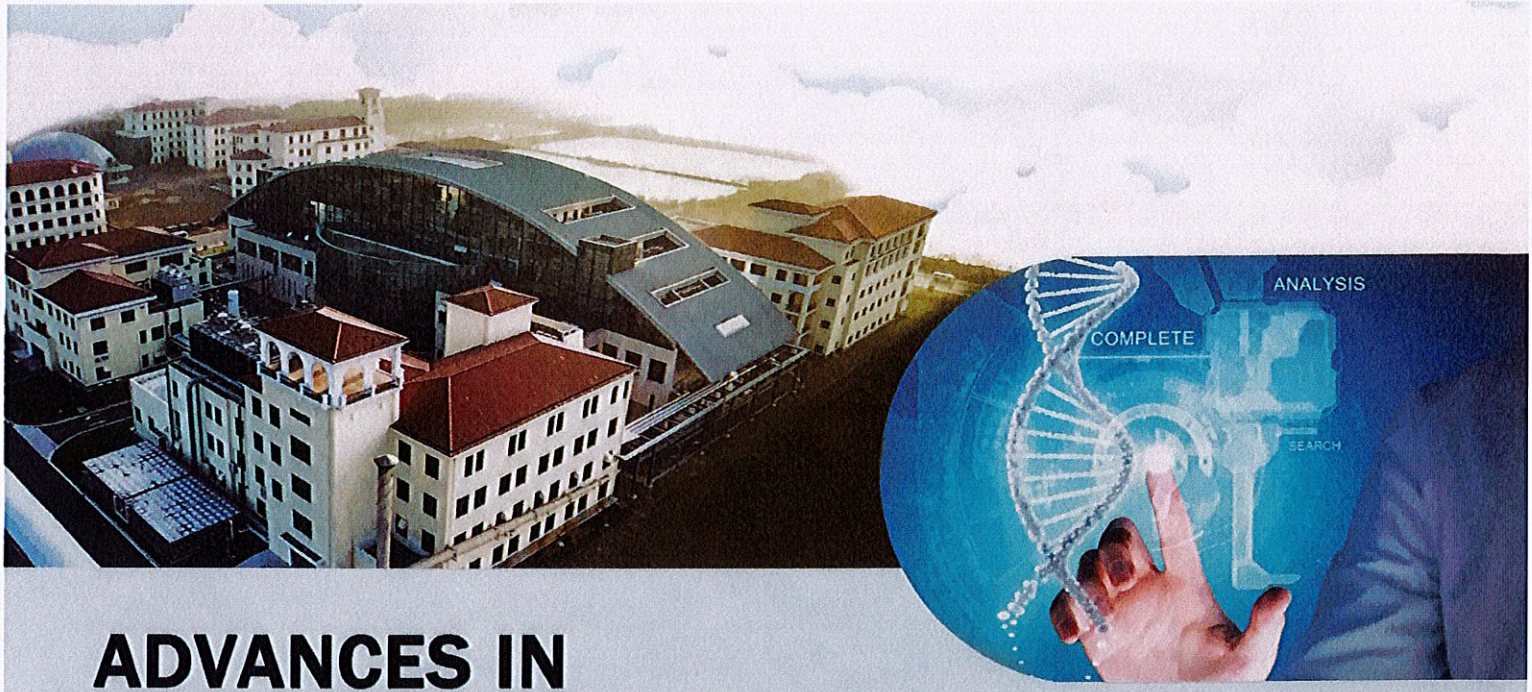

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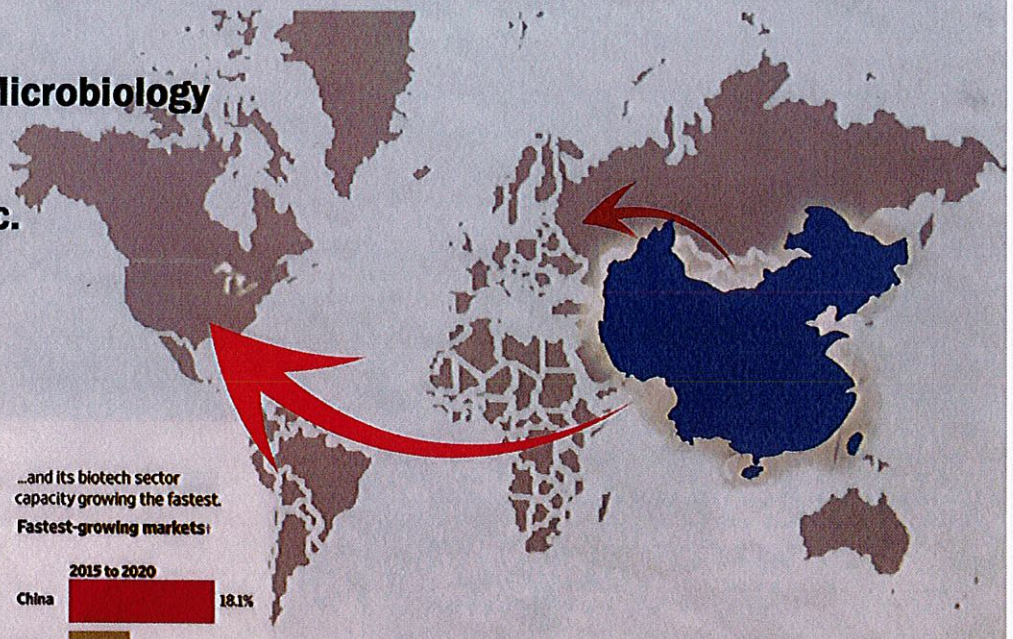

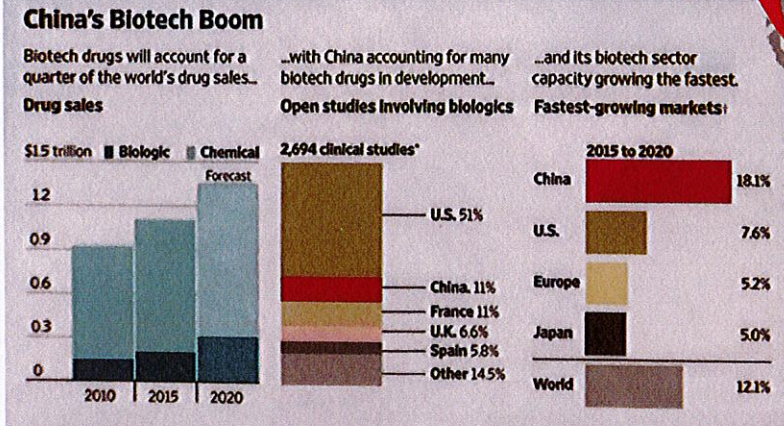

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4-3 Current Challenges and Opportunities of Biopharma Quality Management in China

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ABSTRACT

In this chapter the author gives a brief history of China's biopharmaceutical industry and reviews the history of pharmaceutical quality management in the US/EU and its global impact. The author points out multiple challenges facing quality management in China's biopharma sector, including lack of experience and talent, a rapidly changing regulatory environment, as well as cultural issues in management. The author also sees opportunities for progress in this field with the growing CMO platforms and the emerging CQO business.

KEYWORDS

Contact Manufacturing Organization (CMO), Cost, Quality and Outcomes (CQO), International Conference on Harmonisation (ICH), Market Authorization Holder (MAH), Good Manufacturing Practices (GMP)

1. The Evolution of the Biopharmaceutical Industry in China

Biopharmaceuticals are therapeutic products developed using the scientific principles of microbiology, chemistry, biochemistry, biotechnology, and pharmacology from live organisms and materials, such as biological tissues, cells, and body fluids. Manufacturing technologies for these therapeutic products have been successfully used to generate biopharmaceuticals with tremendous market success for the treatment and diagnosis of life-threatening diseases such as cancer and autoimmune diseases that are unable to be treated efficiently by traditional medicines.

Between 2002 and 2011, out of the world's 100 major scientific and technological advances, 37 were life sciences related. According to statistics, global sales of biopharmaceuticals exceeded USD $75 billion and 22 biopharmaceuticals were "blockbuster products" with annual sales over USD one billion each in 2007. By the end of 2010, sales of biopharmaceuticals reached USD $140 billion, accounting for 16% of the global pharmaceutical market; this is expected to increase to 33% of the global pharmaceutical market by 2020. Currently, the United States and other developed countries are dominant the global biopharmaceutical market, with 63% of North America and 32% of Europe and Japan, and 5% of the rest of the world, including China.

A brief history of the Chinese biopharmaceutical industry follows:

1.1 The beginning (pre-2005)

The Chinese biotechnology industry was present as early as the mid-1980s. Early products included a number of growth factors and cytokines such as interleukin 2, Erythropoietin (EPO), and growth hormones. Historical data of that period indicated a rather slow progress, with an annual total market value less than CNY 30 billion (USD $4.7 billion) and profit less than CNY four billion (USD $635 million). It was not until 2004, that the export of these drugs reached CNY five billion (USD $794 million), with all of the exports to developing countries. The totality of the biotechnology industry output, therefore, was small and can be characterized as follows: (1) the majority of biopharmaceutical companies were small; (2) the social status of these companies was low; (3) there were no "blockbuster products"; and (4) the geographical distribution of biopharmaceutical companies was prevalent in the eastern part of China.

1.2 Accelerated growth period (2005–2009)

After 2005, the Chinese biopharmaceutical industry entered a period of rapid growth. With the release of the national 11th Five-Year Plan, a total of 22 national bioindustrial parks were successively approved by the National Development and Reform Commission, which provided political, financial, and infrastructure support to the biopharmaceutical industry and led to a growth rate of 29.0% between 2005 and 2009. In addition, the average annual growth rate of revenue reached 30.3%, and the average annual growth rate of profit reached 37.3%, respectively. The drivers of this phase were as follows: (1) industry-specific clustering; (2) biopharmaceutical platforms empowered by related and supporting technologies; (3) enhanced research and development (R&D) capabilities; and (4) government preferential policies.

By 2010, biopharmaceutical industry clusters began to emerge: the agglomeration and development centered on the Yangtze River Delta and Bohai Rim, while the Pearl River Delta and the northeast China cluster were also formed. In addition, the central region provinces like Henan and Hubei, the western

regions provinces like Sichuan and Chongqing also had their industrial bases established.

1.3 The rapid growth period (2011 to the present)

Impacted by the 2008 global financial crisis and 2010 Good Manufacturing Practice (GMP) certification policy revision in the United States and the European Union, there was a marked decline in R&D funding for the biomedical industry in China. Despite a low in sales revenue of biopharmaceutical products in 2010, a new wave of growth in China began in 2011. This was partly driven by a large number of global patent expirations for innovator drugs that were anticipated to occur by 2020. Based on incomplete statistics, more than 600 drugs will have their patent expired by 2020, representing a USD $259 billion market opportunity for companies aimed at developing generic and biosimilar drugs to capture the market share. The global pharmaceutical industry has therefore foreseen tremendous potential for business development. The value of biopharmaceutical R&D, products and services in China, as a result, showed a substantial increase and moved into a rapid growth stage. The specific features of this period are as follows: (1) tremendous market potential; (2) highly dynamic and rapid growth; (3) preferential policies from the government; and (4) clear path towards commercialization.

Throughout decades of development in the fields of science and technology, China has gradually built its overall capability and technology, and narrowed the competency gap with developed countries. In 2017, Chinese government leaders attached great importance to the development of high-technologies including life sciences as their economic transformation strategy. The research, development, and commercialization of biopharmaceutical products became one of the focused areas for "13th Five-Year Plan" of China.

In May 2017, China became a formal member of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). This represented new opportunities and challenges for the China-based pharmaceutical industry. For the past two years, China Food and Drug Administration (CFDA) has introduced laws and regulations that will drastically change the ways of regulating the Chinese pharmaceutical industry in an effort to move towards better alignment with ICH standards and global pharmaceutical leaders. In this regard, the actions of the CFDA show the determination of both the government and the private sector to invest in fundamentals around biopharmaceutical development in order for China to become a viable player in the globalization of the industry. These changes, along with the gradual release of patent protections, will only become more and more exciting and momentous. Meanwhile, the challenges and opportunities will drastically reshape Chinese biotechnology industry in the next five to 10 years.

2. History of Pharmaceutical Quality Management in the United States/ European Union and Its Impact in the World

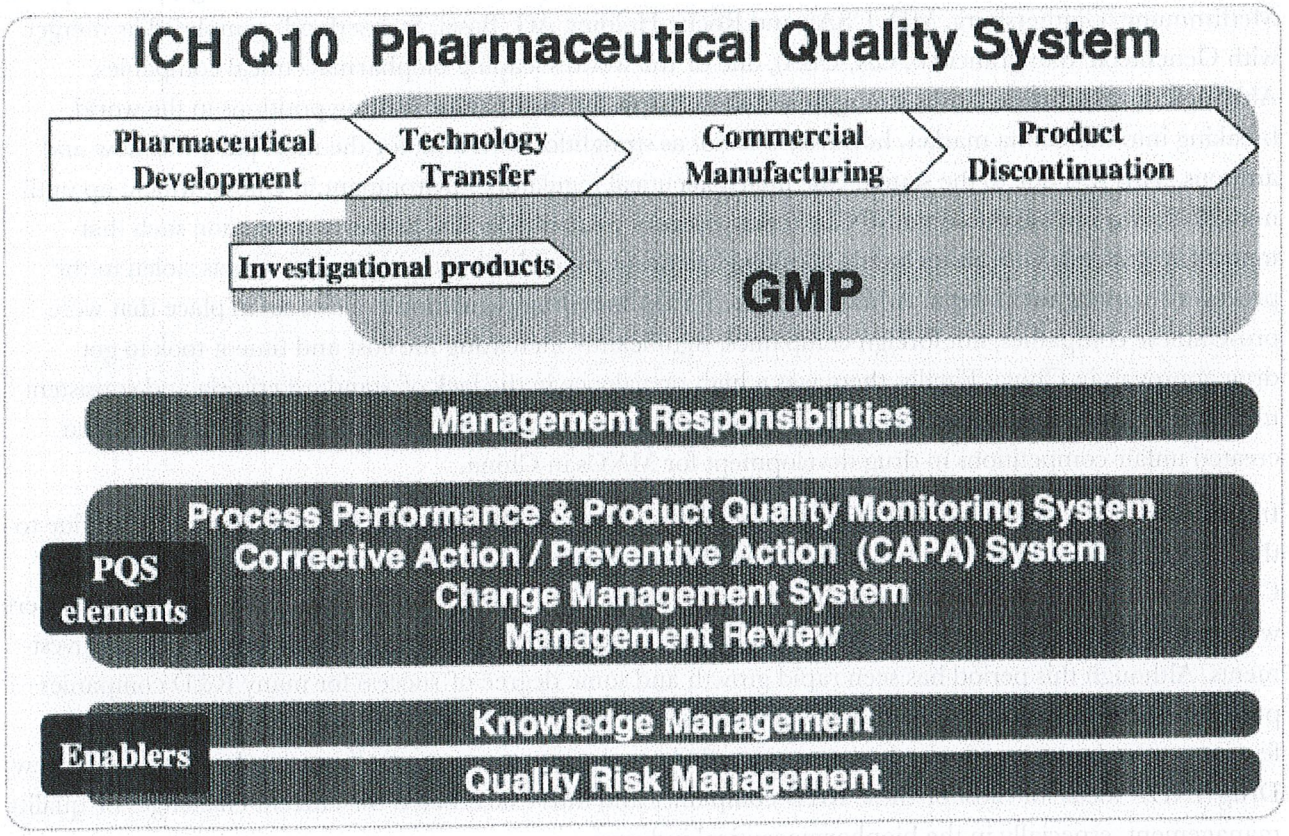
The regulation of the pharmaceutical industry first started in the United States after the thalidomide tragedy, with the cornerstone being passing the Kefauver Harris Drug Amendment by the United states Food and Drug Administration (FDA) in 1962. Since then, legislators have tightened restrictions surrounding the surveillance of and approval processes for drugs to be sold in the United States, requiring that manufacturers prove their products are both safe and effective before market launch. Moreover, current pharmaceutical drug regulations have evolved dramatically throughout the last 50 years or so, with the FDA and its close

followers/collaborators in Europe, Canada, and Japan leading the evolution of the concept, drug approval and monitoring systems, toward a globalized structure and interconnecting mechanisms.

Historically, the development of quality management for the pharmaceutical industry can be divided into three stages: (1) the stage of quality control testing (1970s); (2) the stage of quality assurance (1980s – 1990s); and (3) the stage of establishment and implementation of quality management systems (2002 to the present). The first stage can be summed up as a "testing into quality," where the focus was almost entirely on manufacturing, with some testing at the end in order to select qualified products. The second stage marked the concept of ensuring that equipment and processing were qualified before being used for manufacturing, so the regulatory philosophy was advanced from "check afterwards" to "check the process before manufacturing, check the product testing after manufacturing, and check finally by quality assurance." Although this represented a significant improvement in the quality management concept and methodology at the time, with the rapid growth of the industry, the FDA came to the realization that an unacceptable percentage of marketed products were failing quality standards and, as a result, drug shortages were occurring at an unacceptable rate, compromising the availability of these drugs to the patients who needed them. With the goal of improving the success rate of therapeutic drug production and therefore avoiding drug shortages as well as controlling drug pricing, the FDA rolled out the Pharmaceutical Quality for 21st Century Initiative in early 2000.

This marked the beginning of the third stage of pharmaceutical quality management, which was officially crystallized by the publication of ICH Q10 (Pharmaceutical Quality System) in 2009. The quality management system described therein provides a comprehensive and effective guarantee for the quality of a product by managing all the factors that may affect product quality throughout the life cycle of the product. The establishment and improvement of the quality management system are the inevitable trends and requirements for current pharmaceutical industry. It enhances Good Manufacturing Practices (GMP) for pharmaceutical production, which have become the basic guidelines for pharmaceutical manufacturing and quality control. ICH Q10 sets out a comprehensive model of an effective pharmaceutical quality system (PQS) based on the ISO 9000 quality philosophy, including local GMP regulations and ICH Q8 drug development and ICH Q9 quality risk management, as a pharmaceutical quality system for the pharmaceutical life cycle. It provides a coordinated model in combination with local GMP requirements for the implementation and utilization of all relevant regulations. An ICH Q10 pharmaceutical system model is shown in Figure 1. In the process of implementation, the concept of Quality by Design (QbD), proposed in the second edition of ICH Q8 was utilized, as well as the idea of quality risk management described in ICH Q9. Management involvement also became a key requirement for pharmaceutical company executives to personally take responsibility for the drugs they put out on the market. The key outcome from these combined concepts emphasizes that quality can only be achieved by design and continuous verification of the design: neither the production process nor final quality control testing can make up for poor design and processing defects once the product has been made. Companies must start at the beginning of product development in order to prevent and to solve quality problems.

Fig. 1 ICH Q10 Quality System



Source: International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, November 2010

In summary, a simplified way to describe the evolution of pharmaceutical quality management is the idea that we have moved from "check afterwards" to "check the process" and finally to "check the sources" and, with these evolutional steps, the quality of management has continued to improve and to be more scientifically and risk-based rather than inspection- and experience-based.

The biopharmaceutical industry post-ICH Q10 is even more reliant on comprehensive systematic quality management due to the highly variable nature of biopharmaceutical processes and products. Only when quality is designed into the process and verified and improved throughout the product life cycle can we ensure the consistent supply of life-saving/enhancing pharmaceutical products to patients and the ultimate success of biopharmaceutical companies.

3. Current Challenges of Biopharmaceutical Quality Management in China

As the biopharmaceutical industry matured in leading areas of the world such as the United States, Europe, and Japan, it became clear that both the therapeutic and financial values brought by the relatively safe and effective medicines that were introduced were tremendous. As a result, by the mid- to late-2000s, all major global pharmaceutical companies [i.e., multinational corporations (MNC)] had either completed or advanced their footprints in the biopharmaceutical areas. For example, Pfizer (New York, NY, USA) acquired Hospira (Lake Forest, IL, USA), a perceived leader in the biosimilar area at the time; Merck (Kenilworth,

NJ, USA) acquired Wyeth (Madison, NJ, USA), a vaccine company; AstraZeneca (Cambridge, UK) acquired MedImmune (Gaithersburg, MD, USA); and Roche Holding AG (Basel, Switzerland) completed its merger with Genentech (San Francisco, CA, USA), one of the world's leading biopharmaceutical companies. Although these strategic moves strengthened these respective companies' leading positions in the world, breaking into the China market, however, was not as straightforward and, for the most part, was slow and arduous. This was due to the state of the pharmaceutical regulatory environment in China, which, up until mid-2010, was not conducive to MNCs: there was very weak intellectual property protection such that innovative pharmaceuticals including all biological drugs risked having their product secrets stolen in the process of moving into China. Additionally, the CFDA had drug regulation policies set in place that were pro-Chinese companies, not foreign companies, significantly increasing the cost and time it took to get drug approvals in China. Finally, there was a high prevalence in the lack of standard criteria and consistent measurements working against them, i.e., poor quality practices by pharmaceutical companies in China created unfair competitions in drug development for MNCs in China.

In summary, the Chinese biopharmaceutical industry experienced a period in the early part of 2010, due to the "12th Five-Year Plan" and "13th Five-Year Plan" strategic initiatives from the Central Government of China and, also, an artificial non-competitive environment for the MNCs in China. During this period, there was tremendous support available, both from government policy incentives and from venture capital investments. Although this period has seen rapid growth and some degree of success for many R&D companies—particularly those working in the monoclonal antibodies space, including on biosimilars, biobetters, and a few innovative biologics—it also had an unintended consequence: it created a "speed to Investigational New Drug (IND)" focus for most of these R&D companies and thus exacerbated the current challenges of quality management, especially in the biopharmaceutical industry.

3.1 Lack of experience

As described above, the first wave of Chinese biopharmaceutical industry growth did not achieve its intended outcome of bringing the much-needed newer and safer therapeutics to China for life-threatening diseases such as cancer, diabetes, and cystic fibrosis. Instead, it brought down the reputation of, as well as investors' confidence in the Chinese biopharmaceutical industry. As such, biologics suffered a lull for about 10 years as China fell further behind the United States, the European Union, and Japan. Chinese who were educated in biopharmaceutical-related fields were either forced to move to the traditional chemical drug industry or to find job opportunities outside of China. As a result, when the current wave of biopharmaceutical development started at the beginning of 2010, due to the crash of the Chinese domestic stock and real estate markets and to the recognition of the critical needs of modern medicines for Chinese people by the current central government, the tremendous opportunities were not matched with domestic capabilities in the biopharmaceutical industry.

Coincidentally, around the same time, many United States and European Union pharmaceutical companies were moving towards new business models wherein internal R&D and drug discovery functions were being cut in order to reduce R&D costs and risks from carrying early stage-heavy pipelines. Many Chinese R&D scientists working in those United States/European companies either lost their jobs or saw their career opportunities dwindling abroad. As a result, there was an influx of Chinese American/European scientists returning to China who became instrumental in starting the new wave of Chinese biopharmaceutical growth

in the areas of biologics R&D. During the period of 2008 to 2018, an impressive biotechnology R&D capability was developed in China by small- to mid-sized Chinese companies and government-sponsored research institutes. These R&D efforts, many led by scientists who returned to China from the United States and Europe, have since brought about respectable early-stage drug development pipelines, even though the predominant ones are biosimilars. Also, the CFDA's waves of reform beginning in 2015 significantly improved the efficiency in reviewing IND applications. These combined factors have resulted in a biopharmaceutical industry highly concentrated on pre-and post-IND early-stage products in development (over 70% of the pharmaceutical development programs in China are in Phase I clinical trial stage). Hence, the Chinese biopharmaceutical industry as a whole is entering a phase where selective and successful development of these early-stage products into late-stage products, and, finally, successful commercialization should be the essential focus. Companies that have invested in GMP manufacturing and quality capabilities in addition to clinical expertise are the ones that will reach the end goal amidst fierce competition.

This has highlighted the challenge of overcoming the lack of experience in quality management in the industry: on one hand, the biopharmaceutical history in China has not had much commercial success, so the limited quality management experience has not been significantly impactful, either positively or negatively, to date; on the other hand, the returnees from the United States/European Union pharmaceutical industries are overwhelmingly R&D scientists who have little understanding or experience with GMP and aspects of quality management, in particular with respect to product development and commercialization, so the opportunity to improve experience with quality management is hindered. The overall lack of experience, therefore, remains crippling for hundreds of biopharmaceutical companies in China aiming to move their early-stage drug candidates towards late-stage clinical and commercial successes and is partly due to the failure of many leading R&D companies to transition into clinical manufacturing and commercial operation companies. The low success rate in turn is jeopardizing the great plan, brought about by the recent R&D boom and by significant investments into the industry, of turning ideas into life-saving therapeutics for the 1.4 billion Chinese people.

3.2 The Rapidly Changing Regulatory Environment for the Chinese Biopharmaceutical Industry

Chinese pharmaceutical regulatory policies have been partially responsible for the weak oversight, especially in the areas of quality management and intellectual property protection, prior to 2015. This was revealed through the "clinical self-evaluation policy" issued by the CFDA in July 2016, where more than 80% of the Chinese pharmaceutical products with registered clinical trials had severe quality and compliance issues to the extent that the companies sponsoring the trials had to voluntarily withdraw their applications in exchange for lenient treatment by the CFDA. For the biopharmaceutical industry in particular, when the strategic goal from the central government, led by Chairman Xi Jinping, of transforming China from an exporter of low-tech products to a leader in high technology industries by 2025, biotechnology was one of the named new "focused industries" and policies and regulations became important driving forces for the transformation. The very first *Chinese Pharmacopoeia* was put into effect in 2010 and quickly became obsolete with the advent of the global transformation of the Pharmaceutical Quality System brought on by implementation of ICH Q10. The second version of the *Chinese Pharmacopoeia* was made effective by December 2016 and reflected many of the revolutionary quality management concepts first adopted in the United

States and European Union just five years prior. The CFDA as a government agency, under the new leadership of Bi Jingquan, started the most aggressive overhaul of the old drug regulatory system to date. These efforts included a rapid and significant increase both in the number and qualifications of the CFDA staff and the issuance of new or revised regulatory guidelines in key areas including biosimilar, innovative drugs, new biologics, and cell and gene therapies. Along with organizational expansion efforts and the implementation of new guidelines, the CFDA also reformed its historical working mechanisms in a number of important areas. For example, all new IND applications, which used to be handled by local CFDA offices, are now being handled by the CFDA's central office. In addition, GMP certification, while once a pre-marketing requirement by the CFDA and having a five-year validation period once issued, now has been abolished. Instead, under the new mechanism, the CFDA can choose to conduct GMP audits at any time based on the ongoing performance of a company in terms of product and GMP risks. Of all the regulatory changes, perhaps the most important change yet was the doing away with of the "protectionism" policies that had previously in operation, so that Chinese pharmaceutical companies would henceforth have to compete in the Chinese market on equal footing with companies from other parts of the world. These changes demonstrate the determination of the Chinese government in bringing the China pharmaceutical industry to the world stage and was crystalized by the successful petition of China to be accepted as a formal member of the ICH in June 2017. China is now in a position to participate in global drug regulation harmonization, while, at the same time, gearing up to adhere to international regulatory standards for its pharmaceutical industry.

All these policy changes, implemented in such a short period of time, are eliciting dynamic changes to the current and future landscapes of the biopharmaceutical industry in China. Companies in this new era can only succeed by faithfully adhering to global current GMP, improving their expertise and capabilities in developing and manufacturing high-quality products over product life cycles, in order to become a viable player in the increasingly globalized regulatory environment. This brings about tremendous challenges for the young and inexperienced Chinese biopharmaceutical companies whose knowledge, infrastructure, and talent in these areas remain lacking.

3.3 The Talent Problem

By now (at the beginning of 2018), most Chinese biopharmaceutical companies are aware of the importance of incorporating quality management in their efforts in order to continue their business success, especially those that have products in clinical development stages, i.e., post-IND. The majority of them, however, are led by chief executive officers (CEOs) whose senior management teams have never been personally involved in drug development or commercialization operations, especially when it comes to large-scale GMP manufacturing and quality management. This, in turn, limits their understanding of the type of technical and management talents they need for their business transitions. Even for those who managed to hire the few available talents, the CEOs tend not to give them the necessary support and empowerment the new leaders need in order to operate in their areas of expertise. The lack of empowerment of the new senior leaders, such as new quality leaders, may compromise the successful transition of these R&D companies to clinical manufacturing companies and, ultimately, commercial manufacturing companies.

Challenges in organizational development and leadership team renewal are common amongst all Chinese biopharmaceutical companies, including those that are small to mid-sized and also larger traditional pharmaceutical companies who have been heavily investing in biotechnology in recent years. Companies tend

to underestimate the importance of finding senior leaders/technical experts with successful track records in world-leading biopharmaceutical companies either due to cost concerns or a lack of an understanding of these roles. Making mistakes in such key hiring decisions can not only result in significant delays in clinical development projects but also in the building of the necessary foundations for process and product understanding and controls, which will directly affect product quality in the long run.

The "talent problem" is most serious because the modern pharmaceutical quality management system itself has only been revolutionized in the past decade in leading areas of the world such as the United States, the European Union, and Japan. Therefore, those with current knowledge of biopharmaceutical quality system concepts and methodology as well as those with significant experience in biologics product development and life cycle management are in short demand globally, in general. Amongst those, very few speak Chinese, a huge advantage in the young home-born biotechnology industry, and even fewer still are willing to leave their Western homesteads and professional networks to go work in China full-time. The hundreds of Chinese biopharmaceutical companies, therefore, have to compete for a very small number of biopharmaceutical quality experts available in China. To make the situation even more challenging, those few experts in China also often need to take on senior leadership roles in order to carry out the difficult task of changing the culture and business operational norms of the companies they join—a tall order for most people.

3.4 The Culture Problem

The difficulty in retaining talent in biopharmaceutical quality management is often at least in part a result of corporate culture, which may not be conducive to enabling senior leaders with different educational and professional backgrounds to succeed within an existing company and its power status quo. China, with its long history of feudal societies and centralized political systems, undoubtedly favors "top-down" management styles wherein the CEO has infinite power. Unfortunately, most Chinese CEOs also don't encourage people on their teams to raise issues or cast doubts about their opinions, as such is invariably viewed as "challenging their control." This, along with the "guanxi" relationship-based culture prevalent in Chinese society, ensures many new leaders in quality management are viewed as outsiders, often facing resistance or even bullying from the existing inner circles of the CEOs. Many companies therefore lose their valuable experts in quality control or other technical operational areas such as GMP manufacturing. The resulting rapid turnover of quality leadership in these companies greatly compromises the realization of a consistent and sustainable quality strategy, which further compromises the implementation of quality control systems and operations.

4. Opportunities in Advancing Biopharmaceutical Quality Management in China

Due to the significant challenges described above, Chinese biopharmaceutical companies are still mostly in the "trial-and-error" phases of product development and commercialization. The success of moving towards late-stage clinical development and commercial launch should be and increasingly will become the true dividing line between a successful Chinese biopharmaceutical company and an unsuccessful one in the next five to 10 years. Only the few successful ones would have a chance to gain long-term success in China and also have the possibility of moving into the global market. Chinese biotechnology companies who truly understand the importance of this and invest in high-quality product development infrastructure

from leadership teams to partners [e.g., contract manufacturing organization (CMO), suppliers] have a much better chance to emerge as winners in the highly competitive landscape. Not only will their biological products move smoothly through clinical research phases without any supply issues or safety and efficacy issues resulting from poorly qualified manufacturing processes and analytical methods that are typical of poor quality management, but these companies will also have the quickest path towards passing chemistry, manufacturing, and control requirements for product launch, including GMP inspections. What's more, for these few companies, the realization of commercial success can be easily expanded from local to global markets, achieving a much higher overall commercial value more quickly. These tremendous opportunities for the few companies that actively made investing in quality one of their top priorities will produce unprecedented return for all those involved, especially for the Chinese patients in need of more modern medicines.

For companies with a modernized and strong quality leadership team who are actively developing a quality culture, the advantage over other companies with similar product portfolios will become more and more obvious, especially towards the later stages of clinical manufacturing and product launch into successful initial commercialization. It is important to note that each company can choose different models to arrive at the end goal of commercialization: the Market Authorization Holder (MAH) policy instituted by the Chinese government in late 2015 encourages small R&D companies and even principal investigators from research institutes to move their product candidates through translational research into product development by using contract development and manufacturing services, instead of building their own internal capabilities, before their first commercial success. In this model, however, it is still of great importance for the MAH to acquire adequate quality leadership capabilities in-house that can guide them through their out-sourcing decisions and ensure all deliverables from their partners meet the intended quality and compliance standards as per their specific product requirements.

All companies that have employed solid quality management strategies, leadership, and systems will also be better at anticipating and resolving problems during product development and commercialization due to their risk management and knowledge management procedures—both key elements of a modern pharmaceutical quality system as defined in ICH Q10. As such, damages to their product development due to quality and compliance issues can be minimized, which adds to their competitive advantages amongst their peers.

The current "bottleneck" of biopharmaceutical product realization in China, exacerbated by the shortage of experienced GMP and quality professionals, especially those also with strong leadership capabilities, have created great opportunities for technical service platforms, ranging from all-encompassing biopharmaceutical service companies such as WuXi Biologics (Shanghai, China) and lesser-known similar companies such as MabPlex (Yantai, China) to other biopharmaceutical companies with products in development who are opening their GMP facilities for CMO services. These opportunities give rise to the growing contract service industry in China and such companies are playing increasingly important roles in the cost-effectiveness and ultimate commercial success of the biotechnology industry in China.

The contract services supporting the biotechnology industry in China have unique features due to the history of the biopharmaceutical industry and the regulatory landscape, which are both rapidly evolving. Many Chinese contract development and manufacturing organization (CDMO) service facilities/companies were built before the CFDA regulatory requirements were raised to the current standards and therefore are not

in compliance with the ICH or other current global industry standards. The biopharmaceutical companies using these CMO and contract research organization services need to be highly vigilant about the GMP compliance status of and quality standards that these services are working with. In addition, companies with novel therapeutic products also need to be concerned about employing the services of companies with competing products in an environment where intellectual property protection is not yet fully guaranteed by law or by culture.

A new type of contract service organization, a "contract quality organization" (CQO) has been born in China to provide full service and tailored contract quality management for biopharmaceutical companies as well as service providers looking to upgrade their GMP quality management status. In this business model, the CQO provides the right level and number of quality staff based on the specific needs of the client company, develops quality strategies and plans in line with the company's general business goals, and leads quality system implementation or improvement. More importantly, CQOs are deeply involved in major and minor quality decisions in the GMP operations of their client companies, including GMP training, product control strategies, major deviation investigations, product release decisions, and materials management. Therefore, a CQO service solves a unique problem in China where majority of small and mid-sized Chinese biotechnology companies are not able to find enough talent to form their own internal quality management teams to ensure quality and compliance during product development and initial product launch phases.

Conclusion

The biopharmaceutical industry in China is undergoing rapid growth simultaneously in conjunction with a transformation of its regulatory infrastructure towards a higher and more globally-compliant standard. This is resulting in a critical demand for strong quality management expertise to be available for all the companies transitioning from small-scale R&D operations towards clinical manufacturing and, eventually, commercial manufacturing operations. As human resources in various areas of biotechnology quality management remain extremely scarce in China, only companies that have successfully invested in recruiting and retaining quality leaders of international caliber can ensure not only much higher chances for their product success but also a sustainable supply of high-quality products for the large patient populations in China. Platform service-oriented businesses, such as CDMOs and CMOs specializing in biopharmaceutical R&D, manufacturing, and testing have proven to be highly valuable components of the Chinese biopharmaceutical ecosystem because they allow for the consolidation of the limited capabilities in China into common resources, therefore making them available to many more companies with drug candidates moving into clinical development stages. CQO, a new business model unique to the Chinese biotechnology market, fulfills the needs of customized quality management services for companies of different sizes who are in different stages of development by providing full-service strategic and operational support in all aspects of quality management. Jiayu Biomedical, the first CQO in China (and in the world) was founded in Suzhou, China in May 2017 and has been assisting clients and business partners with their specific quality management needs, which range from GMP facility design and qualification and quality system establishment and improvement to product and chemistry, manufacturing, and control strategy development, especially in areas of process control, analytical method validation, material management, process verification, third-party quality responsibility negotiation. Additionally, Jiayu Biomedical plays a role in major quality decisions during GMP manufacturing, testing, release, and cold chain management. The CQO company has been serving compa-

nies with pipelines representing the forefront of Chinese biopharmaceutical development with therapeutic modalities including but not limited to monoclonal antibodies, antibody-drug conjugates, and cell and gene therapies such as CAR-T. Specialized quality service providers like Jiayu Biomedical are expected to grow in number and become a vital part of the exciting Chinese biopharmaceutical landscape contributing to the selection and consolidation of the best new products into effective therapeutics for China and beyond.