Developing a Pre-IND Packing Strategy to Expedite Clinical Trial Timelines

As biotechnology and pharmaceutical companies seek innovative solutions to expedite their timelines, efficient management of a clinical trial starts with strategic planning. Submission of an Investigational New Drug (IND) application is a major milestone in new drug development. It marks the transition from bench research to clinical studies in human participants. While awaiting the FDA Safe to Proceed letter for their IND, companies are able to take advantage of a Pre-IND labelling and packaging strategy for their clinical study by working with a CDMO operating out of Canada, such as PCI Pharma Services. In this article, we share insights into the IND application process, the benefits of applying a Pre-IND strategy utilising a Canadian-based CDMO, and how this approach can deliver reduced First Patient-In (FPI) timelines by 6–8 weeks.

Understanding the IND application process

Successful IND submissions require careful planning and compliance with FDA regulatory requirements and although not required, a Pre-IND meeting with the FDA is valuable. It is the company's first opportunity to ask specific questions of an FDA review panel pertaining to their specific product, reducing the risk of a clinical hold and delaying time of product delivery to clinic. Pre-IND meetings provide early FDA feedback on regulatory and scientific issues relating to clinical trial design, non-clinical research, and product related CMC questions. The specific feedback will assist in future drug development plans and preparation for submitting a complete IND application.

For companies entering the Pre-IND phase for the first time, seeking support from an experienced CDMO with a specialist regulatory consulting team can prove to be beneficial. Not only can the CDMO team represent the sponsor company at FDA meetings, but they can also provide valuable insight and assist in preparing the meeting package to ensure it contains appropriate information, such as clear focused questions for the review panel to answer, product overview information, design of preclinical and/or initial IND studies, and appropriate clinical / manufacturing and quality control data.

In terms of the process, following IND submission the FDA will review the application within 30 days for safety and assess whether the human subjects are incurring an unreasonable risk. At the end of the review cycle, the agency will either issue a Safe to Proceed letter or inform the sponsor that the study is on clinical hold. If placed on hold, the FDA will provide an explanation within 30 days and the sponsor will need to address the noted deficiencies. Submitted responses will then be reviewed and the FDA will determine whether the hold can be lifted. If the sponsor does not hear from the FDA within 30 calendar days after the initial submission, the IND goes into effect or becomes active on day 31. At that point, the study may proceed as submitted once it has been approved by an Institutional Review Board (IRB) whose purpose is to ensure the protection of the rights and welfare of the clinical trial participants.

During the 30 day review period, it is important to note that the FDA does not allow packaging or labelling of clinical trial material at any US facility. Even if a sponsor has filed an IND and received an IND number, they still must wait until day 31, when the IND application is in effect before they can package their clinical material within the US. In some circumstances, sponsors can import drug product into the US under "quarantine." However, shipping under quarantine does not give the sponsor approval to proceed with clinical packaging and the IND number must be available for import documentation.

Recognising the Benefits of Pre-IND Labelling and Packaging in Canada

Many companies are unaware that a strategy exists allowing upstream labelling and /packaging of clinical material prior to obtaining their IND Safe to Proceed notification from the FDA. The 30 day review period does not necessarily have to be a period of waiting.

While sponsors are awaiting authorisation from the FDA to conduct a human clinical trial in the US, Pre-IND labelling and packaging is possible in a GMP facility operating in Canada. The Canadian site can label and package the Investigational Medicinal Product (IMP) and have finished goods ready to ship to US investigator sites immediately upon receiving the Safe to Proceed notification. This strategy expedites upstream processing and can accelerate timelines for companies with critical FPI milestones.

If a company has not yet filed an IND application and does not have an IND number, it is still possible to send the clinical drug product into Canada for labelling and packaging. Canadian import laws do not require an IND approval nor IND number in the product import documentation.

Importing, Labelling, and Packaging Clinical Trial Material in Canada

The process for importing, labelling, and packaging is relatively straightforward, and an experienced clinical trial service partner can help guide sponsors on the process requirements as well as support the completion of the necessary Health Canada documents.

Once the drug product is manufactured, an Annex A document is filed with Health Canada to notify of the drug product import. According to the Conditions for Provision of Packaging/Labelling Services for Drugs under Foreign Ownership (GUIDE-0067), Part 1 of Annex A must be filed with Health Canada 10 days prior to the arrival of the drug product and accompanying shipment into Canada.

The sponsor then arranges for the physical transportation of the clinical material from the manufacturer to the clinical trial service

facility in Canada for labelling and packaging under GMP conditions. The Canadian-based clinical trial service partner will then hold the finished goods until exportation into the US can occur.

On day 31 following the submission of the IND application, the sponsor can consider the IND approval granted by the FDA. The Canadian clinical trial service partner will complete Part 2 of the Annex A document and file with Health Canada 10 days prior to exportation of the clinical finished goods into the US.

If the FDA does not allow the IND to proceed, the product cannot enter the US. However, any risks associated with labelling and packaging prior to receiving the Safe to Proceed notification are minimal because sponsors are simply reporting the data that they have already collected on the molecule. If the sponsor has solid safety data and promising outcomes from their test data, they will be well advised as to whether their IND will be allowed to proceed.

Understanding Regulatory Requirements for Importing Material into Canada

Canadian regulatory requirements vary based on the status of the IND approval and plans to distribute the product within Canada. The following are required:

- A bill of lading
- Packing slip
- Canadian customs invoices
- An active IND number (if available)
- An end-use letter
- Part 1 of Annex A filed with Health Canada 10 days prior to the arrival of the drug product and must accompany the shipment into Canada (If an approved IND is not in place)

If any of the material is intended to be used in Canada or distributed to Canadian clinical investigator sites, then a No Objection Letter (NOL) is required, which is the Canadian equivalent of the FDA IND Study May Proceed letter. Health Canada provides approval for products used in human studies via a Clinical Trial Application (CTA) and provides a formal response to the CTA via an NOL.

Supporting your Pre-IND strategy with PCI Pharma Services

Our clients come to us seeking solutions for their often complex and unique products and for our renowned reputation in offering unmatched flexibility, a client-centric experience and consultative approach, delivering a seamless clinical service including pharmaceutical development, clinical manufacturing, labelling, packaging, storage and distribution.

As the only Canadian clinical trial services company with the experience and expertise to deliver integrated end-to-end clinical solutions spanning packaging, labelling, kit design, storage (including cold chain), global distribution, returns and destruction, we can ensure that your life changing clinical medicines reach patients when needed upon receiving the Safe to Proceed designation.

Expediting First Patient-In timelines our *speed***solutions**™ combine value-added services and expertise, delivering an integrated approach for every clinical project, aimed at accelerating drug products through the earliest stages of development towards commercialisation.

Complementing our global services across development and manufacturing and clinical trial services, our expert Pre-IND support services to accelerate your project phase include:

- Bespoke Quality and Regulatory Services from support writing IND applications to representation and consulting with regulatory authorities such as the FDA and Health Canada
- Pre-IND clinical solutions facilitating the packaging and labelling of clinical prior to IND approval
- Industry leading expertise in Clinical Supply Project Management with PCI Clinical SMART™
- Faster First-In-Human manufacturing technologies including Xcelodose® microdosing and sterile robotic technologies

Clients can rely on our Pre-IND *speed***solutions**™ to accelerate timelines to meet First Patient-In dosing milestones, providing financial benefits. With access to a global network of manufacturing and packaging facilities with scalable sterile and non-sterile solutions, sponsors can de-risk their supply chain by eliminating the need to transfer to alternative suppliers, regardless of where they are in their drug product lifecycle journey.

As a fully integrated global CDMO, PCI truly spans the drug product lifecycle, connecting development and commercialisation, de-risking supply chains and delivering true speed to market on behalf of our clients. We are a strategic partner of choice and an integral part of the supply chain as the bridge between life-changing therapies and patients.

Sharlett Burgess

Sharlett Burgess is the Quality Director for the PCI Pharma Services sites in Canada. She has responsibility for the clinical site in Burlington, Ontario as well as the Commercial site in Mississauga, Ontario. After completing her studies in chemistry and microbiology she began her career as an analytical chemist working with Eli Lilly for 5 years. She went on to work with AstraZeneca for 15 years in various quality roles in their commercial and clinical business. Sharlett has over 25 years of pharmaceutical experience and has successfully led the Clinical and Commercial sites over the past 9 years at PCI (formerly Bellwyck Pharma Services). She strives for excellence in Quality and Compliance, ensuring that the sites have robust quality management systems that meet client and regulatory requirements.

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