



SINGLE - USE TECHNOLOGIES IN BIOTECH PURIFICATION: THE ADVANTAGES & CHALLENGES

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Case Study – Brineura

B:OMARIN®



- Brineura (cerliponase alfa) is the first & only approved treatment for any form of Batten's Disease.
- CLN2 is an ultra-rare and rapidly progressing brain disorder that affects approx. 20 children born in the US each year.
- Brineura is the first enzyme replacement therapy to be directly administered into the fluid of the brain.
- Brineura is a designated orphan drug in the US & Europe.

“The major challenges with this product”

Challenging



2.5 X Scale-Up

- Small Scale Batches
- < 3 years in the clinic
- Unknown Titres

Consistent



Low Endotoxin Requirement

- Pre Testing of WFI/Buffers
- Specification lower than WFI
- Intravenous infusion

Managing



> 1 batch /week

- Multiple batches in 1 suite
- Cleaning Verification/Validation
- Equipment Turnaround

“The major challenges with this product”

Product



Impacting Compounds

- Rebound during TFF
- Shorter shelf life
- Potential patient impact

Unique



aCSF Formulation

- Specifications on trace compounds
- Unique TFF Approach
- Long Processing Time

Understanding



High Value & Low Volume

- Orphan Drug
- High forecast demand
- Quality v Cost

The Approach



- Single Use where technology allowed.
- Immense workload for Material Qualification of SU components.
- First 100% Single Use Skids on site. Designed for multiple products with quick turnaround.
- Viral Inactivation, Product Hold/Mix, UFDF, Viral Filtration & Filling all 100% Single Use stages.

The Benefits....

- Cleaning Validation kept to a minimum.
- 0 Alert or Action Limits breached in 10 Lots. 0 CFU for Single Use stages.
- Manufacturing Flexibility.
- Novel approach even for regulatory agencies.

The Challenges

- Challenge from agencies on non-standard approach.
- Lot to lot variability of Single-Use components. Inspection of each item is essential.
- Higher level of diligence & understanding required by bio-technicians.
- Vendor engagement & support.

The Learnings

- Inventory Levels / Different Lots are vital to absorb the impact of issues.
- Site inventory & campaign planning becomes much more important.
- Supplier Change Notifications & Vendor Customer Service.
- Still require a lot of automation & more susceptible to human error.

THANK YOU