A Review of China's Life Science and Healthcare Sector 2021: Embracing a Dynamic Regulatory Landscape

- The Chinese government has been taking a series of reform initiatives to enhance the affordability of pharmaceutical products, medical devices and healthcare services.
- NMPA released the first Good Pharmacovigilance Practice (GVP) which means that sponsors or market authorization holders (MAH) are required to conduct pharmacovigilance activities throughout the entire lifecycle of a pharmaceutical product.
- Under the Good Pharmacovigilance Practice, pharma companies must proactively monitor and detect all indicators related to drug safety and robustly address and mitigate any identified risks.

Ting Wu of Haiwen & Partners reviews the regulatory reforms taking place in China's life science and healthcare sector including legislation that has been released to encourage innovation and broaden market access to drugs, implementation of the patent linkage system, increasing antitrust enforcement pressure in the pharma sector, regulating medical devices, cosmetics and online hospitals.

China has been rapidly growing into the world's second-largest healthcare market. Over the past decade, the Chinese government has been taking a series of reform initiatives to enhance the affordability of pharmaceutical products, medical devices and healthcare services to patients by restructuring the legal framework in the life science and healthcare sectors, starting with the *Law on the Administration of Pharmaceuticals* (药品管理法) of 2019 followed by the *Regulations for the Regulation of Medical Devices* (医疗器械监督管理条例) and the *Cosmetics Oversight Regulations* (化妆品监督管理条例) of 2021. By the end of 2021, the fundamental laws and regulations in the life science sector have taken shape and been enforced.

The regulatory reforms in the life science sector are undergoing refinement and expansion, and the objectives are how the restructured legal framework will be enriched, developed and implemented. Instead of observing, life sciences companies must take steps to adjust and adapt their business operations to meet the ever-evolving regulatory requirements.

Rewarding true innovation and products with true value

In November 2021, the Center for Drug Evaluation (CDE) of China's National Medical Products Administration (NMPA) released the guidelines for clinical developments on oncology drugs or cancer therapies (以临床价值为导向的抗肿瘤

药物临床研发指导原则) (the CDE Guidelines). The CDE Guidelines attracted wide attention within the industry and its market reacted strongly.

The Guidelines reiterate that new drug development must focus on creating "true" clinical value and provide better therapy or treatment options with the best standard of care as the measure. What is the "best standard of care" relies on judgement based on scientific and ethical merits on a case by case basis.

The CDE Guidelines have been interpreted to be provide a shake up in crowded and fiercely competitive fields in oncology (such as PD-1/L1 and CAR-T in treatment of cancer cells) and deter the development of me-too drugs, i.e., medication that is similar to a pre-existing drug. The CDE Guidelines basically formalized and re-emphasized CDE's existing practices and positions that new drug development must always be patient-centered and deliver true value. This encourages the industry to develop truly innovative drugs by taking a more "differentiated" approach.

Broaden market access and insurance coverage for innovative drugs

Another highlight in the pharma sector was the announcement of the annual updates to the national reimbursement drug list (NRDL) by National Healthcare Security Administration (NHSA) on December 3, 2021. The updated NRDL will become effective since January 1, 2022.

A total of 74 drugs were added to the updated NRDL with an average price cut at record level by 62% (compared to 51% in 2020; 61% in 2019; 57% in 2018 and 44% in 2017). For the first time, the updated NDRL in 2021 includes several expensive medications for rare diseases, for example, Biogen's Spinraza (nusinersen) for spinal muscular atrophy (SMA) and Takeda's Replagal (agalsidase alfa) for Fabry disease.

Since 2017, the NRDL has been updated annually to include newly approved innovative drugs. With the consolidation of the three major basic medical insurances in 2018, the basic medical insurance scheme in China has covered around 90% of the total national population. NRDL listing negotiation has been increasingly important for innovative drugs because NRDL inclusion is expected to significantly increase the insurance coverage and sales volume for the listed drug in public hospital channels. Despite the price cut during the NRDL inclusion, many pharma companies have been shifting their business focus to innovative drugs when considering the price cliff and negligible profits received from off-patent drugs under volume-based procurement.

First GVP in China

In May 2021, NMPA released the first Good Pharmacovigilance Practice (GVP), which became effective on 1 December 2021. The GVP introduces the concept of "lifecycle pharmacovigilance", which means that sponsors or market authorization holders (MAH) are required to conduct pharmacovigilance activities throughout

the entire lifecycle of a pharmaceutical product, namely from the first human use of the product until the withdrawal of the product from the market. This means pharma companies should have an adequate GVP system in place as early as when the drug is at development stage and before a drug is approved for marketing. Further, not limited to traditional adverse events (AE) reporting, the GVP calls for a systematic approach to detect, assess, manage and mitigate all the safety-related signals. This means that pharma companies must proactively monitor and detect all indicators related to drug safety and robustly address and mitigate any identified risks.

Increasing antitrust enforcement pressure in the pharma sector

China has been taking a series of antitrust enforcement actions against pharma companies in recent years. With the formal establishment of the Chinese National Anti-Trust Bureau and the release of the Anti-Trust Guidelines for active pharmaceutical ingredients (APIs) in November 2021, it is foreseeable that the pharma sector (especially API and drug supply chains) will remain on the agency's list of enforcement priorities.

In 2021, five out of seven enforcement cases in the pharma sector published by the Chinese National Anti-Trust Bureau were related to APIs. Among others, notably, on April 15, 2021, the National Anti-Trust Bureau imposed a historic fine of RMB 764 million (US$116.84 million) on Yangtze River Pharmaceutical Group (Yangtze River), representing 3% of its turnover in 2018. Yangtze River, the parent company, was found to be liable for its controlling role to conspire and instruct misbehaviors committed by its subsidiary. This is the first penalty decision based on the allegation of resale price maintenance. Yangtze River was allegedly trying to maintain the resale price through written or oral means, such as telephone or WeChat conversations, etc. Pricing maintenance has always been a hot topic for pharma companies. This case alerts the industry to carefully manage their distribution and supply chain and restrain from controlling or affecting the resale price by means such as discounts, rebates, fixed profit, or exchanging price information or reaching vertical price agreements with other market players.

Implementation of long-awaited patent linkage system

Following the *PRC Patent Law* (中华人民共和国专利法), on July 4, 2021, NMPA and China National Intellectual Property Administration (CNIPA) implemented a Chinese drug patent linkage system by jointly issuing the *Implementing Measures for the Mechanism for the Early Resolution of Pharmaceutical Patent Disputes (Trial Implementation)* (药品专利纠纷早期解决机制实施办法 (试行)).

To further support the implementation of the drug patent linkage system, on July 5, 2021, the PRC Supreme Court issued the *Provisions on Several Issues Concerning the Application of the Law in the Trial of Civil Disputes Over Patents of Pharmaceuticals*

for Which Registration is Applied (关于审理申请注册的药品相关的专利权纠纷民事案件适用法律若干问题的规定) to specify the judicial proceedings for the drug patent linkage system; and CNIPA issued the *Measures for the Administrative Rulings in Connection with the Mechanism for Early Resolution of Pharmaceutical Patent Disputes* (药品专利纠纷早期解决机制行政裁决办法) to clarify the administrative proceedings for the drug patent linkage system.

The Chinese drug patent linkage system, the so-called Drug Patent Dispute Early Resolution Mechanism, links Chinese drug marketing authorizations to the patent status of an originator's brand name drugs. This system intends to resolve drug patent disputes between originators and generic drug applicants in the early stages through a judicial or an administrative proceeding before the relevant generic drugs are approved for marketing.

Though it remains to be seen to what extent patentees or MAHs of brand name drugs can leverage the Chinese patent linkage system to resolve potential patent dispute at an early stage, this newly established Chinese patent linkage system would procure both innovative and generic drug applicants to proactively and comprehensively evaluate and assess their patent prosecution and enforcement strategies, as well as regulatory and product market access strategies at an early stage.

A new chapter for medical devices regulation

On June 1, 2021, the long-awaited Medical Devices Regulations (New MDR) came into effect. Subsequently, NMPA published implementing rules and drafts such as the *Measures for Medical Device Emergency Approval* (医疗器械应急审批程序), the *Measures for the Administration of the Registration and Record Filing of Medical Devices* (医疗器械注册与备案管理办法), draft *Measures for Regulation of the Manufacturing of Medical Devices* (医疗器械生产监督管理办法), draft *Measures for Regulation of the Distribution of Medical Devices* (医疗器械经营监督管理办法), and draft *Guidelines on Good Clinical Practice for Medical Devices* (医疗器械临床试验质量管理规范). The New MDR together with these ancillary rules and drafts reshape the medical device regulatory landscape in China and begin a new chapter for medical device regulation.

In brief, the New MDR tries to strike an appropriate balance between innovation and compliance, and brings both opportunities and challenges to medical device companies. On the one hand, R&D-driven companies may benefit from multiple measures to speed up market access of products with clinical value, including permitting the use of self-inspection reports in lieu of type-testing reports issued by government-designated testing centers, green channels to accelerate patients in China

to have access to innovative products, expanded compassionate access to investigational medical devices at clinical stage, conditional approvals and priority review of certain medical devices with apparent clinical value or addressing unmet clinical needs, emergency use authorization by NMPA for medical devices not yet marketed in China so as to address public health emergency, etc.

On the other hand, device MAHs are under pressure to build a robust compliance program to fulfill enhanced regulatory obligations under the New MDR. With the rolling out of the MAH system national wide, the New MDR greatly emphasizes MAHs' regulatory obligations to ensure product quality, safety and effectiveness throughout the entire product life cycle. MAHs will be facing increasing severe penalties under the New MDR for their non-compliance, and the New MDR introduces personal liability on responsible individuals of MAHs, including income confiscation and lifetime debarment. For foreign MAHs, if they refuse to fulfill any penalties imposed on them under the New MDR, they may receive an import ban for selling and distributing their products in the PRC market for up to 10 years.

Overarching Cosmetic Supervision and Administration Regulation of China

The Cosmetic Supervision and Administration Regulation of China (CSAR), which became effective on January 1, 2021, replaced the old regulation that had been implemented for over 30 years. In 2021, NMPA issued several ancillary rules to support the implementation of CSAR, including the *Measures for the Administration of the Registration and Record Filing of Cosmetics* (化妆品注册备案管理办法), the *Provisions for the Administration of the Registration and Record Filing Information of New Cosmetic Ingredients* (化妆品新原料注册备案资料管理规定), the *Measures for the Administration of Cosmetic Product Labeling* (化妆品标签管理办法), the *Measures for Regulation of thee Manufacturing and Dealing of Cosmetics* (化妆品生产经营监督管理办法), the *Provisions for Regulation of Cosmetics for Children* (儿童化妆品监督管理规定), and the *Technical Guidelines for Cosmetic Safety Assessment* (化妆品安全评估技术导则).

The CSAR reflects the NMPA's risk-based approach to regulate cosmetic products. For example, NMPA only requires certain high-risk new ingredients (e.g., preservatives, sunscreen ingredients, colorants, hair dyes and whitening agents) to go through the registration process while low risk new ingredients can be notified with NMPA. Further, imported general cosmetics now can be exempted from animal testing requirements if its safety can be supported by adequate safety assessment and a Certificate of Good Manufacturing Practice (GMP). From Jan. 1, 2022, all cosmetic product applicants are required to submit product safety assessment documents when they register or notify cosmetic products with NMPA or its local counterparts.

Notably, CSAR lifted the bar for the labelling and claims of cosmetic products. It requires that any functional claims of cosmetic products must be supported by

sufficient scientific evidence. Cosmetic product manufacturers will have to disclose a summary of such scientific evidence on the designated websites.

Not surprisingly, similar to the New MDR, CSRA also enhances cosmetic license holders' regulatory and compliance obligations in relation to product safety and quality throughout the entire product life cycle. Foreign cosmetic license holders may delegate part of such regulatory obligations to a Chinese local agent; however, foreign cosmetic license holders could be subject to product import bans of up to 10 years) for their violation of CSRA and refusal to accept penalties under CSRA.

Reigning in the surge of online hospitals

With the promulgation of three key regulations concerning online hospitals and telemedicine in 2018, the number of online hospitals is surging and has reached a new high in 2021. From June 2021, over 1600 online hospitals have been providing medical consultations and prescriptions through online platforms. However, the role and boundary of services offered by online hospitals have been contentious.

The National Health Commission released the draft *Rules for the Regulation of Telemedicine* (互联网诊疗监管细则) in Oct. 26, 2021 with the aim to further guide and standardize online medical practices (New Telemedicine Rules). Among others, the New Telemedicine Rules require all physicians and patients to disclose and verify their identity on telemedicine platforms. The medical services provided by physicians must not be replaced by AI software or non-physicians.

In particular, physicians are prohibited from linking their income to pharmaceutical products and medical examinations, and they must not improperly refer patients to online hospitals or request patients to purchase medicines or consumables at a pharmacy designated by them. This restriction challenges existing practices regarding how physicians can be motivated and paid through telemedicine services. The New Telemedicine Rules call for a more transparent and orderly development of online hospitals and telemedicine services.

Outlook for 2022

With fundamental laws in the life science sector coming into shape, it is expected that more legislation will be introduced to enrich and restructure the legal framework in order to reform initiatives at a deeper level. Increasingly it is likely there will be more implementing rules accompanying newly amended laws and regulations for drugs, medical devices and cosmetics. The regulatory paradigm for online healthcare services is becoming more transparent. The draft measures are expected to be finalized in 2022 and the regulatory trends in life science and the healthcare sector will continue to embrace innovation, encourage transparency and orderly market competition, and endorse market players that can offer high value to patients and at the same time meet with compliance requirements.