Acta Pharmaceutica Sinica B 2019;9(5):1084−1085

Chinese Pharmaceutical Association
Institute of Materia Medica, Chinese Academy of Medical Sciences

Acta Pharmaceutica Sinica B

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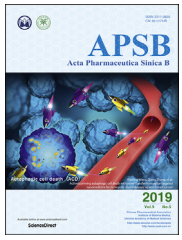

POLICY FORUM

New era of drug innovation in China

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Received 15 May 2019; accepted 11 June 2019

In 2018, the China National Medical Products Administration (NMPA) approved new drug applications (NDAs) of 48 new drugs, which was the highest annual approval rate by the Chinese regulatory agency in the past 20 years. Nine of the 48 new drugs, including fruquintinib, anlotinib, toripalimab and sintilimab, are global new molecular entities (NME) that were developed by Chinese pharmaceutical companies. Chinese regulatory reform since 2015 has enabled increased innovative drug research and development in China. Over a hundred drug-related administrative laws, regulations and guidelines have been issued by the Chinese central government and the NMPA (formerly CFDA before 2018) since 2015, which has unleashed a new era of drug innovation in China.

1. Redefining the new drug classification

In the past, any drugs that had not been marketed in China were considered as new drugs under the Chinese drug classification, even though they might have been previously approved and marketed in other countries or regions. The previous drug classification facilitated Chinese patients' access to new drugs but, at the same time, hindered Chinese innovation in drug development. Prior to the 2015 reform, the pharmaceutical industry and the Chinese regulatory agency had to devote tremendous resources to applications and approvals of the new drugs, lots of which had already been approved and marketed outside China. With the reform, new drugs are defined as globally new innovative drugs that have not been approved and marketed anywhere worldwide. Both global and local pharmaceutical companies will compete on equal footing with international standards and processes.

2. Participation in International Council for Harmonisation

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines had been referenced in NMPA regulations in the past. However, limited experiences in innovative drug development and incomplete understandings of the ICH guidelines restricted the effective promotion and implementation of ICH guidelines in China.

As of June 2017, the NMPA officially joined the ICH. All new drug research and development in China will follow ICH guidelines, including investigative new drug (INDs) applications and NDAs. In addition, NMPA representatives of ICH Expert Working Groups (EWGs) have participated in the revision and development of several ICH guidelines since 2017. As a member country, China will implement ICH guidelines based on the timeline accepted by

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Peer review under responsibility of Institute of Materia Medica,Chinese Academy of Medical Sciences and Chinese Pharmaceutical Association.

https://doi.org/10.1016/j.apsb.2019.06.002

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the ICH Management Committee. The NMPA will adopt drug regulations that are widely harmonized by international counterparts. Under internationally harmonized principles and regulations, pharmaceutical companies that focus on innovative drug research and development will have more opportunities to thrive in China.

3. Reform of IND review processes

Before 2015, the waiting time for review of IND applications in the Center for Drug Evaluation (CDE) of NMPA was usually longer than that of similar applications in FDA (U. S. Food and Drug Administration) or EMA (European Medicines Agency). While the 120 CDE drug reviewers managed a workload several folds higher than their international counterparts, the waiting list for IND reviews was still extensive. Ultimately, long waiting time resulted in a weakened environment for drug innovation and delayed marketing of new drugs. Since the reform, the review timeline for IND applications has been reduced to 60 working days. If there are no "stop" comments on the clinical plan within 60 days, sponsors can start clinical trials by an implied approval. So far, more than one hundred clinical trials have been approved in this manner.

To facilitate the IND reviews, sponsors are encouraged to request a pre-IND meeting for regulatory consultation and to open lines of communication before IND application. In the pre-IND meeting, the pharmaceutical company will receive constructive regulatory opinions and advice, which will enable the sponsor to proactively address potential CDE concerns ahead of the IND review. In addition, the pre-IND meetings can provide valuable regulatory insights to the sponsors and then effectively accelerate their innovative drug research and development. The pre-IND meeting can also provide the regulatory agency a closer view of technical advances and new drug pipelines across the industry.

There will be an increased emphasis on clinical trial data in the evaluation of novel therapies. Potential drug candidates with high benefit−risk ratios will be encouraged to proceed to clinical trials. The regulation of clinical trials will be managed holistically across all clinical development phases, instead of focusing on individual phases. Additional nonclinical studies during clinical trials may be required based on clinical trial progress and findings.

4. Priority review and approval

Priority review and approval is a new pathway established by the NMPA for medical products with urgent clinical needs. The NMPA will release the priority review list regularly based on the predicted clinical need and the potential value of the drug candidates. Drug applications selected for the priority review will receive accelerated review and approval. Conditional marketing approval for the urgent medical need will be granted to those products with excellent clinical data in early or middle phases of clinical trials.

5. Synchronised global research and development

In past decades, global clinical trials of new drugs in China lagged behind other regions and marketing approval of new drugs in China was delayed for years. The historic ambiguity of the Chinese regulatory attitude towards international nonclinical and clinical data was a major factor for the delay. With the reform, the NMPA will equally accept and review all international nonclinical and clinical data that are qualified and traceable for IND and NDA applications as locally generated data. The global pharmaceutical enterprises and the technology-based innovative biopharmaceutical companies which are interested in both global and Chinese markets can drive synchronous drug development much more efficiently than before. Global research and development will enhance the technology innovation across the industry and facilitate patient access to new drugs in China.

6. Expanding employment opportunities

The regulatory reform in the NMPA has expanded opportunities in drug innovation. With the reform, more international pharmaceutical companies will conduct clinical studies in China and more Chinese pharmaceutical companies will globalize their drug development. Job opportunities for professionals in drug development will expand within and outside China because of the international harmonization of Chinese regulations. Pharmaceutical professionals in China will benefit from the growing industry brought forth by the Chinese regulatory reform. Increased professional expertise and dedication will build a solid foundation of sustainable development for the pharmaceutical industry in China.

The current regulatory reform in NMPA integrates the international pharmaceutical regulations and respects the professional contributions for drug innovation across national boundaries.