PILOT PLANT MASS SPECTROMETER FOR DRYING ACTIVE PHARMACEUTICAL INGREDIENTS

AstraZeneca

Gisoo Pasha Moghaddam

Priority topic area: Energy and Climate Action

1 – Aim

The AZ pilot plant is responsible for manufacturing active pharmaceutical ingredients used in clinical trials. With an ambition to increase from 30 batches a year to 100 batches, we were tasked with **increasing facility throughput whilst minimising CO_2/kg of product** in line with **AZ's target to be net zero by 2045.** This aim is also directly linked to **Sustainability Development Goals** (SDG): 9 - guided drying introduces a new process innovation that improves asset utilisation,12 - Condition-based drying reduces resource use by avoiding over-processing and unnecessary utilities, 13 - Lower energy demand leads to reduced operational emissions, supporting decarbonisation goals.

We knew that our drying unit operation method needed **to be optimised to reduce wasted utility consumption**. To do this I project managed the start-up, commissioning and change management of the mass spectrometer, figure 1 shows the kit.

Figure 1 – Picture of Mass Spectrometer on plant.

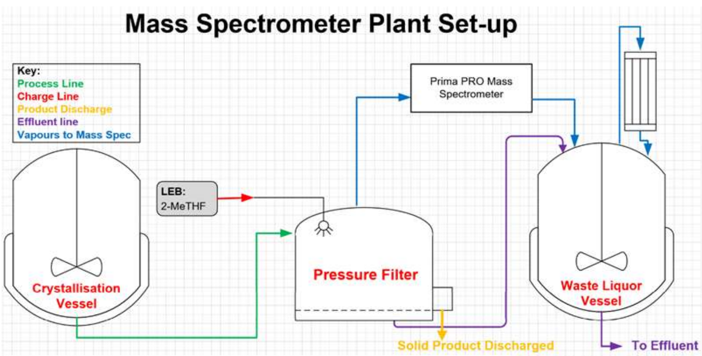

Figure 2 – Mass Spectrometer process block diagram.

2 – Methodology

The current process had bottlenecks as the drying process had to be stopped, the unit depressurised and a sample taken several times by operators to confirm end point. Stopping drying meant having to wait for the vessel to reheat and yield was also wasted on sampling.

Figure 2 shows the spectrometer set-up. Installing the spectrometer meant we could analyse real-time data on the concentration of vapour coming from the pressure filter/dryer.

Hot N_2 gas dries the powder, monitoring the rate of solvent vaporisation with the mass spectrometer allows us to determine drying end-point.

3 – Outputs

I led the first use of the mass spectrometer for a campaign where the process description stated 16hrs minimum drying time.

Instead, the operators used the 'live' graph in figure 3 and sampled after 2Me-THF (solvent present in slurry) levels dropped and stabilised, whilst N_2 levels increased.

A single sample was taken, avoiding yield loss and saving operational time. The sample passed the drying threshold first time!

The drying only took 8hrs 17mins, saving **~50%** of the steam and N^2 that would have been consumed.

This equates to **125 kWh of steam** and **4404 litres of $N_{2\,(liquid)}$** saved.

This one batch saved **812 kg of CO_2**, which is equivalent to 2,068 miles driven by an average petrol car[1].

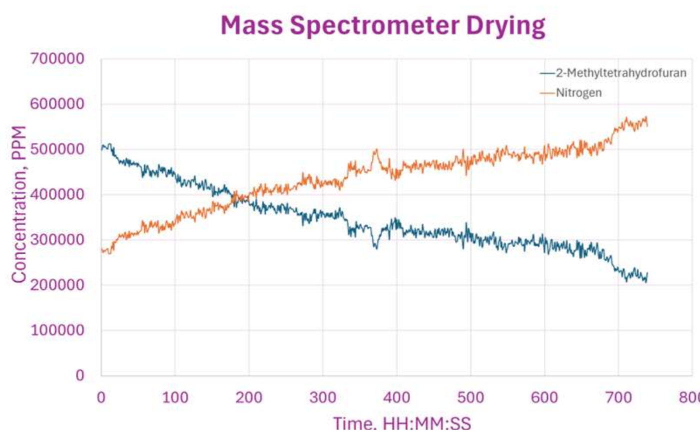

Figure 3 – Plot of Mass Spectrometer live software data.

Drying time reduced by 50%

125 kWh of Steam & 4404 L Nitrogen saved

812 kg of CO_2/batch saved

Potential saving of 81 tonnes CO_2/yr when at 100 batches

4 – Benefit to society

Assuming an **average 50% reduction** in steam and nitrogen per 100 batches, this saves **81 tonnes of CO2 per 100 batches**, which is equivalent to **207,000 miles driven** by an average petrol car[1].

However, drying times vary by process, and some solvents may be incompatible with spectrometer materials. So, this kit may not suit every campaign. I will address this by replacing components as needed or demonstrating, through further use and experimentation, that solvent contact is limited as only gases contact the materials.

5 – Next steps

I aim to work with our global teams to implement the spectrometer design across manufacturing sites.

With this trial I have confirmed installation in an 24/7 plant making 2000 kg/year, with the potential to also go into another plant predicted to make 120 tonnes/year.

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Acknowledgements

Thanks to Rachel Dawson, Graham Rutherford, Caroline Morgan and all at AZ that worked on this project.

References

1. Greenhouse Gas Equivalencies Calculator | EPA - https://www.epa.gov/energy/greenhouse-gas-equivalencies-calculator

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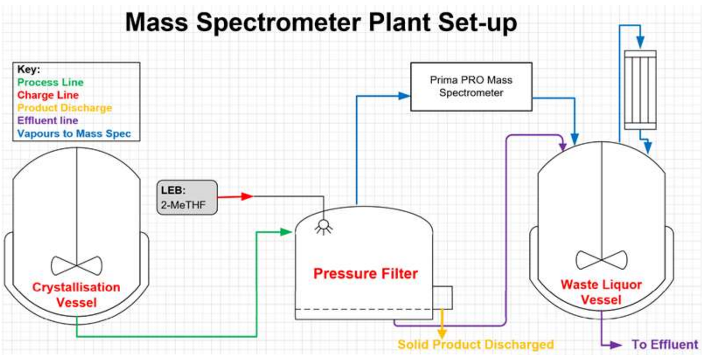

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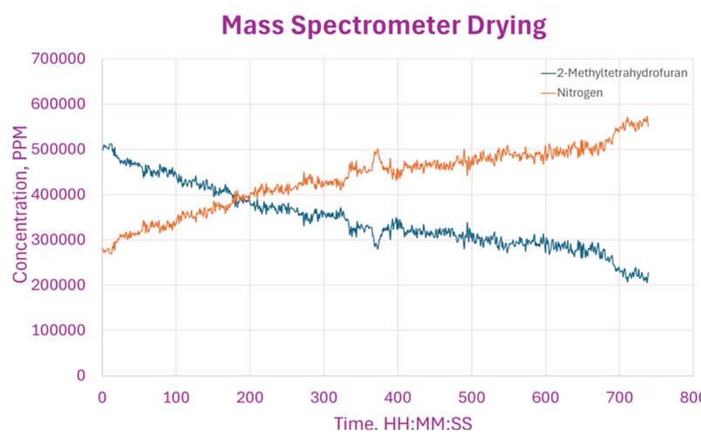

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