



# Drug Product Release

You need to ensure that your biopharmaceuticals, pharmaceuticals and medical devices are produced according to the strict requirements of Good Manufacturing Practice (GMP) and that the release testing packages are carefully designed to demonstrate that compliance. The Biopharmaceutical Services (BPS) group at Charles River provides release for the clinical products we manufacture for our clients and also to support any external requirements for release testing, whether for complete programs or for selected studies only. The BPS group provides release services for the European Union (EU), United States (US) and other regulatory-distinct markets and can act as a single site for your global release testing.

We provide a full range of product release support, from addressing biosafety concerns and analyzing potency using suitable bioassays, to determining purity and other biochemical characteristics. Our commitment to providing rapid turnaround times for all testing helps minimize the period between production and release. We offer assays in compliance with European Pharmacopoeia (Ph. Eur.) and US Pharmacopoeia (USP) monographs, as well as new assay development and validation.

## EU Release

All marketed products or investigational medicinal products (IMPs) manufactured outside the EU require re-testing at an EU-based facility. Charles River can provide this service through its local European facilities. In addition, testing programs may include differing combinations of microbial testing, biochemical analysis, purity, safety and potency testing, as required by the client for market entry.

## Technology Transfer

Controlled management of technology transfer is key to efficiently establishing an effective lot release program at a contract research organization (CRO). BPS achieves this management by initiating discussions with clients regarding their methods at the earliest stages and undertaking careful study of how the process is actually conducted. This methodology allows us to transfer and establish client methods at our facility in the shortest timeline, and to maintain control of these methods throughout the life of the product. Our experience with technology transfer, focus on communication and rigorous generation of documentation and study performance enables us to support you in the most effective and timely manner possible.

## Purity and Impurities

- HPLC/SE-HPLC
- Affinity/ion chromatography
- Mass spectrometry
- SDS-PAGE
- IEF and blotting techniques
- Capillary electrophoresis
- Immunoassays
- Protein concentration
- Residual DNA/host protein
- *In vivo* pyrogen
- LAL endotoxin
- Cytotoxicity testing
- Microbial testing

## Physicochemical Properties

- pH
- Viscosity
- Appearance
- Subvisible particulates
- Osmolality

## Identity

- Gene sequencing
- Peptide mapping
- Glycosylation profiling

## Bioassays

- *In vitro*
  - Reporter gene
  - Immunoassays
  - Cell proliferation
  - Cell survival
  - Monocyte activation test
- *In vivo*
  - Pharmacopoeial studies
  - Vaccine potency testing
  - Protection bioassays
  - Immunogenicity assays
  - Stability
  - Abnormal/general safety toxicity

## Biochemical Analysis

Typically, a release testing program is comprised of key quality-indicating assays determined during earlier characterization studies. Utilizing a range of techniques, these assays cover areas such as identity, purity and impurity, physicochemical properties and dose form-specific tests.

## Potency

Potency is a crucial release specification for biopharmaceuticals. Physical techniques, typically used to determine whether proteins have folded correctly, cannot be easily applied to final product for regulatory compliance purposes. Therefore, bioassays are frequently used as a suitable alternative method to measure activity and potency.

Bioassays may be either *in vitro* or *in vivo*. *In vivo* bioassays measure appropriate clinical end points after dosing with the product, while *in vitro* bioassays detect a quantifiable end point after the product is added to an appropriate cell line. The bioassay staff at Charles River can validate partially developed *in vitro* bioassays and develop or transfer *in vivo* bioassays as required.

## Experience

BPS is a highly experienced team, committed to successful long-term relationships with our product release clients. We have gained valuable experience over the past 10 years generating data in support of more than 1,000 batches of various protein products.

## Typical Release Testing Package

- pH determination
- Visual assessment
- Determination of volume in syringes and vials
- Osmolality determination
- LAL test for bacterial endotoxins or *in vivo* pyrogen testing
- Monocyte activation test
- Spectrophotometric determination of polysorbate 80
- Protein concentration
- SDS-PAGE with western blot
- Isoform analysis (IEF, C-IEF)
- Size-exclusion HPLC of proteins (purity, impurity profiling and quantification)
- Cation-exchange HPLC of proteins (purity, impurity profiling and quantification)
- Reverse-phase (RP) HPLC of proteins (purity, impurity profiling and quantification)
- Reporter gene bioassay
- *In vivo* potency and stability testing
- Sterility and other microbiology tests
- General safety/abnormal toxicity
- Residual DNA/host protein

