphs
LibreOffice	Liberation Sans Narrow	**Ostravex 40 mg/mL — 0123456789**	Vial labels 2R
LibreOffice	Caladea	*Ostravex 40 mg/mL — 0123456789*	Metric clone of Cambria

LibreOffice	**Carlito**	Ostravex 40 mg/mL — 0123456789	Metric clone of Calibri
LibreOffice	**DejaVu Sans Mono**	`Ostravex 40 mg/mL — 0123456789`	Audit-trail exports
LibreOffice	**Gentium Book Basic**	*Ostravex 40 mg/mL — 0123456789*	Multilingual leaflets
LibreOffice	**Rubik**	**Ostravex 40 mg/mL — 0123456789**	Training material
LibreOffice	**Noto Serif**	Ostravex 40 mg/mL — 0123456789	Fallback for Greek αβγ and Cyrillic абв

***Table** : Approved typefaces: Windows system faces and fonts bundled with LibreOffice.*

4.2 Character effects

Shadowed · **Outline** · Embossed · Engraved · Overline · Wave underline

Double wave · bold dash underline · dotted · ~~strike~~ · ~~double strike~~ · ~~slash~~ · ~~X-out~~ · highlight

Small Capitals Heading · A L L C A P S · t r a c k i n g +3 p t · tracking −1 pt · scaled 60 % · scaled 150 %

H2O · 10^{6} CFU · rotated 90° · emphasis dots · Lining 0123456789 · ffi fl ligatures · Thin / **Semibold** / **Black** / *Italic*

Mixed sizes: 6 pt 8 pt 12 pt 18 pt 28 pt — coloured teal orange plum — link: example.invalid/f7

4.3 Right-to-left and East Asian lines

בניין 2, קו מילוי — תעודת הכשרה F7 (עברית)

شهادة التأهيل F7 — خط التعبئة رقم 2 في المبنى (العربية)

Mixed direction: lot 26 מספר אצווה F7-0412 then Arabic رقم التشغيلة inside a left-to-right paragraph.

无菌灌装线确认报告 — 第二条灌装线（简体中文，Microsoft YaHei）

無菌充填ラインの適格性確認報告書（日本語、Yu Gothic） 무균 충전 라인 적격성 평가 (한국어, Malgun Gothic)

無菌充填ライン 第二号機 品質保証部 承認済

The frame at right sets Japanese text vertically (top-to-bottom, right-to-left), as used on the narrow side panel of the export carton. **Ruby** annotations appear above 充填 in the line above, and the combined-characters run 十二月 packs three characters into one em box.

4.3.1 *Labelling rules*

Artwork may only use the faces in Table . Effects such as relief, outline and shadow are reserved for screen mock-ups; printed labels use solid ink only, because thermal-transfer printers cannot reproduce them reliably[4].

5. Environmental monitoring results

Viable monitoring used settle plates, contact plates on gloves and active air samplers at fourteen locations. Non-viable particles were counted continuously at three points in the Grade A zone, with the alarm limits set at 80 % of the regulatory action level for particles of 0.5 µm and 5.0 µm. Results are summarised by grade in Table . The Grade and Limits header cells are rotated; the limits column contains a nested table.

Grade	Location	Non-viable (counts / m³)		Viable (CFU)		Limits
		≥ 0.5 µm	≥ 5.0 µm	Air (per m³)	Glove print	
A	Filling zone	312	0	0	0	0.5 µm 3 520 5.0 µm 29 CFU <1
	Stopper bowl	288	0	0	0	
	Transfer isolator	405	2	0	<1	
B	Background room	21 400	88	2	3	**Grade B:** 352 000 / 2 930 / 10
	Gowning airlock	33 900	140	4	—	
C	Preparation area	187 000	1 210	31	—	**Grade C:** 3 520 000 / 29 300 / 100
	Corridor C-02	211 000	1 560	44	—	

***Table** : Environmental monitoring by grade (rotated header cells, merged headers and grade cells, nested limits table).*

5.1 Sterilisation lethality

The accumulated lethality of the stopper autoclave cycle and the logarithmic reduction achieved by the decontamination cycle are computed as follows:

$$F_0 = \Delta t \sum_{i=1}^{n} 10^{\frac{T_i - 121.1}{z}}$$

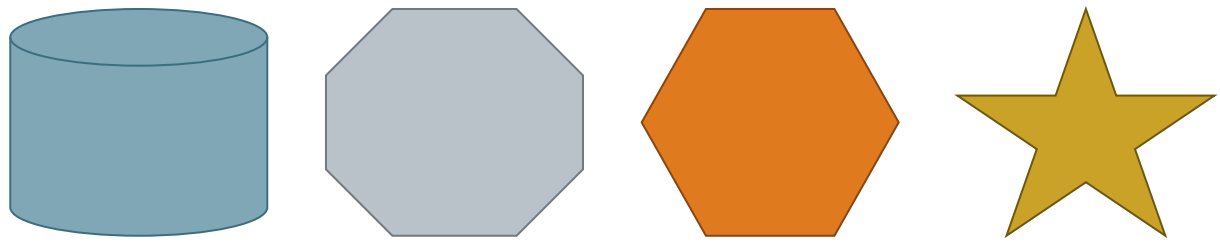
$$LRV = \log_{10}\left(\frac{N_0}{N}\right) = \frac{D_{value} \cdot t}{D_{value} \cdot 1} \quad N(t) = N_0 \cdot e^{-kt}, k = \frac{\ln 10}{D}$$

with T_i the product temperature in °C at interval i, z = 10 K and D the decimal reduction time. All 48 biological indicators were inactivated, demonstrating a reduction of at least six logarithms[5].

The freeze-dryer cycle was challenged at the minimum and maximum shelf loads. Product temperature, measured by wireless probes at the edge and centre of the shelves, stayed at least 3 °C below the collapse temperature for the whole primary drying phase.

6. Engineering views in three dimensions

Equipment outlines are drawn as extruded custom shapes so that the same artwork can be reused in the training deck. Each tile below varies one extrusion parameter: depth, rotation, projection, lighting, surface material and extrusion colour.



5 Indicators incubated 7 days at 55–60 °C; positive controls grew within 24 hours.

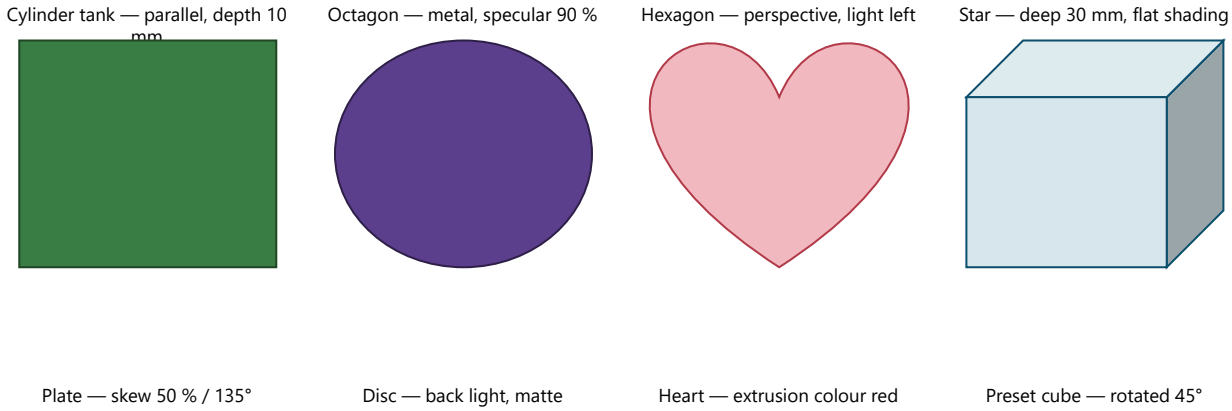


***Figure 4**: Extruded custom shapes: eight extrusion parameter sets (depth, angles, projection, light, metal, colour).*

***Figure 5**: Fontwork arch with parallel 3-D extrusion and an extrusion colour.*

6.1 Transfer flow drawing

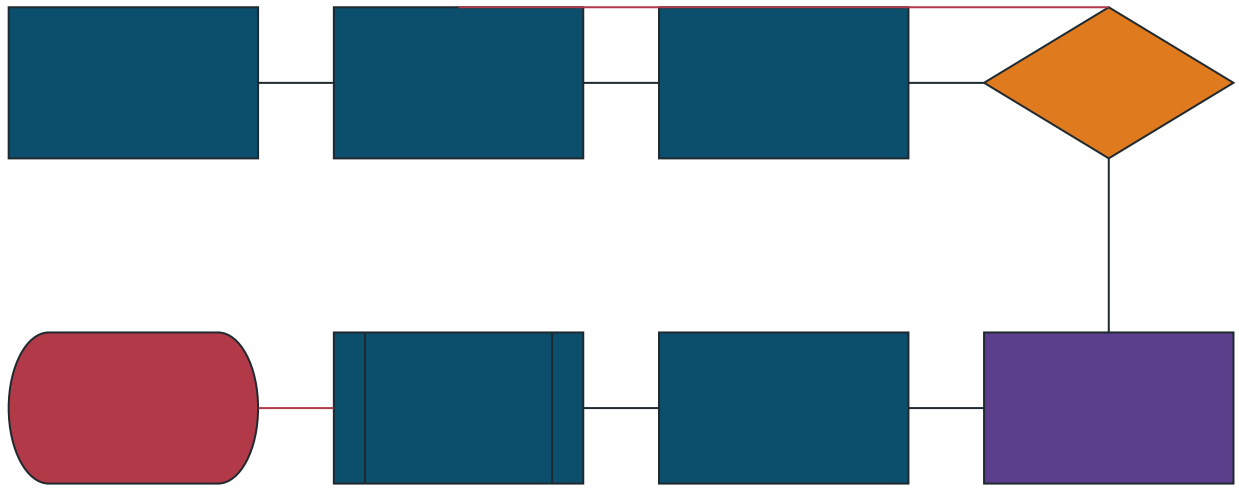


***Figure 6**: Transfer flow with glue-point connectors: standard routing, a dashed reject path and a curved rework loop.*

6.2 Particle counts in three dimensions

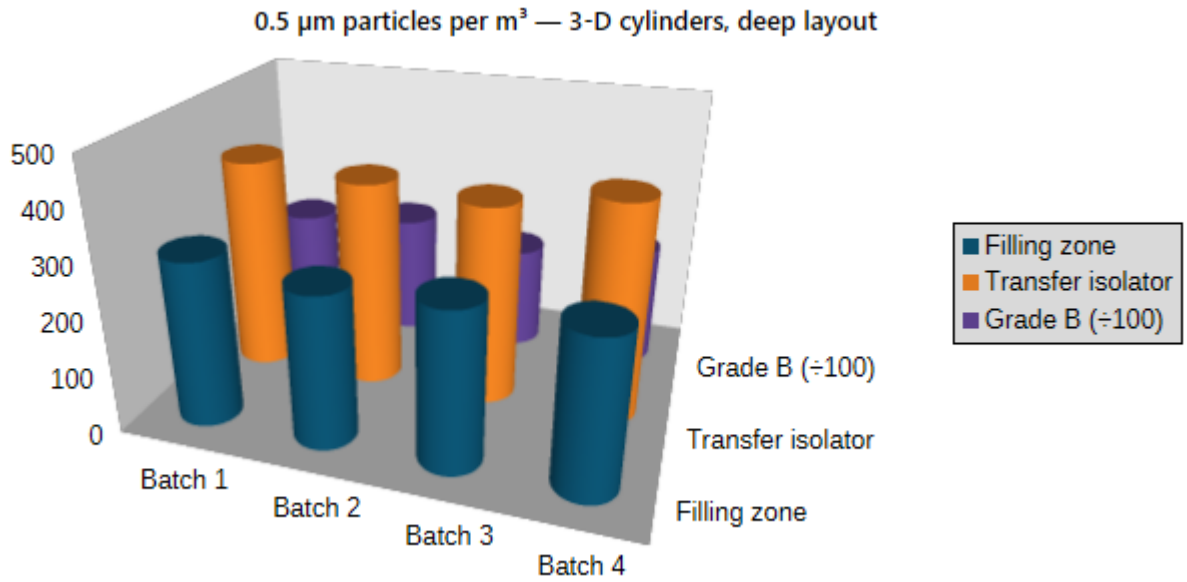


***Figure 7**: Embedded chart: 3-D clustered cylinders, deep layout, Gouraud shading, rotated perspective.*

6.2.1 *Embedded calculation sheet*

Needle	Target (g)	Mean (g)	Sd (mg)	Cpk
1	2,15	2,153	4,1	1.46
2	2,15	2,148	3,8	1.67
3	2,15	2,151	4,4	1.52
4	2,15	2,149	3,9	1.71

***Table** : Embedded Calc spreadsheet object computing per-needle capability (live formulas).*

7. Annex A — qualification matrix

The matrix lists every test of the protocol against the three batches. It is printed on a landscape page style with a double page border, and its header row repeats if the table breaks.

Test	Description	Batch 1	Batch 2	Batch 3	Criterion	Owner	Date	Status
IQ-01	Utilities connection	Pass	Pass	Pass	—	Eng.	2026-04-02	Closed
IQ-07	Isolator leak class	0.2 %/h	0.2 %/h	0.3 %/h	≤ 0.5 %/h	Eng.	2026-04-11	Closed
OQ-03	VHP cycle, 48 BIs	48/48	48/48	48/48	48/48	Micro.	2026-05-06	Closed
OQ-09	Airflow velocity	0.46 m/s	0.44 m/s	0.47 m/s	0.36–0.54	Eng.	2026-05-14	Closed
OQ-12	Smoke study	Pass	Pass	Pass	No reverse flow	QA	2026-05-20	Closed
PQ-01	Media fill 1	0 / 11 520	—	—	0 positives	Micro.	2026-06-03	Closed
PQ-02	Media fill 2	—	0 / 11 520	—	0 positives	Micro.	2026-06-24	Closed
PQ-03	Media fill 3	—	—	0 / 11 520	0 positives	Micro.	2026-07-15	Closed
PQ-05	Fill-weight Cpk	1.74	1.69	1.71	≥ 1.33	Proc.	2026-08-01	Closed
PQ-08	Lyophiliser mapping	ΔT 0.8 K	ΔT 0.9 K	ΔT 0.7 K	≤ 1.5 K	Eng.	2026-08-12	Deviation DV-F7-0419
PQ-11	Inspection reject rate	0.58 %	0.66 %	0.61 %	≤ 1.0 %	QC	2026-08-20	Closed

***Table** : Qualification matrix (landscape section).*

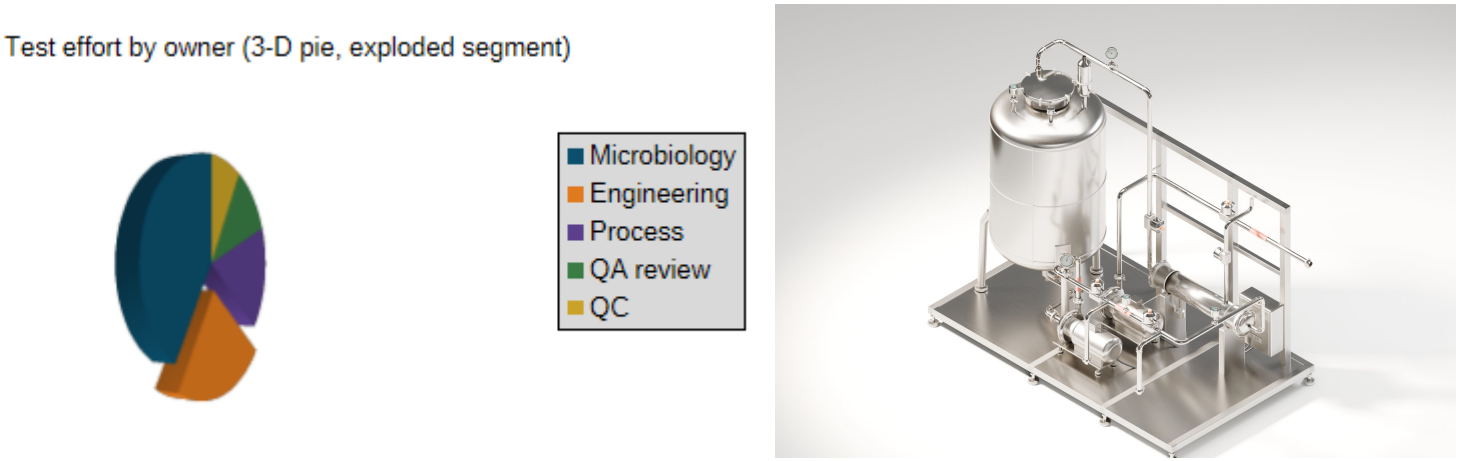


***Figure 8**: Left: 3-D pie with exploded segment. Right: WFI skid, isometric rendering.*

8. Glossary

Aseptic processing — Handling of sterile product, containers and closures in an environment that prevents microbial contamination.

BI — Biological indicator: a carrier inoculated with a known population of resistant spores.

Cpk — Process capability index relative to the nearer specification limit.

Grade A — Critical zone for high-risk operations, with unidirectional airflow.

Intervention — Any operator action inside the critical zone; inherent or corrective.

Isolator — Enclosure with a fully sealed barrier, decontaminated by an automated cycle.

Lyophilisation — Freeze-drying: removal of water by sublimation under vacuum.

Media fill — Process simulation using a growth medium in place of the product.

RTU — Ready-to-use: pre-sterilised containers delivered in sealed tubs.

VHP — Vaporised hydrogen peroxide, the decontamination agent of the isolators.

WFI — Water for injection, produced by distillation and held hot.

Worst case — A set of conditions with the highest chance of failure within operating limits.

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End of report. Endnotes follow on the next page.

2 Reconciliation was performed under procedure SOP-QC-2207. The detection probability for 100 µm glass particles was 0.97 at the 95 % confidence level.

4 Printer qualification PQ-LBL-031 limited the minimum stroke width to 0.25 mm at 300 dpi.