

Injectables – A *sure*-SHOT solution to your needs

At Piramal Healthcare Ltd, we believe in providing services with high quality and fast turnaround...every time. With our mission of “quality on time” we crave to augment the human knowledge for evaluating and solving challenges for developing Injectables.

Research capabilities

PHL offers contract manufacturing and development services for Injectable dosage forms. We are experienced in developing injections for NCE up to class IV i.e. upto 0.1 µg/mL; and for generic molecules for regulated markets, including pediatric dosage.

An injectable dosage form development program generally includes preformulation studies, compatibility studies, formulation development, method development analysis, microbial method (BET, sterility, preservative efficacy) development, stability studies including freeze-thaw studies, scale-up studies (10L), tech transfer, extractable and leachable studies and primary and secondary packaging development, cGMP manufacturing of clinical trial materials, and formal stability studies according to ICH Guidelines.

At PHL, we have the insight into the complex, scientific requirement, and the multidisciplinary skill sets required for the same. We offer end-to-end programs and /or any of the disciplinary of the program for Injectable dosage development.

Our capabilities include manufacture and development of sterile liquids and lyophilized products. Our internal standards and systems, keep us in line with the international guidelines, with the same time, providing with equivalent flexibility to harmonize with the clients' requirements.



Arnold H. Glasow had once said *“Success is simple. Do what’s right, the right way, at the right time.”* At Piramal Healthcare we have added upon the quote and believe in “doing the right thing, in the right way, at the right time at the very first time.” Thus, providing formulation development services that are complemented by impregnable integrity and confidentiality, that fulfill the regulatory requirements and that deliver flawlessly on time.

Personnel capabilities:

PHL is powered by a team of prominent leaders and qualified scientist with background in pharmaceutical science and allied areas, which provide expertise in every facet of dosage form development.

The R&D department is efficiently led by Dr. Vandana Sonavaria who has more than 15 years of experience in formulating challenging injectables.

At PHL all our scientists are aligned to the vision of knowledge, action and care. This spirit helps us to challenge our own standards and perform better, in our endeavor for a compassionate cure. Their knowledge about technical and commercial requirements paves way for advances in the science of injectable drug delivery.

Laboratory capabilities

a) Formulation lab:

Our R&D has the latest equipment required for development and testing these formulations. Our formulation laboratory boasts of sophisticated equipment like:

- D O meter- D0110
- Nephrometer Spectronic 20 D+ Digital
- Headspace O2 analyzer -898 025
- Rheometer (LV DV III ULTRA-Brookfields)
- Osmometer-OSMOMAT 030
- pH meter (Eutech)
- Turbidimeter -2100 AN
- Tachometer-DT 209X
- Glove box , Mini 220W KH- 34750-25
- Lyophilizer- Genesis 25 SQ EL, CIP
- High Intensity Lightmeter-EA30



b) Our analytical laboratory developed per regulatory requirements and conforming to GLP is equipped with:

- Gas chromatograph (Shimadzu GC 2014)
- HPLC [Waters Alliance system with UV / PDA detector and Empower client network server (2695 / 2487 - 2996). Shimadzu LC solution with UV detector (LC-2010A HT)]
- FTIR (Shimadzu FTIR -8400S)
- Particle counter - HIAC Royco, USA- Roycomodel 9705
- Particle size Analyzer- Malvern Wet analyzer
- UV Spectrophotometer- Shimadzu UV1700

c) Our state-of-art pre-formulation laboratory is furnished with:

- Cryogenic Differential scanning calorimetry (Perkin Elmer Diamond DSC Autosampler)
- Cryogenic microscopy (Leica)
- XRPD (Bruker AXS, Germany, D8 Advance)
- TGA (Perkin Elmer, USA- Pyris 1 TGA)
- DVS (Surface management systems -DVS Advantage)

d) Our Microbiology laboratory is equipped with:

- Autoclave- (Vaiktron- customized with rotary drum, raining type and HP/HV and standard cycles)
- HLAf (Klenzaid- 1590-48-24-30)

e) Our extensive range of stand-alone and walk-in stability chambers (Thermolab) offer:

- Conditions as per ICH guidelines
- Photostability conditions
- Allow flexibility to absorb conditions that are specially designed per customers' requirement.

Development Strategy

As Piramal Healthcare we understand the latest trends and requirements and the pitfalls potentially occurring during development, industrialization and commercialization of an injectable dosage form.

Development processes that can be handled in R&D on Small volume parenterals involving vials and ampoules and large volume parenterals involving infusion bags are as follows:

- Terminal sterilization
- Aseptic filtration
- Scale of batch sizes: Easily handle batch size of as low as 50mL up to 10L



The principle of Design of experiments (DOE) is applied to achieve Quality by design (QbD) in formulations developed. The designing is conducted by evaluating a matrix of potential parameters in respect to the active ingredient being formulated. This allows for achieving our goals of low cost service offerings with efficiency for on-time delivery and quality in the services.

Two different tools for formulation development are used based on the clinical phase of the active ingredient.

a) Development steps for NCE:

- 1) Reviewing available data from the client.
- 2) Focusing on characterizing and understanding the molecule for developing injectable for IND or NDA filing. For this, preformulation studies like solubility studies and characterization using XRPD, TGA, DVS and DSC play a vital role.
- 3) The formulation development is generally initiated in the following order after weighing out variety of options and paradigms:
 - A) Clear Solution:- Aqueous and non-aqueous
 - B) Suspension [Nanosuspension]
 - C) Emulsion
 - D) Lyophilization
- 4) Conducting stability studies on the developed formulation at conditions as per ICH guidelines and/or as per customers' requirement.
- 5) Manufacturing of clinical batches.

b) Development steps for Generic molecules:

- 1) Literature search: orange book, PDR, USP, Martindale, Florey's Analytical profile of drug substances, FOI data Sci-finder search, other physiochemical properties of molecules
- 2) Characterization of the RLD samples for pH, tonicity, fill volume, viscosity, density, appearance, head space oxygen, impurities, assay, toxicity and packaging material
- 3) Excipient compatibility studies and API evaluation with respect to Drug Master File, polymorphs, and impurity profile.
- 4) Formulation development involves:
 - A) Evaluation of manufacturing process with respect to sequence of excipient addition, temperature, mixing time, etc.
 - B) Determination of D- value: Autoclave cycle development.
- 5) Analytical method development and validation as per ICH guidelines



6) Stability studies for stopper compatibility, effect of oxygen, pH, metal ions, light, PET, extractables and leachables and compatibility with manufacturing components, at conditions as per ICH guidelines.

7) Pivotal Batch studies: Mixing time for achieving homogeneity, hold time study for bulk, admixture stability, freeze thaw and light sensitivity.

Partnerships:

As rightly said by Woodrow Wilson, *"I not only use all the brains that I have, but all that I can borrow"*. PHL has the maturity and versatility to work with partners in a variety of options.

PHL has partnerships with manufacturers having USFDA approved sites for conducting manufacturing of clinical trial batches and subsequent commercialization.

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