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Water Cooler Chat

Importing Clinical Supplies into China

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YOUR BRIDGE BETWEEN LIFE-CHANGING THERAPIES AND PATIENTS

PCI Clinical Trial Services hosts a weekly virtual ***Water Cooler Chat*** series, where our subject matter experts host informal discussions around a number of clinical supply hot topics.

Importing Clinical Supplies into China

Rich Nelson, Sr. Manager, Global Logistics, recently discussed the different aspects to importing clinical supplies into China including: the unique import requirements that China has, the benefits of running clinical trials in China, and moving clinical supply between Hong Kong and China

China's sizeable population makes it an alluring market for pharmaceutical markets. There are many aspects that make it an attractive location to run clinical trials, as well as some challenges that we will explore in this article.

What are the benefits of running clinical trials in China?

There are three main benefits to adding China to clinical studies:

- Massive populations in urban areas. Many of China's cities are home to populations larger than several US states, which improves the success rate of patient recruitment. If patients drop out of a study, the likelihood of finding another patient is also higher.
- China has a large and growing network of clinical trial sites that sponsors can select from. There is also a highly qualified population of private investigators, laboratory professionals, and project leaders[1].
- Access to a genetically unique set of patients. The Han, who make up 92% of the Chinese population, are genetically homogenous. Minority ethnic groups such as the Kazakhs, Mongols, and Uyghurs show higher levels of genetic diversity than the Han[2]. In 2003, a study found that approximately 8% of men living in the region of former Mongolia, or 0.5% of the world population were likely genetic descendants of Genghis Khan[3].

With these three benefits, the upside to doing a clinical study in China is enormous – if one can overcome the challenges that managing clinical trials in China presents.

What are the challenges of importing clinical supply into China?

China has unique challenges not seen elsewhere when it comes to supplying clinical trials. Applying for the import permit requires a substantial set of documents that are listed in Figure 1. Unique requirements to China's import

[1] *Bao, Jing. Advantages and challenges conducting clinical trials in China. 4th International Conference on Clinical Trials. Sep 11-13, 2017. San Antonio, USA.*

[2] *Sioyang Liu, Shujia Huang et. al. Genomic Analysis from Non-invasive Prenatal testhing Reveal Genetic Associations, Patterns of Viral Infections, and Chinese Population History. Vol 175, Issue 2, Oct 4, 2018. https://www.cell.com/cell/fulltext/S0092-8674(18)31032-8*

[3] *Tatiana Zerjal, Yali Xue et. al. The Genetic Legacy of the Mongols. Vol 72 Issue 3, Mar, 2003. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180246/*

SHELF LIFE FROM DATE OF IMPORT

China also requires clinical materials to have at least 12 months of shelf-life from the date of import. Without proof that the material is viable for at least 12 months, the material will be rejected. This can be an issue for phase I and II studies that may have limited stability data.

application are the first leg airway bill and the Certificate of Origin (CoO).

China requires the first leg airway bill of your drug to verify the actual cost of the material. For most sponsors, this will be the airway bill of the shipment from the manufacturer to the packaging vendor. This value is used to verify that the invoice price for the shipment into China is not less than the market value that you paid for the drug. This is their way of ensuring the proper amount of taxes are being paid.

The CoO is a letter that is issued by the government agency that oversees the area that the drug manufacturer is located in. It is a certificate that merely states that the drug manufacturer exists, and is licensed to perform certain functions in a certain geography. While this is not a complex document, it is not a commonly requested item globally. If local government agencies are not accustomed to providing this, extra time could be needed to acquire this document.

Once all the documents for the import permit are gathered, they must be translated into Mandarin prior to submission. Upon issuance of the import permit, the trial sponsor has two weeks from the date of issue to complete the importation of the clinical material into China. If this is missed, the import permit application must be submitted again. Luckily, issuance timing usually takes only a couple of days.

The customs process includes an extremely intense inspection where custom officials verify that material referred to in the import permit matches with the actual kits and packages that arrive for import. China also requires clinical materials to have at least 12 months of shelf-life from the date of import. Without proof that the material is viable for at least 12 months, the material will be rejected. This can be an issue for phase I and II studies that may have limited stability data.

Figure 1. Common Documents Needed for Import Permit Application

- ✓ Certificate of Assessment (CoA)
- ✓ Certificate of Compliance (CoC)
- ✓ Certification of Manufacturing Facility
- ✓ Clinical Trial Application (CTA)
- ✓ Certificate of Origin (CoO)
- ✓ First leg airway bill

**All documents must be translated into Mandarin*

Do the same import & export rules that apply to China apply to Hong Kong?

In 1999, the UK's ninety-nine year lease of Hong Kong expired, and the control of Hong Kong was given back to the Chinese government. Since then, Hong Kong has been left as a free economic zone, and therefore the same rules and regulations that apply to mainland China do not apply for Hong Kong.

This has two main effects on the shipment of clinical supplies. First, China is known as a one-way transport country, which means that clinical supplies can be shipped into China, but cannot be exported. What goes to China stays in China. The exception to this rule is that material can be shipped from China to Hong Kong. Second, if a sponsor's clinical sites are in Hong Kong but not in mainland China, they can be supplied from anywhere in the world. Shipping into Hong Kong is very easy, as no extra depot involvement is required.

By contrast, politics prevent the shipment of clinical supplies from China to Taiwan.

Does China still keep a clinical kit for state identity testing purposes?

In the past, China has been known to reverse engineer products and not respect intellectual property. It used to be a provision in Chinese trade that a sample of any imported materials would be taken for state identity testing. A trial sponsor would have no legal recourse to stop the manufacture of copycat material until the drug was on the market.

Luckily, this does not happen anymore. In February 2020, there was a change in general Chinese trade agreements so that Chinese patent laws now apply to medicines. This means that if someone manufactures a pharmaceutical company's drug, the company can file an injunction to stop the copycat's manufacturing activities.

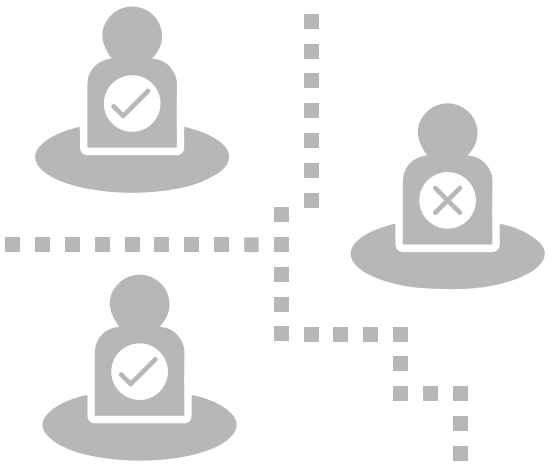

Figure 2. Depot Strategy: China

CLINICAL SITE LOCATION	SUPPLYING DEPOT
Mainland China	Mainland China
Hong Kong	Anywhere
Taiwan	Anywhere except mainland China

There are many benefits to running clinical trials in China, from the large potential patient pool to the large commercial prospects of drugs that come out of successful clinical trials. It is important for trial sponsors to understand the challenges that running a clinical trial in China presents, from preparing the import permit to developing valid depot strategies.

About Rich Nelson, Sr. Manager Global Logistics, PCI Pharma Services

Rich Nelson has over 15 years of clinical and commercial distribution and logistics experience. In his current position at PCI, Rich works with clients to provide seamless global distribution for their investigational drug products, ensuring cost-effective and time-efficient delivery throughout the clinical trials process. Rich has a B.A in Criminal Justice and Law Enforcement from Monmouth University.

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