Quotient Sciences

Molecule to cure. Fast.™

Information sheet

Drug Substance Synthesis and Manufacturing

Tactical deployment of best-in-class synthesis technologies to minimize chemistry costs and move your drug substance supply off the critical path.

At Quotient Sciences, we understand that every molecule and program is different, and that there is no single manufacturing solution. We take an agile and flexible approach with our customers programs, offering bespoke drug substance synthesis and manufacturing, helping to accelerate molecules from candidate selection to clinical proof-of-concept and onwards towards commercial scale. Our drug substance team works closely with our customers to ensure they have made the right decision, for the right molecule, at the right time.

Our 40+ years of expertise in a wide range of synthetic organic chemistry coupled with extensive experience in flow chemistry, synthetic biology and biocatalysis can significantly save months of development time for our clients.

Our Expertise

Over 90% of our Process Research and Development team are qualified to PhD level and have over 100 years' combined experience in drug substance manufacture. Quality is built into everything we do, starting with the design of your synthesis. We develop routes to drug substances with regulatory compliance, efficiency, and cost in mind. Where appropriate, we undertake experimental design, parallel reactor and computational modelling approaches to shorten development timelines.

We are a trusted partner in the manufacture of your drug molecule, offering standalone and fully integrated services spanning preclinical to commercial drug substance from milligrams to multi kilogram scale.

Capabilities include

- Glass and PTFE 5L, 20L and 100 L GMP reactors to provide near universal chemical compatibility
- GMP processing capabilities from 100g (5L scale) to 7kg (100L scale) per batch
- Continuous processing capabilities up to 5kg per day
- Cryogenics to -80 °C
- High pressure hydrogenation to 50 bar up to 3kg per day
- HF-Calorimetry
- Parallel reactor capability
- PAT reaction monitoring
- Large scale GMP chromatography (up to 500g)
- CFR21 compliant data logging

Our Integrated Approach to Drug Substance

In addition to a wide array of open access analytical equipment, our chemists work in partnership with our Quality Control team to ensure that robust data is generated quickly and efficiently throughout the project to support further development. For integrated Drug Substance & Drug Product projects, cross functional project teams “bridge the gap” between drug substance and drug product, shortening program timelines by sharing knowledge and materials from project initiation and continue to work side by side for the duration of the project, ensuring that nothing gets missed along the way. Our experienced chemists and formulators work hand-in-hand with our manufacturing scientists across our global network of sites to ensure seamless program delivery, on-time and on budget.

Services offered

- Route Scouting
- Process research and development
- Pre-formulation
- Salt & polymorph screening
- nonGMP and GMP drug substance manufacture
- Analytical method development and validation
- Experimental design (DOE)
- Stability studies
- Impurity synthesis
- GTI assessment
- IMPD/IND dossier preparation
- Technical investigation
- Formulation development – preclinical and clinical
- Clinical drug product manufacturing

Case studies

API development for a US biotech client

A US Biotech was developing combined small molecule & biologic immunotherapy treatments. Quotient rapidly developed a scalable route towards an analogue of a new drug substance, with a definition of an optimal salt form for formulation. We developed two process route options & selected one based on scalability and process economy. An API free base was generated, and a rapid salt screening protocol undertaken. A solubility study was conducted showed optimal solubilization at a set pH. The drug substance analogue showed superior solubility to the prime API. The client was delighted & has filed provisional IP.

Drug substance salt selection

A US Biopharmaceutical was seeking drug substance and salt screen selection for their molecule. We manufactured the drug substance and screened a selection of corresponding pharmaceutically acceptable salt forms. We assessed each salt form for salt formation, solubility, hygroscopicity, crystallinity, polymorph tendency, chemical stability & particle size/morphology. From the resulting salt forms, a candidate was selected that exhibited optimal characteristics for formulation and bioavailability. The API was manufactured, and a series of salts subsequently produced. An optimal salt form was identified, manufactured & progressed to a formulated product for clinical use.

Thermal rearrangement – A continuous approach

Quotient Sciences was seeking to improve the yield and purity of a US Biotech's API intermediate using flow chemistry. The thermal rearrangement of 7.5 kg of an API intermediate was technically challenging & a labor intensive process in batch with a typical yield of 50% and a poor impurity profile. Initial reaction conditions were Diphenyl ether, 180°C, 2 hours (followed by acid-base extraction & solvent switch into dichloromethane then ethanol), which was complex and garnered low yielding. A process innovation was applied to run continuously using a scalable coil reactor with superheated ethanol as solvent. Yield & purity of the product were increased, and overall throughput was improved due to shortened residence time & number of human manipulations was reduced. As a result, the implementation of flow chemistry led to significant time and cost savings.

Integrated drug substance & drug product project

A US Biotech client was developing combined small molecule & biologic immunotherapy treatments. The client's initial drug substance required a complex synthesis and the drug product isolated as an amorphous solid with poor solubility and no salt form available. Rapid development of a scalable route towards an analogue of a new drug substance took place in 15 weeks, with definition of an optimal salt form for formulation. Two process route options were developed & one was selected on the basis of scalability and process economy. Six salt forms tested and the new analogue showed superior solubility to the prime API and similar activity towards the biological target. A shorter synthesis was developed, and solubility of the final drug form was markedly improved. This case study demonstrates the power of an integrated drug substance / drug product development capacity.

Who is Quotient Sciences?

Quotient Sciences is a drug development and manufacturing accelerator providing integrated programs and tailored services across the entire development pathway. Cutting through silos across a range of drug development capabilities, we save precious time and money in getting drugs to patients. Everything we do for our customers is driven by an unswerving belief that ideas need to become solutions, molecules need to become cures, fast. Because humanity needs solutions, fast.

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