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Will US Clinical Study Diversity Guidance Cloud Chinese Firms' Prospects For Going Global?

by Brian Yang

The latest FDA guidance will have profound impact to Chinese biotech sector at a time when going global and a US approval is vital to its very survival.

Although the US FDA didn't name any specific countries or markets, the latest clinical study diversity guidance titled "Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies" will have profound impact to aspiring Chinese biotechs. For one, a US FDA approval is considered a must for any Chinese biotech eyeing to have their products marketed outside China.

Since the success of *Legend Biotech* and its US partner *Johnson & Johnson*'s chimeric antigen receptor T-cell therapy Carvykti (ciltacabtagen autoleucel), which shocked the ASCO annual conference in 2017 with its impressive efficacy data, many Chinee biotech companies have prioritized the US approval as their ultimate goal after a domestic Chinese approval.

Key Takeaways:

- Chinese biotechs eyeing US market need to adjust to the new FDA clinical study diversity guidance, adding challenges to a sector hit hard by economic downturn and capital crunch.
- Although waivers are possible, they will be "very rare" and earlier filing is required.

Many companies are conducting studies in the US, in hopes of eventually making deals with more established drug makers to launch their innovative antibodies or cell therapies in the world's largest pharma market.

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- The guidance could impact Chinese biotech's interests in the US, but it's still too early to tell.

However, the journey has not been easy and the latest FDA guidance further clouds their prospects.

Several major Chinese players, including *Eli Lilly*'s local partner *Innovent Biologics*, have been dealt with setbacks while pursuing a US FDA approval. Innovent's PD-1 checkpoint inhibitor, immuno-oncology antibody Tvyvt (sintilimab), was rejected by the agency. In a complete response letter, FDA cited the biologic license application's China-only data. Rather than conduct the multiregional trial the agency requested, Lilly opted to discontinue develop for sintilimab, which had been studied in non-small cell lung cancer but did not, according to the FDA, address an unmet medical need.

The latest guidance, developed under a Congressional mandate in the latest user fee legislation, would make such BLAs even harder, at a time when getting such an approval is the No.1 goal for many aspiring bioventures in China.

Sponsors can submit comments on the draft guidance on clinical trial diversity action plans until 26 September 2024.

"More Data Doesn't Cut It"

"Drug development in US differs greatly than in China," noted Ali Pashazadeh, co-founder and CEO of investment advisory firm Treehill Partners, in an earlier interview.

For any Chinese biotechs eyeing to go global via product approvals or dealmaking, they must have the US regulatory framework in mind. "More data doesn't cut the deal," noted the executive. (Also see "*China Biotech Podcast: BIOSECURE Updates, Genmab/ProfoundBio Deal*" - Scrip, 15 Apr, 2024.)

In other word, it's not about data but whether the data fully represent the diversity of American patients with the condition for which the therapy was intended.

For any Chinese biotechs eyeing to go global via gaining US FDA approvals, they may have to focus on having sufficient ethnical representation in their patient enrollments. In the past, however, Chinese companies had largely relied on producing promising clinical data and believed such data would convince regulators, but that is not enough any longer, insiders say.

That translates into data sufficiently representing four aspects of diversity emphasized by the US agency in the guidance: namely age, sex, racial and ethnic demographic characteristics.

Local Response

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Li Jing, co-founder and CEO of Vela Vigo, a Shanghai-based antibody developer, told the *Pink Sheet* that the latest guidance sent a clear signal that to secure a US approval, Chinese biotech must closely follow this and other guidance.

"[Clinical study diversity] has been mentioned before, and now it's becoming clearer – to make deals in the US and globally, [Chinese] biotechs have to be in compliance with the US FDA's latest guidance," Li said.

It also presents more challenges, such as including local US patients in their study designs, he added.

The message is clear: getting a US approval or making a global deal means Chinese companies must adopt and adapt to US requirements, not counting on FDA's regulatory flexibility, he emphasized.

"Frankly speaking, you have to be more US-centered if you want to secure an FDA greenlight."

'Very Rare' Waivers

Chinese companies, however, can still apply for waivers for their innovative assets that are indicated for conditions prevalent among Chinese and Asian populations.

The guidance specified that "a waiver is necessary based on what is known or what can be determined about the prevalence or incidence in the U.S. of the diseases or condition," such as gastric cancer, hepatic cell carcinoma, and certain types of hepatitis.

Also, Chinese companies have early-stage studies conducted in Australia, and late-stage trials in China and the U.S. might be able to meet the new requirements, depending on the new drug's indications, noted Katherine Wang, APAC-based partner of international law firm Ropes & Gray.

However, a US FDA official pointed out that such waivers would be "very rare." (Also see "*Clinical Trial Diversity Action Plan Waivers Will Be 'Very Rare,' US FDA Official Says*" - Pink Sheet, 19 Jun, 2024.)

Because the agency is required to issue a waiver or deny it within 60 days of the receipt, early communication with FDA is important. (Also see "*Diversity Action Plans Should Be Brief And Waiver Requests Filed Early, US FDA Says*" - Pink Sheet, 26 Jun, 2024.)

US Interests To Drop?

Could the new guidance significantly alter Chinese biotech's going global plan, prompting them to turn attention to other markets outside the U.S. or even refocus on domestic market?

Given Washington's accelerating decoupling move from reliance on China for biologics manufacturing and services, underscored by the BIOSECURE Act, Chinese companies may start diversifying to other markets such as EU for Southeast Asian countries. (Also see "*Can BIOSECURE Maintain Its Virality In The TikTok Era?*" - Pink Sheet, 1 Jul, 2024.)

Nevertheless, clinical and regulatory insiders asked by *Pink Sheet* expected limited disruption. Amid a severe and lingering capital crunch, dealmaking with global partners wherever they locate has become the last straw for many Chinese biotechs to grasp for survival.

The general feeling is that there will be time for any necessary adjustments to meet the regulatory approval or dealmaking needs.