neuland

Innovative Process Solutions and Cost-Efficient Scale Up to Produce a High-Purity Pharmaceutical Intermediate for Phase 3 Clinical Trials

Developed a lower-cost process, scaled-up to produce six, 250-kg batches of high-purity intermediate packaged in a humidity-controlled environment.

Case Study

Key outcomes

Developed an improved process with a safer, inexpensive reagent

Identified and controlled impurities to < 0.1% each, with > 99% purity overall

Delivered six, 250-kg batches of pharmaceutical intermediate, one week ahead of schedule

Packaged in humidity-controlled environment to control hygroscopicity

About the client

A US-based company committed to developing and expanding access to innovative medicines for cancer and immune-inflammatory diseases.

Client objectives

The Client was looking for a reliable partner to develop a low-cost, high-quality process to produce a high-purity intermediate and to manufacture and package the intermediate at large scale for GMP manufacturing of drug product for Phase 3 clinical trials.

Existing challenges: Non-scalable flammable reagent, inefficient process

The Client's existing lab-scale process for a pharmaceutical intermediate used a flammable reagent that was unsafe at larger scales. A new process with a safer reagent was needed to produce a high-purity intermediate at a scale large enough for clinical trial manufacturing, while maintaining cost-efficiency. For optimal performance in the Client's manufacturing process, the intermediate was required to have:

Lower than 0.1% of each impurity

A residue on ignition of less than 0.1%

Less than 10 ppm of iron

A low moisture content in the packaged intermediate

Neuland's approach: Focus on cost-efficiency and consistent quality, facilitating large-scale manufacturing

At the start, the scientific team at Neuland evaluated several alternative reagents that would be safer to use at large-scale. They established a 1:1 ratio of iron powder and ammonium chloride in water to be a cost-effective reagent that could help efficiently provide high yield without a risk of flammability or explosion under the reaction conditions. Certain process modifications were made to control the red color inherent to iron and to prevent filter clogging.

A filtration aid was employed, which made the filtration step faster, making the process more cost-efficient. The team addressed the issue of color by using a carbon absorbent to capture the iron oxide in the process prior to isolating the intermediate. This approach resulted in an intermediate that was lighter in color, with consistent color from batch to batch, and with less than 10 ppm of residual iron. This low level of residual iron was important to the Client to mitigate the risk of any interaction in subsequent drug manufacturing steps.

The carbon treatment solution identified by Neuland also helped to reduce the individual impurity levels to below 0.1%. The team further reduced the residue on ignition (ROI) by incorporating an extra water wash to effectively remove inorganic salts. The elegant combination of these simple in-process steps brought the inorganic residue level to below 0.1%, as measured by ROI.

Scale up delivers consistent high yields

Following the successful optimization of a 200-gram lab-scale process using the iron-based reagent, which yielded high-purity intermediate with over 70% yield, the Client requested further scale-up. Neuland's team then executed a pilot-scale, 10-kg demonstration batch using the refined process. This batch met all specifications and achieved a consistent 70-75% yield, proving the robustness of the process. Subsequently, Neuland scaled up to commercial manufacturing under GMP conditions, achieving a steady 70-75% yield with high purity at this larger scale.

Neuland's commercial-scale equipment included a reactor capable of producing an 870-kg batch in the first step of the multi-step process. The company's commitment to ongoing capital investment enables efficient large-scale production.

Neuland's commercial packaging operations are equipped to handle challenging materials, such as the hygroscopic pharmaceutical intermediate in this case. To prevent the material from absorbing moisture from the air during the final packaging step, Neuland implemented dehumidification in the packaging environment, successfully packaging 30-kg containers with low moisture content.

Outcome: High-purity pharmaceutical intermediate meeting client requirements

Neuland's team developed and scaled-up an improved process with a safer, inexpensive reagent that produced consistent yield of the pharmaceutical intermediate in the range of 70-75%. Neuland's scientists identified and controlled impurities to less than 0.1% each, with greater than 99% purity overall. The optimized process successfully reduced inorganic residue level to below 0.1%, as measured by ROI, and reduced residual iron to less than 10 ppm, resulting in a consistently light color that met the Client's requirements. A humidity-controlled packaging environment allowed the hygroscopic material to be successfully packaged in 30-kg packages with low moisture content.

Neuland's scientific team devised cost-effective solutions that will benefit future commercial production. Their efficient work resulted in project completion one week ahead of client's request, achieving scaled-up manufacturing in just eight months from the initial development phase.

Conclusion: Lower-cost, high-quality intermediate delivered on time

Neuland swiftly identified a safe, cost-effective, and efficient process that was successfully scaled up to produce a high-purity intermediate suitable for clinical manufacturing. The team developed an innovative process solution to ensure high-quality material production, cost-efficiency, and reduced development timelines.

About Neuland

A global CDMO, Neuland delivers success for biotechnology and pharmaceutical clients seeking complex APIs and Intermediates at all phases of the product life cycle. Their strength lies in overcoming complex chemistry challenges to advance drugs to market, having completed more than 150 NCE projects for custom APIs and developed more than 300 API processes. In business more than 40 years, with 500+ clients in more than 80 countries, Neuland boasts an impeccable record of quality standards. Make Neuland your strategic partner for improved process efficiency, quality, and ultimately, faster time-to-market for your drug product.

To choose Neuland as your strategic partner for developing high-quality pharmaceutical intermediates, connect with us:

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