

Pilot Scale Manufacturing approach for novel low GWP propellants

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Summary

Facilities filling new low GWP propellants, such as Zephex® 152a should be constructed and operated considering the risks associated with filling of flammable gases (see Figure 1).

A pilot 5L scale manufacturing laboratory has been constructed by Koura at Thornton Science Park, UK, to aid customers who wish to perform early R&D work supporting transition to using the new propellants.

	Lower Toxicity	Higher Toxicity
Higher Flammability	● A3 (propane)	● B3
	● A2 (152a)	● B2
Lower Flammability	● A2L (1234ze, 1234yf)	● B2L (ammonia)
No Flame Propagation	● A1 (134a, 227ea)	● B1 (R-245fa)

Figure 1. ASHRAE (Standard 15/34, ISO 817) safety categories for a range of refrigerants/propellants.

Approach

To safely handle P152a at laboratory scale and upwards a combination of laboratory (personal) and process safety is required (see Figure 2). In the UK, the HSE require compliance with hierarchy of risk reduction as detailed in DSEAR and relevant ACOP e.g., L138. Appropriate risk assessments (using tools such as HAZID, HAZOP, LOPA etc.) must be undertaken to identify hazards, risks and mitigations in event of Loss of Containment (LOC).

As an example, Bow Tie diagrams (see Figure 3) can be used, to identify factors and controls which reduce the risk of primary event (LOC) occurring as well as mitigation measures to limit the consequences should LOC occur.

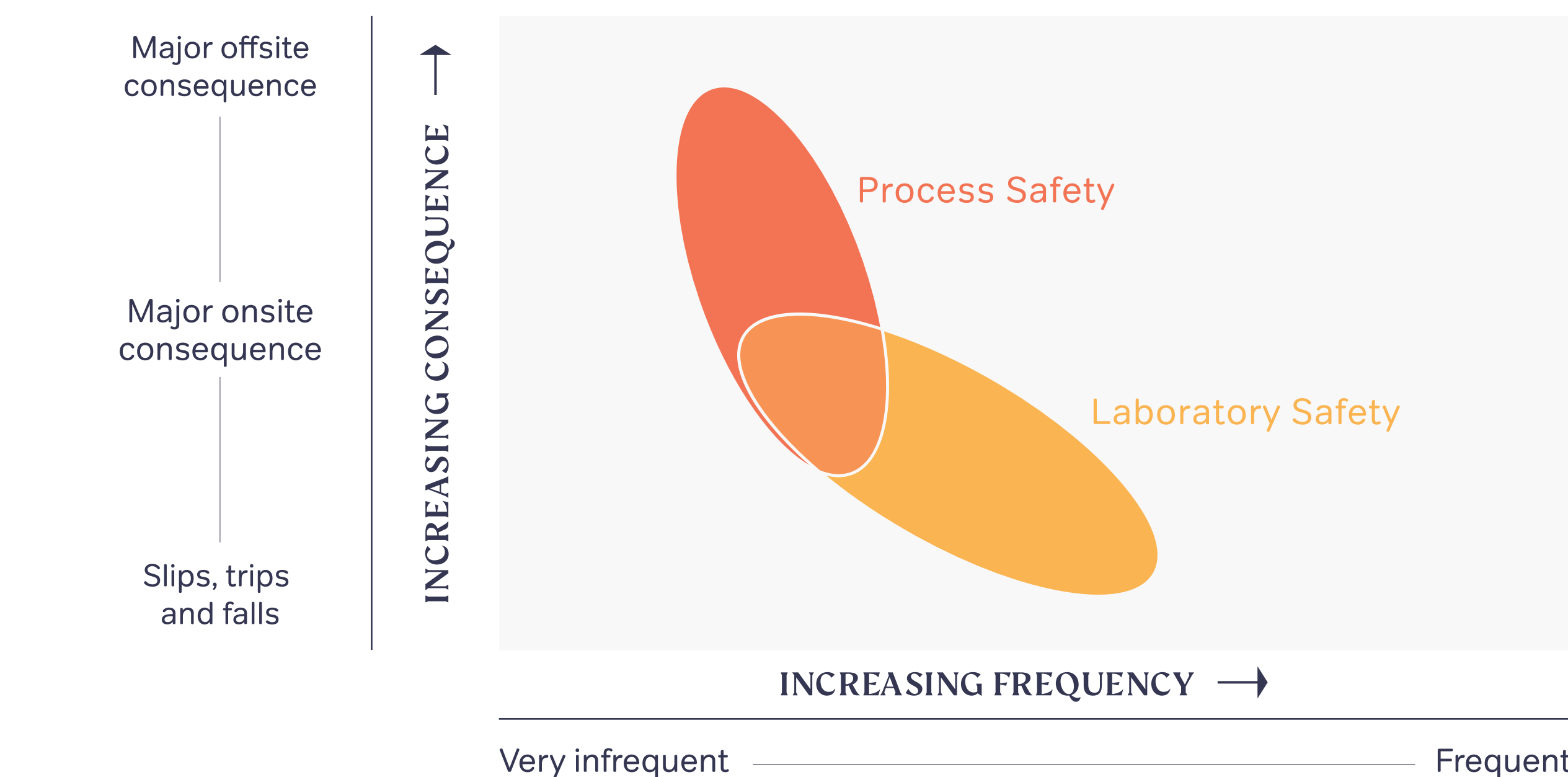


Figure 2. Risk Profile Overlap between Process and Laboratory Safety.

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Considerations

Local codes of practice and guidance should be reviewed, such as UK LPG COP and BAMA when developing the approach as well as SEP/GEP.

Receipt and Storage – minimize inventory in the facility. Store cylinders outside in covered secure areas. Movements assessed using TBRA.

Production – controls to prevent LOC – equipment design, self-contained relief streams, controls to prevent overfilling, leak checks, procedures, training.

Production – mitigations in event of LOC - ATEX zoning, equipment selection, earthing, gas detection, static dissipation, once through high flow ventilation and control system with alarms/shutdown logic. Controls over API/excipient handling are also important to prevent electrostatic sparking (e.g., limit use of insulated materials, dispense under N2).

Storage of filled units – stress testing/check weighing to remove gross leakers, storage in flow wrap laminate with molecular sieve.

Maintenance – PPM schedule and lifecycle approach.

Waste – recovery of all waste for processing by specialist contractors.

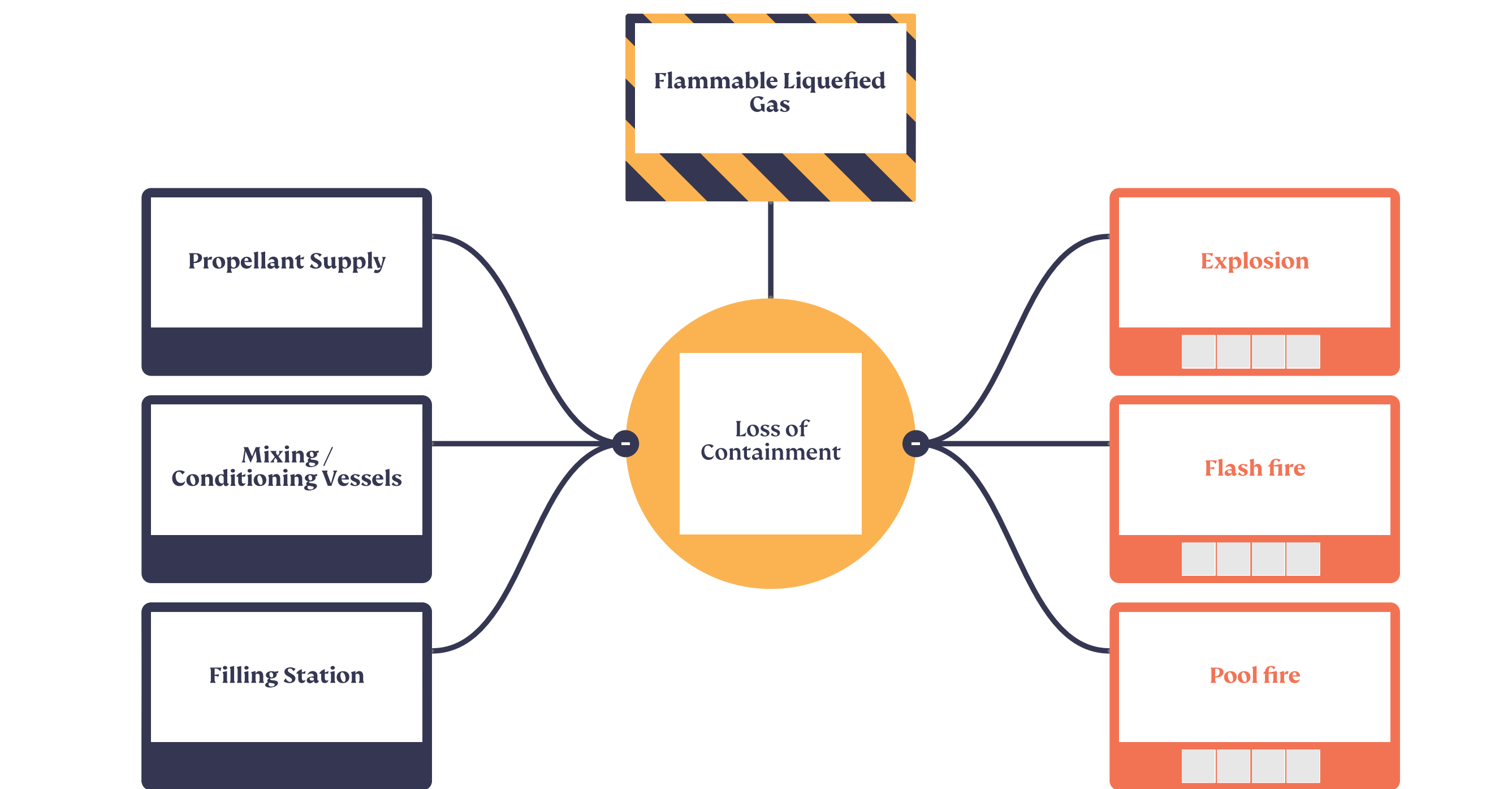


Figure 3. Example bow tie diagram.

Conclusion

Koura's approach to filling of pMDI in our 5L scale pilot facility has been presented, which is considered appropriate for filling of new low GWP propellants including P152a at this scale. These principles are scalable and can be applied to new and existing facilities.

Figure 4. ATEX Zoning Assessment (Left) of Koura 5L Pilot Facility (Right).

