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Introduction of changes in National Medical Product Administration: NMPA

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General Introduction

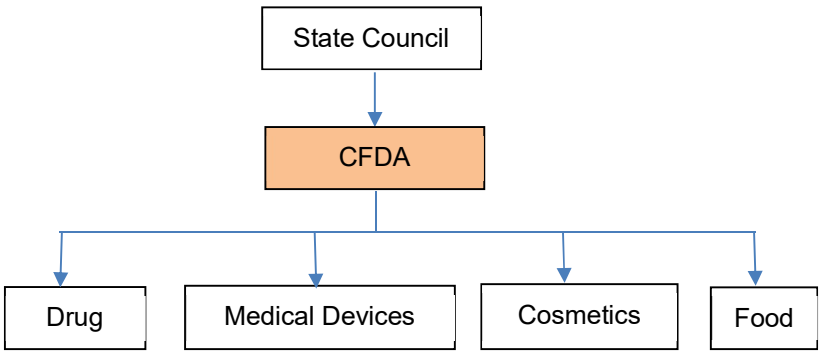
The NMPA (National Medical Products Administration) was known as the CFDA (China Food and Drug Administration) before the Chinese government reform of 2018.

Two major changes have occurred as a result of the reform:

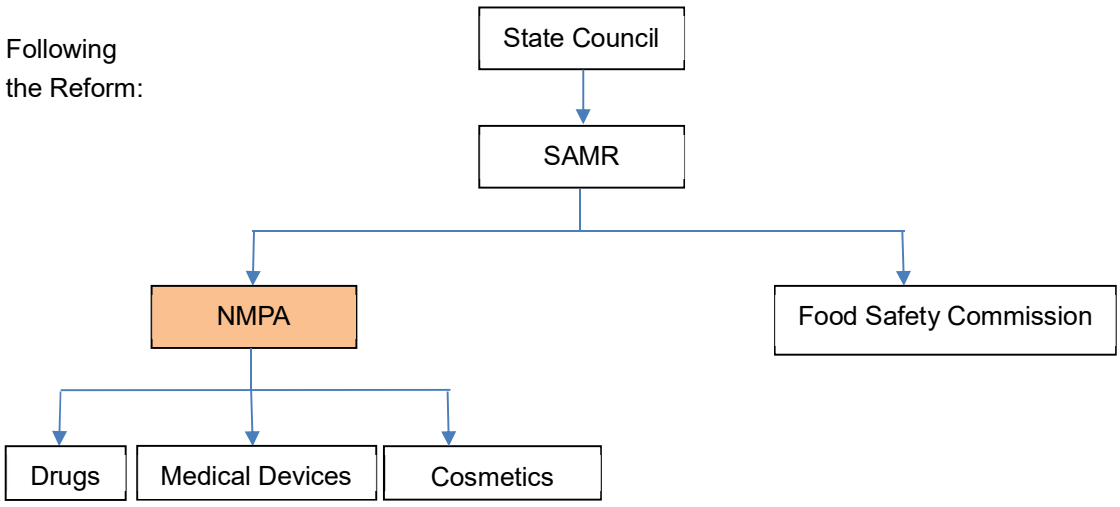
1) Food is no longer under the authority's administration;
2) Prior to the reform, the CFDA was directly under the state council's administration. Now, the NMPA is under the administration of SMAR (State Administration for Market Regulation) (SAMR), a ministerial level bureau.

Organization chart prior and following the reform:

Prior to the Reform:



Following the Reform:



Now NMPA performs administration and surveillance to drug, medical device and cosmetics. As a vice-ministerial level governmental body, it consists 11 departments and 17 affiliated institutions.[1]

1 Please refer to the NMPA official website at: http://english.nmpa.gov.cn/NMPAorganizations.htm

Head of the NMPA is the Commissioner, Ms. Jiao Hong, Mr. Hong Has four vice commissioners:

- Mr. Li Li, CPC Secretary, Vice Commissioner
- Mr. Xu Jinghe, Vice Commissioner in charge of Medical Devices
- Mr. Chen Shifei, Vice Commissioner in charge of Drugs
- Ms. Yan Jiangying, Vice Commissioner in charge of Cosmetics

Below are the main medical products related departments and affiliated institutions:

Product	Pre-market Administration	Post-market Surveillance	Approval Body
Drugs	Drug Registration Department	Drug Regulation Department	Center for Drug Evaluation (CDE)
Medical Devices	Medical Device Registration Department	Medical Device Regulation Department	Center for Medical Device Evaluation (CMDE)
Cosmetics	Cosmetic Regulation Department	Cosmetic Regulation Department	Cosmetic Regulation Department

Along with strengthening international cooperation and connection to international standard, most of NMPA websites are available in English. For a comprehensive understanding of the NMPA structure, please refer to

http://english.nmpa.gov.cn/NMPAorganizations.html

Some of the main functional departments' English websites are listed below:

Drugs	
Registration Department	http://english.nmpa.gov.cn/2019-07/18/c_377593.htm
Regulation Department	http://english.nmpa.gov.cn/2019-07/18/c_377597.htm
General Administration Rules	http://english.nmpa.gov.cn/drugs.html
Center for Drug Evaluation	http://www.cde.org.cn/linshi/regulatEn/regulatMainEn.jsp
Medical Device	
Registration Department	http://english.nmpa.gov.cn/2019-07/18/c_377598.htm
Regulation Department	http://english.nmpa.gov.cn/2019-07/18/c_377599.htm
General Administration Rules	http://english.nmpa.gov.cn/medicaldevices.html
Center for Medical Device Evaluation	https://www.cmde.org.cn/CL0001/ English introduction only available on WeChat
Cosmetics	
Regulation Department	http://english.nmpa.gov.cn/2019-07/18/c_377600.htm
General Administration Rules	http://english.nmpa.gov.cn/cosmetics.html
Imported Non-special Purpose Cosmetics	http://cpnp.nmpa.gov.cn/enterprise/index.jsp (Chinese

Filing	only)
Imported Special Purpose Cosmetics Registration	http://cprp.nmpa.gov.cn/enterprise/index.jsp (Chinese only)

Drug Administration

The revised Drug Administration Law entered into force on December 1, 2019. Listed below are several highlights:

i) Drug Marketing Authorization Holder (MAH)[2]

A drug marketing authorization holder refers to any enterprise or drug development institution, which obtains a drug registration certificate. The MAH shall be responsible for the following activities: non-clinical research, clinical trial, production and distribution, post-market study, adverse reaction monitoring/report/handling.[3]

MAH system has been implemented, meanwhile drug GMP (Good Manufacturing Practice) and GSP (Good Supply Practice) will be gradually no longer be relevant. The MAH will be responsible for drug safety, efficacy and quality control throughout the whole process involving development, production, distribution and use. To achieve this, drug traceability system must be established within the chain of MAH, manufacturer, distributor and medical institutions.

For overseas companies being the MAH, a Chinese domestic company must be appointed and entrusted to perform MAH obligations. A joint liability will be shared between the Chinese domestic and foreign company.

The drug marketing authorization can be transferred to different body upon NMPA approval.

ii) Drug Evaluation and Approval Priority

Drug evaluation process will be optimized as part of the new revised law by introducing expert consultation, communication

2 https://www.kwm.com/en/cn/knowledge/insights/major-changes-in-the-newly-revised-drug-administration-law-20190830
3 Article 30 of Drug Administration Law
2 https://www.kwm.com/en/cn/knowledge/insights/major-changes-in-the-newly-revised-drug-administration-law-20190830
3 Article 30 of Drug Administration Law

and opinion exchange mechanism. Drug review conclusion and approval basis will be subject to social supervision, which focuses on making drug review transparent, disclosing drug review information to public to ensure fair evaluation and process legitimate.[4]

Articles 16, 26 and 96 specifies several circumstances for drug benefiting from evaluation priorities, including:

i. drugs for children's use;

ii. drugs treating seriously life-threatening disease;

iii. drugs meeting urgent public health needs;

iv. drugs meeting urgent clinical needs; and

v. new drugs for preventing and treating major infectious diseases and rare diseases.

iii) Imported drugs

According to the general provision, drugs can be imported through any port permitted for drug importation, designated by NMPA, the Customs and the State Council. The process is detailed below:

i. drug importer must file the import request with local NMPA;

ii. the local NMPA is to issue an "import drug approval" upon NMPA entrustment;

iii. the Custom process custom clearance upon "drug import approval" issued by local MPA where the custom located;

iv. drug inspection might be randomly conducted by the Customs

Upon approval, drugs for urgent clinical needs can be imported to China. For personal use, a small amount of drugs can be brought into China.

iv) Drug Emergency Evaluation

[4] Article 27 of Drug Administration Law

In the beginning of 2020, along with COVID-19 outbreak, NMPA established and emergency approval track for drugs for public health needs and new drugs for preventing and treating major infectious diseases, as stipulated in Article 26 and 96 of Drug Administration Law. The specific procedure is regulated by "CFDA Drug Special Approval Procedure"[5] (Ministry Order No.21) issued in 2005.

Note the following key points:

i. Whole procedure including "application and plant visit"; "registration and testing"; "technical assessment"; "clinical trials"; "production approval and surveillance";

ii. For unregistered drugs in China, R&D matters are required to disclose to NMPA by applicant;

iii. A special expert group will be established by NMPA.NMPA will be the only authority responsible for the whole process;

iv. Although each procedure's duration is much shortened, the purpose of special procedure is not to lower drug entry requirements

For example, From the beginning of 2020, NMPA urgently approved 5 drugs entering clinical trial, including Remdesivir and Favipiravir, in a fast track of two months.

[5] Original text please refer to http://www.nmpa.gov.cn/WS04/CL2174/300621.html

Comparison between the old and the new Drug Administration Law:

	Old Drug Administration Law	New Drug Administration Law
supervision system	drug adverse reaction report system - in case a serious adverse reaction occurs, the incident must be reported to local authority	drug traceability system - the information is traceable throughout the whole process of development, production, sale and use
Responsible Body	Producer- Good Manufacturing Practice certificate; Distributor- Good Distribution Practice certificate	The MAH will be responsible for the whole life cycle of the drug. GMP and GDP certificate are no longer needed
Penalty (the value of the fine has increased)	Fine- -e.g. producing or selling counterfeit drugs will lead to a fine, worth 2-5 times of the product's value	Fine--e.g. producing or selling counterfeit drugs, will lead to a fine, worth 15-30 times of the product's value
Innovation	No special provision for innovative drugs	Innovative drugs are encouraged- Article 16:states supports new innovative drugs that provides special and direct treatment to disease; encourages TCM treatment innovation; and innovation of pediatric drug.

Medical Device Administration

Medical devices companies accounts for a large part of Israeli health care industry.

i) Basic Understanding of Medical Device Registration

Domestic medical devices are administrated by different levels of the NMPA in accordance with their level of risk; imported medical devices are all administrated by central NMPA, regardless of their level of risk.

The relation between manufactures' location and the administration is detailed below:

	Imported Medical Device	Domestic Medical Device
Manufacture Site	Outside of China	In China
Regulatory MPA Level	Class I: Central NMPA Class II: Central NMPA Class III: Central NMPA	Class I: City-level NMPA Class II: Province-level NMPA Class III: Central NMPA

Clinical trial for Class II and III medical devices require a highly time consuming registration process. Updated "Clinical Trial Exemption List" has been published by NMPA in 2018 and revised in December 2019. Currently over 1,003 medical devices and 416 In Vitro Devices (IVD) products are exempted from clinical trials.[6]

NMPA has released an announcement on the "Technical Guidelines on the Acceptance of Data from Overseas Clinical Trials of Medical Devices".

[6] http://www.nmpa.gov.cn/WS04/CL2201/372788.html

According to the announcement, overseas clinical trial data can be used when an applicant submits a medical device registration request in China. Instead of going through clinical trials again, an evaluation report must be submitted to justify different aspects that may affect clinical trial results, such as races, ethnic groups, age, gender, social and healthcare environment etc.

ii) Special Evaluation Procedure for Innovative Medical Devices

Innovative Medical devices evaluation shall go through a special fast track. Comparing with the regular track, the total evaluation and approval period could be shortened[7]. This procedure was revised and came into force on 1 December 2018[8].

To start an application process, the following key supporting documents are required:

i. IP rights certificate of the product;
ii. Summary of R&D process and outcome;
iii. Technical notes of the product;
iv. Product risk analysis;
v. Applicant enterprise qualification.

In order to prove innovation, the following materials need to be submitted:

i. Papers publicized on academic periodicals and journals which fully explain the clinical practice value of the product;
ii. Similar product marketed domestic and abroad, including analysis and comparison;
iii. Innovative contents of the product and their significant value in clinical practice.

Practically, a reliable Chinese partner and an urgent need for the device for public health reasons are both important factors that may

[7] http://www.cmdi.org.cn/publish/default/zhixuntop_1/content/20190111093559172 62.htm
[8] http://www.nmpa.gov.cn/WS04/CL2138/331560.html

positively affect evaluation process.

iii) Guiding Principles for Technical Review of Mobile Medical Device Registration

This principle released in December 2017 specifies three categories of Mobile Medical Devices ;(i) Mobile Medical Devices; (ii) Mobile Independent Software, such as the cloud computing for disease diagnosis; and (iii) Mobile Medical Auxiliaries. Basically, health management and recording devices without treatment functions cannot be classified as Mobile Medical Devices. The guiding principle does not get into much detail regarding to Mobile Medical Device description. However, the medical device must fit into catalog published by NMPA August 2017[9]. If the product doesn't suit into this catalog, applicant can apply for classification determination from the CMDE (Center for Medical Device Evaluation).

Cyber security is a critical factor for the evaluation of mobile medical devices. User data confidentiality and internet accountability must comply with the national standard[10].

iv) Medical Device Registrants System

According to the NMPA notification issued on 1 August, 2019, pilot areas of medical device registration system has been extended to 21 provinces[11].

According to current practice, a medical devices producer must apply to local MPA to get "Medical Device Production License" before manufacturing. MPA registration certificate is a necessary criteria for applying production license.

Under the medical devices registration scheme, the medical devices registrants doesn't have to be the manufacturer of the device. With "Medical Device Registration Certificate", the registrant can

[9] http://www.nmpa.gov.cn/WS04/CL2138/300389.html
[10] Refer to GB/T 29246-2012
[11] http://www.nmpa.gov.cn/WS04/CL2197/339662.html

entrust capable company to produce and be responsible for the medical device in its whole life circle. In this way, the manufacture of the medical device doesn't have to be confined within local MPA administration. For example, if the registrant is in Beijing, it can entrust any company within the 21 pilot provinces to manufacture the medical device. The registrant can be medical device producer or research institute, with quality management, risk control ability, be responsible for product quality and safety management.
This will benefit NMPA's surveillance, as the registrants will play an important role in product quality and safety enforcement. As a result, NMPA will be able to focus more on the whole industry rather than each individual product.

v) Fast Track through "Boao Lecheng Pilot Zone"

On February 2013, the State Council approved the establishment of "Hainan Boao Lecheng International Meidcal Tourism Pilot Zone". As a result, some private hospitals started operation there, such as "Boao Super Hospital"; "Boao Evergrande International Hospital"; "Changsheng International Medical Center", etc.

The Hainan government and the local MPA support the pilot zone by issuing favorable policies for imported medical devices entering into the different hospitals within the pilot zone. For example, the procedure at the "Boao Super Hospital" will be as following:

i. internal evaluation will be done by the hospital, to assess how advanced the device is and whether the device is irreplaceable; if the internal evaluation is positive, the Boao Hospital will submit an application to the Hainan MPA, which will go through a preliminary assessment and issue the approval paper for Customs clearance;
ii. in case the medical device requires NMPA approval in order to be sold in markets outside the Boao Hospital, clinical trial policy at the hospital's site is more relaxed. for instance, if

normally 300 samples are required to be tested, Boao's policy allows for only 100 samples to be required.

Comparing with the NMPA's generally strict rules, and taking into account the unfamiliarity of the Chinese market, the pilot zone can provide a good opportunity for foreign companies making their first steps at the Chinese market.

vi) Medical Device Emergency Approval

The relevant regulation is "Medical Device Emergency Approval Procedure" (CFDA [2009] No.565)[12]. This procedure applies to public emergency needed products. During COVID-19, as of 5 May and under this procedure, NMPA approved 30 test kits; provincial MPA fast approved 348 protective clothing, 173 medical protective masks, 879 surgical masks, 1,255 medical disposable masks and 301 infrared thermometers[13].

For foreign products that are not marketed in China, "Opinions regarding to Emergency Import of Unregistered Medical Device" issued by NMPA, determined that if the provincial level COVID-19 prevention and control mechanism think the import is necessary, then provincial MPA, Industry and Technology Information Bureau, Health Commission and Custom can allow the importation. The imported product must comply with US, EU or Japan standards. Safety declaration must be made.[14]

12 http://www.nmpa.gov.cn/WS04/CL2197/324626.html
13 http://www.nmpa.gov.cn/WS04/CL2590/
14 http://mpa.ah.gov.cn/zwgz/gsgg/99420161.html

Cosmetics

From the origin perspective, cosmetics can be divided into domestic and imported cosmetics; for different functions, cosmetics can be classified as "Special-Purpose Cosmetics" and "Non-special Purpose Cosmetics".

i) Special-Purpose Cosmetics" refers to cosmetics that are used for hair nourishment, hair coloring, hair perm, hair removal, breast beauty, body building, deodorization, speckle removal and sun protection. Production of Special-Purpose Cosmetics must get NMPA approval documents first.[15]

   For imported Special-Purpose Cosmetics, the importer must submit requested documents to get NMPA approval.

ii) For imported "Non-special Purpose Cosmetics", "a foreign company shall set up a representative office or designate a local Chinese company as the responsible entity for filing, assisting in monitoring adverse reactions and be responsible for product safety"[16].

On 10 Sept. 2019, NMPA issued the "Work Specifications for Cosmetics Registration and Record-filing Inspection", which rules that Cosmetic Inspection and Testing Institutions must obtain a "CMA (China Inspection Body and Laboratory Mandatory Approval)" certificate before being able to conduct inspection work.

For imported cosmetics, as specified in the "Measures for Import and Export Cosmetics Inspection, Quarantine, Supervision and Administration" promulgated on 23 Nov. 2018, the inspection and quarantine will be conducted according to compulsory requirements of China's national technical code and agreements or protocols signed

[15] Article 10 of Regulations on the Hygiene Supervision over Cosmetics (Revised in 2019)
[16] http://www.cnstandards.net/index.php/measures-of-non-special-purpose-cosmetics-filing-draft/

between China and the exporting countries.

For cosmetics imported the first time, following documents must be provided:

i. if subject to hygiene license, then hygiene license must be provided;

ii. if subject to filing, then filing record must be provided;

iii. for cosmetics not subject to hygiene license nor filing, then safety assessment report and certificate of origin must be provided;

iv. package for sales must provide Chinese label and foreign label translation;

v. product name, quantity/weight, specifications, production location, batch no. and usage period must be provided for finished product non-sales package.

Summary

The Israeli Economic Mission to China in Beijing is constantly following changes in the Chinese regulation. We recognize changes in the NMPA policy, as presented in this paper. The NMPA investment more effort on the legislation process; in order to keep medical products' administration and surveillance in comply with practical business activity and economic development, and adopts mechanisms on product quality and safety control.

After NMPA joining IMDRF and ICH, gradually implementing drug MAH, medical devices registrant system, opening pilot zone for clinical Real World Evidence, we can see Chinese medical product administration is more in line with international standard.

For more information or if you have any questions, please contact us at: Beijing@israeltrade.gov.il