

Navigating China's market entry: Bridging studies for foreign medical product registration – strategies and considerations

As China emerges as a crucial market for medical products, foreign companies face unique challenges in navigating its complex regulatory environment for product registration.

When incorporating China registration into global development plans, bridging studies typically serve as the most efficient method to connect data between Chinese and non-Chinese populations, thereby maximizing clinical development efficiency.



Based on International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) E5 and E17 guidelines to support China registration, a comprehensive analysis of China regional data is recommended to identify significant differences from global data. Subsequently, it is advisable to examine the following factors contributing to uncertainty and assess their impact on potential consistency:

- › **Statistical analysis method:** Consider whether the analysis method could be affecting the inconsistency
- › **Clinical study conduct:** Evaluate if there are any aspects of the clinical Study conduct that might influence the consistency of the results
- › **Regional inconsistency:** Investigate if there is regional inconsistency due to known intrinsic and extrinsic factors (e.g., clinical practice and genetics) that affect benefit-risk profiles
- › **Randomized data impact:** Explore how the randomized nature of the data itself might influence the consistency of the results (e.g., difference in gender ratio between China vs. global)

The China Center for Drug Evaluation (CDE) advocates for the early inclusion of Chinese participants in global clinical development programs. During the exploratory phase, no specific Chinese sample size is mandated. This early integration allows for:

1. Identification of PK and PD differences between Chinese and global populations
2. Accumulating data to support proposed dosage regimens
3. Enabling more precise participant recruitment strategies for later-phase studies in China

This approach enhances clinical data quality and potentially streamlines drug development for the Chinese market.



According to the ICH E5, a bridging study is defined as a supplemental study performed in the new region to provide pharmacodynamic or clinical data on efficacy, safety, dosage and dose regimen in the new region that will allow extrapolation of the foreign clinical data to the new region. Such studies could include additional pharmacokinetic information.¹

In alignment with China’s regulatory requirements for drug development, a **PK bridging study** is highly beneficial for drugs that:

- › Have completed early-phase clinical development outside China (without Chinese participant data)
- › Are currently undergoing pivotal studies (excluding Chinese participants)
- › Have already been marketed outside of China

This approach is particularly useful when the drug development process lacks data from Chinese participants. By leveraging these PK bridging studies between Chinese and non-Chinese populations, companies can effectively expand their presence in the Chinese market while maintaining alignment with their international strategies, potentially streamlining development timelines and enhancing overall efficiency.

In the process of foreign medical product registration in China, the CDE follows the ICH E5 and E17 guidelines, with significant emphasis on ethnicity sensitivity assessment. Within this crucial evaluation, PK bridging studies emerge as a cornerstone, providing vital data that informs and shapes the regulatory decision-making process.

Based on the China CDE reviewer’s opinions,² the following are the considerations of PK bridging study design:

Best practice	› Traditional PK profile comparison (Chinese vs. non Chinese populations) + population PK (PopPK), which includes Chinese data in the developed model and assesses whether ethnicity is a covariate
Typical practice	› Traditional PK profile comparison
Other choice	› Chinese PK profile + PopPK without Chinese data › PopPK (in cases where intensive PK sampling is not feasible)
Rare case	› Adhering to the patient-first principle, it may be acceptable to proceed with only an assessment based on ICH E5 Appendix D, despite the lack of PK comparison data
Other consideration	› For PK comparison data, Chinese regulatory authorities are primarily concerned with the Chinese vs. non-Chinese data, rather than Asian vs. non-Asian data

Strategies for incorporating China into global clinical development programs

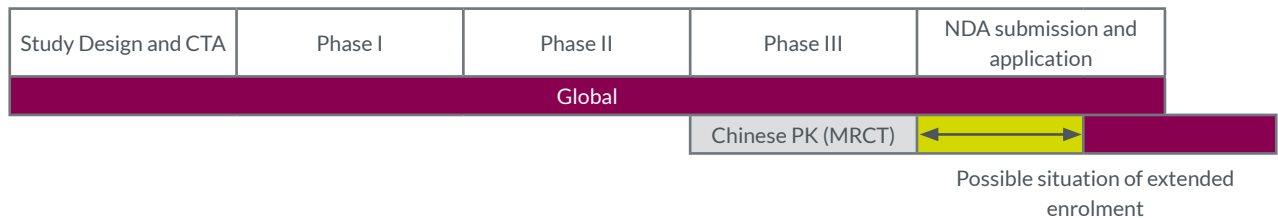
Currently, foreign sponsors primarily employ **three distinct clinical development pathways** for product development and registration in China:

Pathway 1: Participate in global early-stage clinical studies. Implement synchronized development strategies across all stages to ensure concurrent registration and market launch. (~10% of foreign medical products registering in China following this Pathway). Currently, there is a growing trend among pharmaceutical companies to select China for early-phase development, driven by considerations of speed and cost-effectiveness.

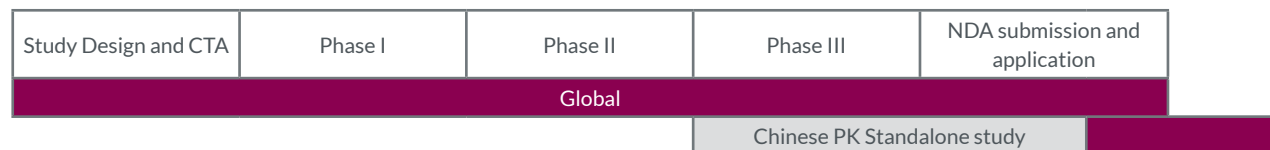
An alternative approach involves including Chinese populations in global first-in-human (FIH) studies from the outset. In both scenarios, China can participate in clinical studies concurrently with global development timelines.



Pathway 2: Participate in a global registrational multiple region clinical trial (MRCT). Implement synchronized development strategies in later stages to facilitate concurrent registration and market launch (~60% of foreign medical products registering in China following this Pathway). Given China's large patient pool, robust infrastructure, and high-quality clinical sites, the incorporation of Chinese populations post-Phase II is strategically advantageous. In this case, conducting a Chinese PK bridging study is typically necessary.



Pathway 3: Plan early for bridging and standalone clinical study needed for China registration, to shorten approval lag between China and global (23% of foreign medical products registering in China following this Pathway). In this case, conducting a Chinese PK bridging study is also necessary.



Note: Standalone study will lead to an increased overall R&D cost and extended timeline

Other pathways: e.g., post-approval approach (~7% of foreign medical products registering in China following this Pathway).

Regarding the patient study in China, APAC regional study or a study conducted exclusively in China with patient enrollment could follow either the synchronized Pathway 3 or post-approval pathway. APAC regional studies require standard statistical significance, with Chinese participants comprising at least 50% of the study population. China standalone bridging studies aim to show consistency with global pivotal study results. Due to their smaller scale, sample sizes for these bridging studies should be discussed with the China CDE statistical division.

When including the Chinese patient population in pivotal studies, the study design, particularly regarding Chinese sample size, should adhere to ICH E17 guidelines. The design process should also consider factors such as population and patient ratios, epidemiological data, and variations in disease incidence and subtype distribution.

In MRCT, Chinese participation of 10-20% generally satisfies China registration requirements.³ Similar to practices in the US and EU regulatory agencies, for products addressing significant unmet medical needs, sponsors can negotiate with the Chinese regulatory authority regarding the possibility of supporting registration with a reduced number of local patients. However, this is subject to case-by-case discussions with the China CDE and requires statistical input for each specific study.

China bridging study considerations for different pathways

Early enrollment of the Chinese population during early phase studies

As previously discussed in “**Pathway 1: participate in global early-stage clinical studies**,” it is crucial to consider including Chinese participants in global early-phase clinical trials. This inclusion allows for timely comparative analysis of data from Chinese and non-Chinese populations. Presented below is the proposed study design for global clinical trials enrolling both Chinese and Caucasian populations:



Obtain Chinese PK data prior to pre-Clinical Trial Application (CTA) consultation with the China CDE (e.g. may facilitate the reduction or waiver of China-specific bridging studies).

Standalone PK/PD study in China

Conduct a standalone PK/PD study in China to support cross-study comparisons with global data. The PK and PD data obtained from Chinese participants should be thoroughly compared with those from non-Chinese populations. For oncology products seeking approval, if the available data inadequately addresses the safety and efficacy profile in Chinese patients, a randomized study involving 2-3 dose levels may be necessary. This study should include a separate Chinese cohort or a dedicated Chinese study to address population-specific factors.

As we have explored the importance of bridging studies in global drug development, it is crucial to examine specific regional considerations. China, with its large population and growing pharmaceutical market, presents unique challenges and opportunities in this context. In the upcoming Part 2 of our exploration, we will delve into the specific aspects of bridging studies in China, focusing on key study design considerations that can ensure successful drug development and regulatory approval in this important market.



References

1. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. Ethnic factors in the acceptability of foreign clinical data E5(R1). Geneva: ICH; 1998. Available from: https://database.ich.org/sites/default/files/E5_R1_Guideline.pdf
2. Jian Li, Jinbo Yang, Yuzhu Wang, Consideration and assessment on ethnicity differences in pharmacokinetics, Clin J Clin Pharmacol, Vol 36, No. 6, March 2020.
3. Zhanjian Dong, Naiqing Zhao, Suiheng Lin, A method to allocate sample size into each region in multiregional clinical trial, Fudan Univ J Med Sci, 2009 Mar, 36(2) Multi-regional Clinical Trial

With Heart™

Ready to discuss the strategy for your foreign drug registration in China? Our ex-NMPA/CDE regulators are always available for a conversation.

[Connect with us](#) to learn more.

Parexel International Corporation
2520 Meridian Pkwy, Durham, NC 27713, USA
+1 919 544-3170
info@parexel.com

Offices across Europe, Asia, and the Americas
www.parexel.com

© 2025 Parexel International (MA) Corporation

parexel®