Quotient Sciences

Molecule to cure. Fast.™

Information sheet

Aseptic Development and Manufacturing

Parenteral drug products, also known as injectables, are a rapidly growing area in the pharmaceutical market. Injectables include intravenous (IV), subcutaneous (SC), or intramuscular (IM) routes of administration, and are the preferred dosage form for drugs that are incompatible with the gastrointestinal (GI) tract (e.g. biologics and vaccines), require a highly localized effect (e.g. in chemotherapy), or require a rapid effect (e.g. in an emergency).

The development and manufacture of parenteral drug products require specialized facilities and equipment in order to ensure patient safety. Since injectables bypass many of the body's natural defenses, such as the GI tract, they must be supplied as sterile products that are free from bacterial contamination. This is achieved through aseptic manufacturing, which requires careful planning, thoroughly trained personnel, and dedicated facilities.

Our expertise

At Quotient Sciences, we have over 30 years of experience in the development of parenteral drug products, from candidate development through to clinical trial manufacturing via aseptic filtration techniques. Our innovative approach enables rapid development and manufacturing of sterile solution formulations for parenteral administration, with a strong emphasis on environmental and process controls.

We have the expertise to develop, manufacture, test, release, and supply a range of formulations (IV, SC, and IM administration) for a variety of clinical study types, including first-in-human (FIH) healthy volunteer studies assessing safety, tolerability, and pharmacokinetics (PK), as well as radiolabeled formulations for human absorption, distribution, metabolism, and excretion (ADME) studies. These services can be utilized as a standalone offering or as part of a fully integrated drug development program for our customers.

Our approach

In early development, simple dosage forms are typically used to quickly obtain Phase I clinical data. We plan ahead to ensure a seamless transition to scalable dosage forms for proof-of-concept (POC) patient studies and beyond, improving the likelihood of formulation success.

Our experienced scientists are always looking downstream, ensuring our customer's target product profile (TPP) is top of mind. The dosage forms we develop, and their associated manufacturing processes, are fully documented and discussed prior to the manufacture of representative (technical) batches. This not only confirms the suitability of the proposed process but is also used to establish a shelf life for the clinical products. Good Manufacturing Practice (GMP)-compliant clinical products are manufactured with comprehensive support from our in-house quality control (QC) and quality assurance (QA) teams and can be released by a qualified person (QP) prior to shipment of the investigational medicinal product (IMP) to the clinic. Alternatively, aseptically prepared drug products can be manufactured in our United States Pharmacopeia (USP) 797 and 800-compliant compounding pharmacy.

Clinical testing and manufacturing support

At our clinical pharmacology facilities in both the UK and US, we develop and prepare sterile drug products for immediate dosing within our Phase I, healthy volunteer clinics. This is done at a small scale to support FIH studies (typically up to 25 units of 10-mL vials or >10-mL bags/syringes). With a strong emphasis on environmental and process controls, there is strong scientific justification and risk analysis to support reduced product testing and setting a very short shelf life. We follow just-in-time (JIT) manufacturing processes and deliver drug products to our clinics, which at our Nottingham facility are located in the same building as our manufacturing facilities, for dosing within 48 hours.

Using our unique, integrated drug development and clinical testing platform, Translational Pharmaceutics®, we can perform rapid "make-test" cycles to manufacture, release, and dose sterile drug products. This facilitates real-time decision-making based on emerging clinical data and provides flexibility to adjust formulations within a study, which ultimately simplifies the supply chain, shortens timelines, and reduces R&D costs.

In the UK, we have laboratories where parenteral formulations are developed and GMP manufacturing facilities where they are processed by double aseptic filtration. Bulk preparation and initial filtration are performed in a Grade C (Class 10,000) environment within the GMP facility. The final filtration stage is typically direct into a pre-sterilized, pyrogen-free final container closure system and performed in Grade A (Class 100) isolators located in the Grade C (Class 10,000) GMP environment.

We can also manufacture and ship sterile drug products (25–150 units of 2–20-mL vials) for Phase I/II, FIH (healthy volunteer/patient) studies at third-party clinics across Europe, the UK, and the US. When supplying sterile drug products to third-party clinics, we develop a formulation and establish at least a 1–3-month shelf life for the product to ensure the required 2-week QC release-testing period can be accommodated in the clinical planning.

Our state-of-the-art facilities are licensed by the UK Medicines and Healthcare products Regulatory Agency (MHRA) to manufacture sterile IMPs, including radiolabeled, high-potency, and some cytotoxic and controlled substances. The facilities contain warehousing, dispensing, manufacturing, clinical labeling, and packaging rooms. These rooms are fully qualified and maintained as appropriate, with Grade A facilities available for the manufacture of sterile products. All areas are controlled to specified temperature and humidity limits with appropriate air pressure differentials between rooms, all of which are continuously monitored and recorded. In addition, routine cleaning and environmental monitoring schedules are followed.

In the US, at our clinical pharmacology site, we have an International Organization for Standardization (ISO) 7 pharmacy cleanroom suite that contains two ISO 7 buffer rooms for sterile compounding. There is a positive-pressure ISO 7 buffer room, which contains an ISO 5 laminar airflow workbench (LAFW) for non-hazardous, sterile filling. There is also a negative-pressure ISO 7 buffer room, which contains an ISO 5 biosafety cabinet (BSC) for hazardous, sterile filling.

Microbiological testing

At Quotient Sciences, we have expertise in the development, validation, and application of pharmaceutical microbiological methodologies as part of our sterility assurance assessment. These can be applied to the release and stability testing of drugs and maintenance of the manufacturing facility, including environmental monitoring and manufacturing support. As this can all be performed within a single organization, there is no need for technology transfer activities. In addition, we are equipped to perform microbiological testing on radiolabeled, high-potency, and some cytotoxic and controlled substances.

Applications and case studies

Peptides

To obtain therapeutic plasma levels, peptides usually require injection. At Quotient Sciences, we have developed a number of peptide formulations for injection via IV, IM, and SC routes.

For example, one of our clients, Stealth BioTherapeutics, had already developed an IV formulation of their peptide drug target, and they asked us to develop a SC formulation to enable patient self-administration for a different indication. It was important to ensure the tolerability of the formulation while achieving similar PK parameters. Using our Translational Pharmaceutics platform, we developed a formulation design space to enable flexibility to adjust both the dose and volume of injection administered to healthy volunteers, with decisions about what would be dosed in the next dosing period informed by the PK and tolerability data from the previous dosing period. The outcome was that we identified a SC formulation that was well tolerated and hit the required target PK parameters in less than 7 months.

IV microtracer studies

At Quotient Sciences, we offer IV microtracer studies, which can be used in early clinical development to define IV PK and absolute bioavailability for non-parenteral drugs without needing to develop a conventional IV formulation. This involves administering an unlabeled oral therapeutic dose alongside a ^{14}C-labeled IV microtracer dose. High-sensitivity analytical techniques, such as accelerator mass spectrometry (AMS), are used to quantify the low concentrations of ^{14}C-labeled drug in plasma arising from the microtracer dose. This approach supports earlier and more informed decision-making in clinical development and provides significant overall cost and time savings.

For example, one of our clients, Galapagos, integrated an IV microtracer study with the human ADME study for Ziritaxestat. We developed the IV formulation and then manufactured and release-tested the drug product just prior to dosing in our clinic. By extending the analysis of samples from the study to include the IV mass balance, and by comparing to data generated in the ADME period, we were able to assist Galapagos to evaluate not just absolute bioavailability of their oral drug product but also fraction absorbed, fraction surviving hepatic elimination, and fraction surviving gut metabolism. This provided a comprehensive understanding of the absorption and elimination of the drug from the body after administration.

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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