Route scouting for a cost-effective process development.

Introduction

Process development is often undervalued at the early development phases due to the time or budget constraints. When inefficient research processes often get moved into ADME TOX or early clinical studies, it can lead to negative implications:

Implications of poorly developed processes:

- Higher costs and longer production times for initial clinical supply
- Bridging studies may be required if alternative routes are developed
- Risk of failed batches if the process is not robust
- Inefficient processes are not moved into commercial
- Raw materials or reagents require special handling or are not readily available

Thermo Fisher Scientific implemented a dedicated team, the Chemical Process Research Group (CPR Group), at its Regensburg (Germany) API site that performs specifically early process research on new routes with dedicated analytical equipment and resources.

Our approach to route scouting

Synthetic Design	Feasibility	Demonstration batch	Scale up to support CTM
• Literature search • Raw material consideration (cost / availability / form) • Waste material considerations	• Proof of Principle, gram scale • Screening of catalysts, reagents and solvents	• 10 to 100 g scale (suitable for ADME and TOX) • Initial impurity assessment (cost / availability / form) • Safety studies • Solid State Characterization	• Additional process • Analytical development • Clinical supply • Polymorph / Salt screening

+1 919 226 3200 • thermofisher.com/patheon • pharmaservices@thermofisher.com

Published 04/23

What we do differently

Process research on new routes, driven by manufacturing experience for clinical and commercial scale API
Parallel screening of multiple synthesis routes to identify a scalable and robust process for the target molecule
Emphasis on atom efficiency, safety, and commercial viability
Tackle projects with a dedicated team of experts who understand the future challenges of upscaling

The Regensburg API site has 50 years of process development and manufacturing experience and an extensive track record of delivering new or optimized routes.

It offers a wide range of laboratory equipment and analytical tools to ensure rapid route development in close collaboration with in-house quality unit:

Reaction calorimetry (DSC, EasyMax 402)
Laminar Flow cabinet to handle Tox Cat. 3A substances (OEL 1-10 µg/m3)
Biotage flash chromatography
HPLC (UV, MS, CAD, RIv)
GC (FID, MS)
Parallel and flow reactors

In addition, there is the posibility of scale-up and chemical production of intermediates and APIs for ADME TOX, Phase I and Phase II clinical trials under cGMP, as well as ISO conditions. Every year we transfer ~30 projects to manufacturing which results in more than 100 chemical steps per year. Many routes developed at the site have been later transferred to other sites within the API network for larger scale production, and eventually moved into the commercialization.

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Published 04/23

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