

Indiana CTSI-NIPTE Clinical Supply Acceleration Service

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Abstract

The Indiana CTSI and National Institute for Pharmaceutical Technology and Education (NIPTE) have established a partnership to make both groups more effective in assisting the translation of drugs from bench to bedside. NIPTE is a non-profit organization consisting of several major colleges of pharmacy and chemical engineering departments. It was created to promote research in pharmaceutical technology, engineering and product development. Its capabilities include the knowledge, expertise and facilities to synthesize drug (API), develop a formulation, and prepare clinical supplies of that formulation. This poster outlines the Indiana CTSI-NIPTE partnership approach to accelerating translation and summaries for two completed projects.

Introduction

A clinical trial cannot proceed without the availability of affordable high quality clinical supplies manufactured in compliance with applicable regulatory controls. The goal of the CTSI-NIPTE partnership is to manage the needs for clinical supplies for CTSI investigators. In addition, this partnership focuses on developing processes and formulations, and ensuring availability of high-quality clinical supplies, in a time-efficient manner. The NIPTE-CTSI partnership will ensure that the manufacture of clinical supplies will never delay clinical trials.

The manufacture of clinical supplies requires three steps:

1. Development of a manufacturing process and synthesis of the drug (API)
2. Conversion of the API to a bioavailable formulation
3. Manufacture of clinical supplies and placebo.

Indiana CTSI-NIPTE Program

The ICTSI-NIPTE process begins with a request to the ICTSI Translational Technology Resources (TTR) representative. The TTR representative first contacts IU Health Investigational Drug Services (IDS) to check if they can provide Clinical Supplies. If not, NIPTE will perform a feasibility assessment to include regulatory compliance and budgetary and time constraints. If the project is feasible, NIPTE will obtain quotes and work closely with the ICTSI TTR and IDS representatives, as well as the investigator, to complete the project. This can involve three steps:

Step 1. Synthesis of API

The drug, either a small molecule or macromolecule, must be synthesized in large enough quantities to enable preclinical toxicological testing and manufacture of clinical supplies. The Institute for Therapeutics Discovery and Development, University of Minnesota, has capabilities for chemical process development, scale up and cGMP manufacturing of small molecule and protein-based drug substances.

Step 2. Formulation Design

In many cases during modern drug development a formulation must be developed to render the drug soluble. It has been estimated that over 60 percent of drugs under development are poorly soluble. NIPTE scientists at Purdue University, as well as other universities, have extensive experience in formulation approaches, including amorphous formulations, cocrystals and salts that solubilize the drug. NIPTE scientists design the correct formulation to achieve maximum blood levels for both toxicology and human trials.

GMP Manufacture of Clinical Supplies

After finding a bioavailable formulation, it must be scaled-up to make clinical and toxicological supplies. Two NIPTE schools, the University of Iowa and the University of Maryland, have facilities capable of manufacturing clinical supplies. Additionally, NIPTE scientists have extensive expertise in clinical supplies manufacture. NIPTE is ideally positioned to provide assistance in a wide range of clinical supply needs.

Regulatory Capabilities

The CTSI-NIPTE partnership also provides regulatory assistance based on the extensive regulatory experience of the team. NIPTE provides assistance with INDs and regulatory submissions, the ICTSI Regulatory Knowledge and Support program provides IRB advice, and IU Health IDS provide sign-off on records and label requirements.

Project 1. Treatment for Autism

Autistic disorder (autism) is a neurodevelopmental disorder causing marked impairment in social relatedness, communication and behavior. The goal of this study is to test acamprosate as a treatment for autism. This project includes a single-blind pilot study that aims to generate prospective pilot data on the potential efficacy and tolerability of acamprosate in 12 youth with autism ages 5 to 17 years. The hypothesis of this study is that treatment with acamprosate will treat core symptoms of autism in humans.

Clinical supplies of acamprosate were prepared by overencapsulating commercially available tablets. Placebo was prepared in the same way. The drug was packaged in 250-500 capsules per bottle and handled by IU Health IDS. The long-term goal of this proposal is to conduct a federally funded, large-scale controlled trial of acamprosate in autism.

Project 2. N-Acetyl Cysteine in Schizophrenia

N-acetyl cysteine (NAC) is an attractive molecule for the proposed study because it is an established neuroprotective agent and NAC modulates glutamate release. Sixty early stage psychosis patients will be randomized on a 1:1 basis to a 12-month, double blind, placebo controlled study to determine the efficacy and mechanism of action of NAC. NAC and matched placebo will be supplied in unmarked capsules. Dosing will begin at 600 mg/d and titrated up by 600 mg/d each week until a maximum dose of 3000 mg/d (BID) is reached.

Conclusion

The Indiana CTSI-NIPTE program combines sourcing of the drug substance (API), formulation design and clinical supplies manufacture in a fast development regime. In this way clinical supplies can be rapidly prepared for clinical trial.

Investigators are encouraged to contact the Indiana CTSI-NIPTE program early to ensure the best possible outcome. Formulation, synthesis and manufacturing, as well as cost and regulatory approvals, are potential roadblocks to clinical trial initiation, so it is important to involve the team as early as possible.

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