

# REGULATORY SHIFT IN CHINA: EVOLUTION OF NMPA

## **ABSTRACT**

The paper aims to provide an outline and review of the major regulatory changes that NMPA has undergone in China since 2015 to speed up new products production and registration in accordance with international norms, as well as to raise the profile of Chinese medical products on a global scale. In the past, China's regulatory framework has been extremely difficult. Since 2015, China's health authority has been changing the organisational structure in China to bring Chinese therapeutic items up to international standards in terms of suitability, protection, and reliability, as well as to more likely locate individuals' general prescription drug requirement and expand access to new drugs and treatments from across the world. All the regulatory changes are making it easier to produce innovative products by implementing international standards and technological criteria, increasing review and approval transparency, and speeding up the new drug evaluation and approval, medical devices, and other products. The Chinese Ministry of Health has also issued guidance to help with drug production, including contact for drug development and technical assessment, introduction of electronic common technical documents, and post-approval safety surveillance. To promote the production of innovative products, regulations for priority review and approval, data protection regime, imported medical product registration, and new product classification are in place. China's regulatory system is constantly being reformed. It is possible to achieve simultaneous growth and approval in par with existing regulatory markets in the near future.

**Keywords:** NMPA, Regulatory, Reforms, Standards, innovative products, approval transparency

## **INTRODUCTION**

China is considered to be an epitome where tradition meets technology. It is evident that cultural preservation and innovations towards an advanced future go hand in hand in this country. This can even be said about the health care system in place. Even though majority of

people still practice traditional medicine, the domestic demand for effective drugs, and novel medical devices have increased <sup>[1]</sup>. This can be due to the growing old-age population and the countries economical status on a global level. This has resulted in tremendous changes as the whole healthcare is evolving towards a new universal healthcare<sup>[2]</sup>.

This also means that China is constantly changing and expanding with vast opportunities in terms of manufacturing, import and export of innovatory products, drugs, cosmetics, and medical devices. It is no secret that initially the walls around the Chinese market were looming high due to its language barrier and the regulations that were a bit difficult to comprehend and incorporate as it deviated so much from the harmonized approval process, it appears to be individual and tedious <sup>[3]</sup>.

The product registration process varies from that of many other countries in that all imported drugs, whether sold internationally or not, must contain evidence from local clinical trials; in terms of quality, there are substantial differences between global standards and certain domestic products and suppliers; the period it takes to evaluate and approve new medicines is longer than in most other major countries<sup>[4]</sup>.

Regional Chinese industries have historically been uninterested in the development of innovative new products due to strong competition in the generics market, and their current capacity for doing so is limited which can related to Indian market<sup>[5]</sup>.

These companies have previously focused on bioequivalence (BE) trials for generic drug registration, but with due to the regulatory shift and the evolution of CFDA into NMPA new standards, they will have to begin focusing on generic consistency and efficacy. As a result, any data that is deemed incorrect or incomplete will not be accepted, potentially causing current licenses to be revoked. This can also pave way for the industries to consider new innovative products in future <sup>[6]</sup>.

## **ADMINISTRATION IN CHINA**

Pharmaceutical policy in China has historically been relatively disjointed and uncoordinated between provinces, autonomous regions and national levels. They have various levels of

authority based on the hierarchy. NMPA have published norms to dissolve and maintain a unified chain of command amongst the regions [7].

Below is a brief outline of the administration in China [8]:



**Figure 1: Political Map of China**

A three-level system division amongst the country currently exist namely provinces, counties, and townships. The country is divided into regions, independent nations, and municipalities, all of which report directly to the Central authorities. China is currently divided into 23 provinces, 5 autonomous regions, 4 municipalities directly subordinate to the Federal Government, and 2 special organizational entities.

Navigating legal documents can present to be a bit different since rule (guizhang) and regulations (xingzheng fagui) are published in forms of circulars, notice, decree and letters [9].

## **DISCUSSION**

The aim of this shift is to encourage systemic change and improvise the pharmaceutical industry, bringing drugs, devices, and cosmetics which already on the market in China as well those that need to be formulated up to international effectiveness, protection, and quality standards <sup>[10]</sup>.

These reforms aimed to:

- Rectifying the current accumulation of registration applications.
- Create a global-development environment that promotes research and innovation of novel medications;
- Increase the transparency & consistency of the evaluation and approval process <sup>[11]</sup>.

Reforms	
2016	Self-inspection of clinical data
	Priority review
	Additional capacity at CDE
	Marketing Authorization Holder rationalization/new classification/definition of new drugs
	Generic drug quality and efficacy consistency Evaluation (GQCE)
2017	Opening up of first-in-human (FIH) Phase I trials to global development
	Simplified process for gaining a marketing approval
	Clinical trial management
	Acceleration of drug and medical device registration review process
	Drug and medical device life cycle management
	Protecting innovators' rights
2018	NHC Rare Disease list
	NMPA elected member of ICH Management Committee
	Technical Guideline for Acceptance of Overseas Drug Clinical Trial Data
	Adjusting the Approval Process for Drug Clinical Trial Evaluation (Circular 50)
	MAH pilot project extended one year
	Accelerated approval
	Independent Vaccine Administration Law
	CDE website
2019	Medical device site qualification notification
	MAH ADR direct reporting system online
	Oncology and rare disease drugs
	eCTD implementation progress and plan

**Figure 2: List of major reforms in NMPA during the 13<sup>th</sup> 5-year plan <sup>[12]</sup>**

**Table 1: Rules and Regulations published under NMPA during the 13<sup>th</sup> 5-year plan for drugs <sup>[13]</sup>**

<b>Drugs</b>				
<b>FILE</b>	<b>NAME</b>	<b>PHASE</b>	<b>IMPLEMENTED BY</b>	<b>ISSUE DATE</b>
<b>General Decree</b>				
<b>Decree No. 28 of 2020</b>	Approaches for Drug Manufacturing Control and Management	Implemented	NMPA	January 22, 2020
<b>Decree No. 39 of 2017</b>	Administrative Measures for Batch Issuance of Biological Products	Implemented	SFDA	December 29, 2017
	Approaches for Drug Manufacturing Control and Management	Implemented	NMPA	November 21, 2017
	Measures for the Administration of Internet Drug Information Services	Implemented	NMPA	November 21, 2017
	Measures for the Administration of Pharmaceutical Business Licenses	Implemented	NMPA	November 21, 2017
	Provisions for Administering the People's Republic of China's Drug Administration Law	Implemented	SFDA	February 6, 2016

<b><u>Registration/Filing</u></b>				
<b>Notice No. 119 of 2020</b>	Online application of drug registration	Implemented	Comprehensive Department of the State Drug Administration	
<b>Notice No. 2 of 2020</b>	The filing procedures and requirements of provincial-level Chinese herbal medicine preparation specifications	Implemented	NFDA	
<b>Notice No. 193 Of 2015</b>	The filling out relevant items in the Drug Production License	Implemented	SFDA	
<b><u>GMS/QMS</u></b>				
<b>Notice No. 160 of 2016</b>	Guiding Principles for On-site Inspection of Good Drug Management Practices	Implemented	SFDA	December 14, 2016
	Pharmaceutical business quality management practices	Implemented	SFDA	June 30, 2016
<b><u>Clinical Evaluation</u></b>				
<b>Notice No. 108 of 2019</b>	The Principles and Procedures of Drug Sampling and Other Documents	Implemented	Comprehensive Department of the State Drug Administration	December 26, 2019
<b>Notice No. 34 of 2016</b>	Clinical trial data verification work procedures	Implemented	SFDA	March 28, 2016

<b>Post Market Surveillance</b>				
<b>Notice No. 78 of 2015</b>	<b>Guidelines for Reporting, Monitoring and Inspection of Adverse Drug Reactions</b>	<b>Implemented</b>	<b>SFDA</b>	<b>July 2, 2015</b>

**Table 2: Rules and Regulations published under NMPA during the 13<sup>th</sup> 5-year plan for medical devices** <sup>[14], [15][16][17]</sup>

<b>Medical Device</b>				
<b>FILE</b>	<b>NAME</b>	<b>PHASE</b>	<b>IMPLEMENTED BY</b>	<b>ISSUE DATE</b>
<b>General Degree</b>				
<b>MJPRC- 20180825-1</b>	<b>Amended Regulation on Supervision and Management of Medical Devices of Medical Devices (Draft)</b>	<b>Draft</b>	<b>Ministry of Justice</b>	<b>June 25, 2018</b>
<b>Decree No.7 CFDA, 2017</b>	<b>Measures for Supervision and Administration of Medical Device</b>	<b>Implemented</b>	<b>CFDA</b>	<b>November 21, 2017</b>

	<b>Production</b>			
<b>Decree 4 CFDA, 2014</b>	Provisions for Medical Device Registration	Implemented	CFDA	July 30, 2014
<b><u>Registration/Filing</u></b>				
<b>Notice, CMDE- 20190103</b>	Operation Specification for Record Filing of Medical Device Master Files	Draft	CMDE	January 3, 2019
<b>Notice, CMDE- 20190103</b>	Record Filing Requirement of Medical Device Master Files	Draft	CMDE	January 3, 2019
<b>Notice, CMDE- 20190103</b>	Guideline for Record Filing of Medical Device Master Files	Draft	CMDE	January 3, 2019
<b>Notice, CMDE- 20190103</b>	Announcement on Record Filing of Medical Device Master Files	Draft	CMDE	January 3, 2019
<b>Notice, No. 83, NMPA, 2018</b>	Innovation Device Approval Procedure	Implemented	NMPA	November 5, 2018
<b>Notice, NMPA- 20180822</b>	Unique Device Identification (UDI) Implementation Plan	Draft	NMPA	August 22, 2018
<b>Notice, No.131, CFDA, 2017</b>	Using Chinese Name for Registrant or File Submitter of Imported Medical Devices	Implemented	CFDA	November 2, 2017
<b>Decree 6, CFDA, 2014</b>	Regulation on Instructions for Use and Labels of Medical Devices	Implemented	CFDA	July 30, 2014
<b><u>GMP/QMS</u></b>				



<b>Notice No.101 NMPA, 2018</b>	Regulations for the Administration of Overseas Inspection of Pharmaceutical & Medical Devices	Implemented	NMPA	December 26, 2018
<b>Notice No.19 CFDA, 2016</b>	Good Manufacturing Practice in Class III Medical Device Manufacturers	Implemented	NMPA	February 5, 2016
<b>Notice No.218 Annex 3, CFDA</b>	Good Manufacturing Practice Guidelines for Onsite Inspection of Implantable Medical Devices	Implemented	CFDA	September 25, 2015
<b>Notice No. 218 Annex 2, CFDA</b>	Good Manufacturing Practice Guidelines for Onsite Inspection of Sterile Medical Devices	Implemented	CFDA	September 25, 2015
<b>Notice No.218 Annex 1, CFDA</b>	Good Manufacturing Practice Guidelines for Onsite Inspection	Implemented	CFDA	September 25, 2015
<b>Notice, No.103, CFDA, 2015</b>	Good Manufacturing Practices on In Vitro Diagnostic Reagents	Implemented	CFDA	July 10, 2015
<b>Notice, No.102, CFDA, 2015</b>	Good Manufacturing Practice for Implantable Medical Devices	Implemented	CFDA	July 10, 2015
<b>Notice, No.64, CFDA, 2014</b>	Good Manufacturing Practice for Medical Devices	Implemented	CFDA	December 29, 2014
<b><u>Clinical Evaluation</u></b>				

<b>Notice CMDE- 20181122-2</b>	Technical Guideline for Comparing the Same Variety of In-vitro Diagnostic Reagents Exempted from Clinical Trials (Draft)	Draft	CMDE	November 22, 2018
<b>Notice CMDE- 20181122-1</b>	Guidelines for Clinical Trials of In Vitro Diagnostic Reagents (Draft)	Draft	CMDE	November 22, 2018
<b>Notice No.6, CFDA, 2018</b>	Medical Device Clinical Trial Design Guideline	Implemented	CFDA	January 8, 2018
<b>Notice No. 179, CFDA, 2017</b>	Basic Requirements for Clinical Evaluation Materials of IVD Exempted from Clinical Trial (Draft)	Implemented	CFDA	November 8, 2017
<b>Decree 25, CFDA, 2016</b>	Good Clinical Practice for Medical Device	Implemented	CFDA/National Health Commission	March 23, 2016
<b><u>Guideline &amp; Standard</u></b>				
	Current China NMPA Clinical Pathways for Medical Device Registration (Draft)			November 18, 2020
	Drug-Medical Device Combination Products in China (Draft)			September 21, 2020
<b>Notice No.7, CMDE, 2019</b>	Guideline on AI-Aided Software	Implemented	CMDE	July 3, 2019
<b>Notice No.50,</b>	Guideline for Technical Review of Medical Device	Implemented	CFDA	August 18, 2015

<b>CFDA, 2015</b>	Software Registration			
<b><u>Post Market Surveillance</u></b>				
<b>Decree 1 Annex 9, NMPA, 2018</b>	Guidance on Inspecting Medical Device Adverse Event Monitoring Activity	Draft	NMPA	September 20, 2018
<b>Decree 1 Annex 7, NMPA, 2018</b>	Guidance on Focus Points when Monitoring Medical Device Adverse Events	Draft	NMPA	September 20, 2018
<b>Decree 1 Annex 5, NMPA, 2018</b>	Guidance for License Holder on Collecting and Reporting Individual Cases of Medical Device Adverse Event	Draft	NMPA	September 20, 2018
<b>Decree 1 Annex 3, NMPA, 2018</b>	Guidance on Medical Device Adverse Event Monitoring Scope	Draft	NMPA	September 20, 2018
<b>Decree 1 Annex 1, NMPA, 2018</b>	Guidance on Medical Device Adverse Event Monitoring	Draft	NMPA	September 20, 2018
<b>Decree 1, NMPA, 2018</b>	Measures for the Administration of Medical Device Adverse Event Monitoring and Re- evaluation	Implemented	NMPA	August 31, 2018
<b>Decree 29, NMPA, 2018</b>	Measures for the Administration of Medical Device Recall	Implemented	CFDA	January 25, 2017

**Table 3: Rules and Regulations published under NMPA during the 13<sup>th</sup> 5-year plan for Cosmetics** <sup>[18][19][20]</sup>

Cosmetics				
FILE	NAME	PHASE	IMPLEMENTED BY	ISSUE DATE
<b><u>General Decree</u></b>				
<b>Announcement No. 265 of 2015</b>	Cosmetics Production licensing	Implemented	SFDA	December 15, 2015
	Cosmetics Supervision and Administration Regulations	Draft	CSAR	June 30, 2020
<b><u>Registration/Filling</u></b>				
<b>Drug Administration Letter (2020) No. 105</b>	Administrative Measures for Cosmetics Labeling	Draft	NMPA	September 21, 2020
	Administrative Measures for Cosmetic Supplementary Inspection Methods	Draft	CSAR	November 12, 2020
	Cosmetic Sampling Inspection Management Regulations	Draft	CSAR	September 27, 2020

<b>Announcement No. 195 of 2017</b>	General Administration on Regulating the Registration and Filing of Cosmetics Related Matters	Implemented	SFDA	November 30, 2017
<b>Announcement No. 31 of 2018</b>	Pilot Implementation of the Filing Management of Imported Non- Special Purpose Cosmetics	Implemented	SFDA	March 8, 2018
<b>Drug Administration Letter (2020) No. 105</b>	Administrative Measures for Cosmetics Labeling	Draft	NMPA	2020-09- 21
<b><u>GMS/QMS</u></b>				
	Cosmetic Production Quality Management Standards	Draft		September 27, 2020
<b>Notice No. 4 (2018)</b>	Regulating the Risk Monitoring of Cosmetics	Implemented	SFDA	January 5, 2018
<b><u>Guidelines and Standards</u></b>				

<b>Drug Administration Letter ( 2020 ) 82</b>	Technical Guidelines for Safety Assessment of Cosmetics	Draft	Department of Cosmetics Supervision, National Food and Drug Administration	July 29, 2020
<b>Drug Administration Letter (2020) 82</b>	Rules for Classification of Cosmetics and Classification Catalogue	Draft	Department of Cosmetics Supervision, National Food and Drug Administration	July 29, 2020
<b><u>Post Market Surveillance</u></b>				
<b>Notice No. 94 (2020)</b>	Cosmetics Adverse Reaction Monitoring Management Measures	Draft	SFDA	September 27, 2020

## **CONCLUSION**

Few changes over the course of these 5 years speaks for itself taking into consideration that in China, there have been an increase in the number of clinical research centres and clinical organisations. In April 2016, China only had 478 clinical trial institutions. In 2019, there were 886 authorized clinical study organizations, an 185 percent rise over the past year.

By introducing in November 2019 the record-setting system for registering and administering clinical trials institutions in China, more and more healthcare facilities will be qualified for clinical trials. This will allow China to address the growing number of clinical trials ongoing in the country, as well as encourage the drug development.

In 2017, the Chinese regulator, the National Medical Products Administration (NMPA) joined ICH, highlighting the convergence of the Chinese regulatory system with international norms.

China is a prominent advocate and defender of globalisation as the world's second largest economy. Chinese pharmaceutical innovation can only be globalised by mutual recognition of clinical trials data from China and the world. Between new medicine licences in the United States and China there existed a delay between five and seven years before 2015. Due to the above-mentioned Chinese pharmaceutical reforms, this time lag was decreased to one or two years, and in certain situations to few months. As part of this internationalisation process, Chinese domestic innovation capacities and achievements are rising rapidly.

China was appointed in 2018 to McKinsey's second-level innovator list, alongside Europe and Japan's creative markets, representing China's remarkable success in pharmaceutical innovation. Previous limits on drug and medical-device innovation have been lifted as the breadth of these reforms' spreads across multiple stages of the products life cycle.

#### **COMPETING INTERESTS DISCLAIMER:**

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

#### **REFERENCES**

1. Feng Z, Liu C, Guan X, Mor V. China's rapidly aging population creates policy challenges in shaping a viable long-term care system. Health Aff (Millwood) 2012;31(12): 2764-73

2. Dai, W., Zhong, M., Lin, W. and Su, L., 2021. Overview on the Amendments of Provisions for Drug Registration in China. *The Journal of Clinical Pharmacology*, 61(1), pp.74-81.
3. Yip WC, Hisao WC, Chen W, Hu S, Ma J, Maynard A. Early appraisal of China's huge and complex health-care reforms. *Lancet* 2012;379:833–42.
4. China.org.cn. Focus on Chinese economy data in 2010. 2011. Available from: [www.china.com.cn/economic/node\\_7109305.htm](http://www.china.com.cn/economic/node_7109305.htm) [Last accessed 30 April 2014]
5. Ministry of Health P.R.China, WHO. China-WHO country cooperation strategy 2013-2015. 2013. 21
6. Woo J, Kwok T, Sze F, et al. Ageing in China: health and social consequences and responses. *Int J Epidemiol* 2002; 31(4): 772–775.
7. Sciences CAoM. China's health care development report (2009-2014). Beijing, China: Sciences CAoM, 2015.
8. Liu ZL, Bo Y, Wei SF, et al. 2014 China medical device industry development blue book. Beijing, China: China Pharmaceutical Materials Association, 2015.
9. CNCBD. Internation comparison of China medical device technology innovation and industry competitiveness. Beijing, China: Science Press, 2010, pp. 416–437.
10. CFDA. Regulations on the supervision and administration of medical devices, <http://www.sfdachina.com/info/69-1.htm> (accessed 7 March 2014).
11. Guo Y, Yang BX and Yang YH. Current situation and developing trend of china medical devices industry. *Chin Med Device Inf* 2011; 17(7): 40–47.
12. Boyer P, Morshed BI and Mussivand T. Medical device market in China. *Artif Organs* 2015; 39(6): 520–525.
13. Chen, L., Li, Y., Liu, C. and Liu, D., 2019. Updates on Drug and Device Regulatory Reform in China. *Applied Clinical Trials*, 28(12), pp.20-22.
14. Yip W, Hsiao W. China's health care reform: a tentative assessment. *China Econ Rev* 2009;20:613–9.
15. Meng Q, Xu K. Progress and challenges of the rural cooperative medical scheme in China. *Bull World Health Organ* 2014;92:447–51.
16. Liu GG, Fukuda T, Lee CE, Chen V, Zhen Q, Kamae I. Evidence-based decision-making on medical technologies in China, Japan, and Singapore. *Value Health* 2009;12(Suppl. 3):S12–7.



17. Meng Q, Xu L, Zhang Y, et al. Trends in access to health services and financial protection in China between 2003 and 2011: a cross-sectional study. *Lancet* 2012;379:805–14.
18. Dong H, Duan S, Bogg L, et al. The impact of expanded health system reform on governmental contributions and individual copayments in the new Chinese rural cooperative medical system. *Int J Health Plann Manage* 2014 May 22. Epub ahead of print.
19. Frew SE, Kettler HE, Singer PA. The Indian and Chinese health biotechnology industries: potential champions of global health? *Health Aff (Millwood)* 2008;27:1029–41.
20. Sun P. Medical device regulation in China and the US: a comparison and a look forward. *Intersect* 2012;5:1–16.
27. He C. Foreign manufacturing investment in China: the role of industrial agglomeration and industrial linkages. *China World Econ* 2008; 16:82–99.