



FACTSHEET

API to regulatory submission in as little as 26 weeks...

Once again, Aptuit is taking a bold, new step to engineer a better drug development process. Aptuit's accelerated drug development service will substantially reduce time to first-in-man clinical trials while improving consistency of results and product knowledge, the two backbones of quality.

Accelerated drug development reduces time from API to regulatory submission (IND/CTA) in as little as 26 weeks for appropriate compounds. These reductions are achieved by tightly integrating traditional silos - API manufacture, toxicology, metabolism/ pharmacokinetics and clinical supplies - into a single project managed by a veteran, dedicated project manager and staffed by professionals with experience spanning the development process.

The accelerated drug development approach is based on a novel discipline we call development science, and centers on four primary elements:

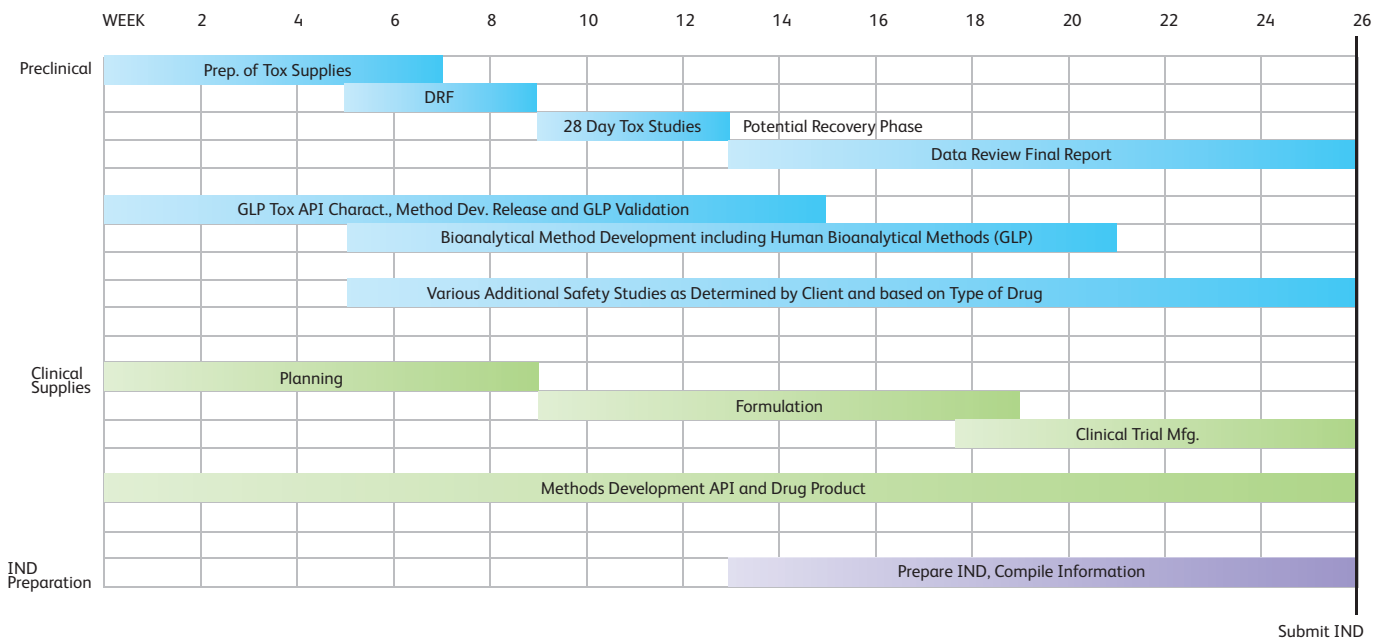
- 1 Eliminating artificial barriers between drug substance (API) and drug product development, merging these into a single track,

called clinical supplies. This approach streamlines pre-Phase I process down to only three development tracks: (a) Preclinical toxicology; (b) Clinical supplies; and (c) IND/CTA preparation. These tracks operate in parallel to reduce time to clinical trials.

- 2 Modern approaches, such as amorphous dispersions, are used to increase the solubility and bioavailability of the test compound.
- 3 Utilizing quality-by-design strategies in the earliest stages and throughout the development cycle. This will enable the facile implementation of such strategies for successful drug candidates at each stage.
- 4 Establishing information for patent filings even during this early timeframe and maintaining the seamlessness and integrity of data throughout.

General Plan

The diagram below outlines how the accelerated drug development process works and approximate time frames for various parallel development tracks.



The chart on the previous page is divided into three tracks: Preclinical, Clinical supplies, and IND/CTA preparation. The preclinical program includes a rigorous Aptuit preclinical study involving 28 day tox studies as well as a complete battery of additional tests, designed and implemented with an eye toward the requirements for successful regulatory submission (IND/CTA) – with non GMP material timelines can be further reduced. The clinical supplies module includes a significant planning component where the type of dosage form for clinical supplies is determined based on the solubility of the API, as well as methods development. Finally, there is an IND/CTA preparation segment during which the IND/CTA will be prepared. All of this is intended to be accomplished in as little as 26 weeks. This plan is based on the assumption that the client is able to provide Aptuit with, for example, 1 kg of GMP drug substance on day one – a capability Aptuit itself is able to resource.

Formulation Approaches

The first approach involves amorphous dispersion in capsules. This approach will increase exposure for the estimated 80% of NCEs with solubility problems. A typical amorphous formulation will be a dispersion of the drug in a polymer. The second approach involves filling a capsule with crystals of the drug. Such a product is the simplest formulation and greatly reduces development time. An automated powder filling device will be used to prepare both of these drug products. The third formulation is a powder in a bottle formulation that is intended to be dissolved just prior to administration. If needed, Aptuit will help develop the vehicle for dissolution or use the client’s preferred solvent.

Quality Overall Summary

The Aptuit approach was developed based on the latest FDA standards for quality. These concepts are briefly summarized in the wheel below. Aptuit’s work on its clients’ behalf focuses on the inner part of the wheel. As shown on the wheel, step 1 is product design as described in the formulation approaches section. A process is then designed to produce the product. Quality-by-design elements are at the heart of the process design, and extensive measures are taken to ensure stability, for example. The process is monitored using sophisticated analytical equipment including in-line Raman probes. This information will be provided in a report suitable for submission to the FDA.

Intellectual Property

Information needed for patent filings is also provided as a standard part of the accelerated drug development offering.

Unique Aspects of Aptuit’s Fast-to-IND Service

- Integrated preclinical toxicology, clinical supplies and regulatory documentation and IND/CTA preparation support services
- Fast turnaround times, reducing time to submission
- Apply quality-by-design principles
- Best possible approaches for poorly soluble drugs including amorphous dispersion in capsule
- Intellectual property support elements

Additional Aptuit Capabilities

Aptuit offers a comprehensive suite of drug development services that range from candidate selection through to market, including consultancy services, API development and manufacture, preclinical and clinical technologies, pharmaceutical services, large and small scale manufacturing, IVRS, and clinical packaging and logistics, across a wide range of compounds, dosage forms and delivery systems.

For information about Aptuit’s services, please call or email:

+1 816 767 3900 North America

+44 131 451 2451 Europe

email: info@aptuit.com

or visit our website: www.aptuit.com

Engineering a better drug development process.

