CASE STUDY: LOWER OPERATIONAL COST BY REDUCING GMP SAMPLING

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SITUATION

In terms of clinical GMP production, we're coming out of decades of high titres and yields with MAbs products, but new biologics present more product-related variance, titres are much lower, and yields are significantly lower as we have to remove all these product variants. As a result, we often end up with less mass than we've had historically. We're also moving towards high concentration formulations, so the final bulks are very small compared to what the industry has experienced historically.

This case study is about changing mindsets, as we're still behaving as if we're working with MAbs but we're living in a different world.

For example, litres of samples can be taken during GMP clinical manufacturing, which reduces the bulks even further and the result is we don't have that much mass i.e., if 5mlis needed to check product quality, a sample size of a litre is taken because it could be useful. We always try to prepare for future eventualities by having too much inventory, however, with that, we're creating a different problem.

ABOUT

Josefine was born and educated in Sweden and earned her PhD in Biochemistry from Lund University, Sweden. She earned her post-doc and has worked at Genentech, South San Francisco for 18+ years. Josefine has led development teams and served as CMC team leader for multiple projects.She has done extensive work and is considered an expert in E. coli derived proteins, ADC and bispecific antibodies. Currently, Josefine is managing critical reagent production at Genentech.

In this case study, Josefine shares her experience of reducing sampling volumes and the knock-on effect of that on cost and speed to clinic

CHALLENGE

During one trial we were sampling around 60% of our bulk, resulting in extra runs being added to the campaign to ensure there is enough clinical material. However, we also know that our clinical facilities are full, so when runs are added, there are other products that won't get into the pipeline because you're filling it up with sampling instead of getting material to the clinic.

A knock-on effect of high sampling volumes is that clinical supply is reduced and there are increased storage and development costs. We have 100s of -80C freezers using huge amounts of energy just for clinical development samples that can have a break of 2-3 years between clinical phases and mostly end up being discarded.

SOLUTION

Communication is essential. We've operated in such overflow conditions with so many resources for so long that the cost has never really been at the forefront. When you have unlimited space in your manufacturing facility it might not have a huge impact but when you're starting to have low yields with low mass and need extra runs, the cost adds up and then it takes longer to get to the clinic and to patients, which is a hidden cost we don't consider.

It's about communicating that the material is very costly with the aim of changing mindsets and behaviours. These behaviour changes are key to reducing the sampling sizes, which seems straight forward but we've been taking these high volumes for decades and many people who have been working in this industry for decades are very risk-averse. So, it's more of a challenge than it seems.

Using development instead of GMP material is another solution to reduce GMP sampling.

Outcomes

1. reduced bulk mass sampling from 63% to 15%
2. reduced number of GMP runs needed
3. no compromise in product quality
4. opened up facility space for additional projects

Overall, people were accepting of the changes. For example, in purification where we had taken litres from each pool, we're now just taking 5ml to have some material available for further analytics if we need it but not high volumes for development work.

When I did some calculations, I realised 63% of the bulk was being taken and showed this to the team, their reactions were the same as mine and we agreed that it was not reasonable, and we managed to cut back to 15%. However, in some situations, we have very high concentrations and sometimes you need a specific volume and not a mass for some assays and the higher in concentration you go, the more mass you lose.

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LESSONS

The knock-on effects of reducing the sampling to 15% mean we can reduce the number of manufacturing runs needed and that in turn opens up the facility so new projects can begin. The costs of this cannot really be calculated because what is the cost of a lost opportunity to put a new product into the facility?

This case study was presented at Evaluating Biopharma's recent virtual networking event 'Bioprocessing Strategies for Operational Efficiency', which included three in depth case studies and two interactive networking sessions.

Details of future events can be found here.

You can watch Josefine's case study in full and on-demand here.

ABOUT EVALUATING BIOPHARMA

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