RAMED NEWSLETTER

on NMPA Policies

(Jan-Sep, 2018)

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Issuance of *Administrative Measures for the Monitoring and Re-evaluation on the Adverse Events of Medical Devices*

To strengthen the monitoring and re-evaluation on medical device adverse events, so as to timely and effectively control the risks of post-marketed medical devices, recently, the State Administration for Market Regulation and the National Health Commission of the People's Republic of China jointly issued the Administrative Measures for the Monitoring and Re-evaluation on the *Adverse Events of Medical Devices* (SAMR Decree No. 1, hereinafter referred to as the Measures), which shall come into force as from January 1, 2019.

The *Measures* clarified the principal responsibilities of holders of marketing license for medical device; separately defined the time limits, procedures, and work requirements for reporting and evaluation in light of the essential requirements, individual adverse events, group adverse events, and periodic risk assessment reports; detailed the requirements for the holders' risk control; and stipulated that the holders should perform re-evaluation actively, strengthen the supervision and inspection of the drug regulatory authorities, and increase the punishment for violations of laws and regulations.

The *Measures* have improved the monitoring system for adverse events and strengthened the obligation of holders to report adverse events directly. The risk control requirements have also been consolidated. It is stipulated that where the product has been spotted with unreasonable risks that may endanger human health and life safety during the monitoring, the holder should take the corresponding measures, such as stopping production, implementing recall, and modifying the Instructions for Use, etc., and should timely publicize the risks related to the safe use of medical devices and corresponding disposals.

The *Measures* established the Intensive Monitoring System, which stipulates that the drug regulatory authorities at or above the provincial level can designate qualified units as the monitoring sites to actively collect the data of products being monitored. The drug regulatory authorities shall take necessary administrative measures in a timely manner against the risks found during the monitoring.

The *Measures* improved the re-evaluation system, clarified the principal responsibility of the holders to carry out re-evaluation on their own accord, and required the holders to carry out re-evaluation actively. Where the results of re-evaluation indicate that the products have defects that endanger personal safety, or the risk-benefit ratio is unacceptable, the holders shall proactively apply for cancellation of the marketing license, and make the public informed in a timely manner.

The *Measures* strengthened the supervision and inspection to severely investigate and deal with illegal acts of nonperformance of

Responsibilities of direct reporting. It also required that provincial drug regulatory authorities shall formulate inspection plans, clarify inspection priorities, and supervise and inspect the system construction and implementation status of adverse event monitoring performed by the holders.

(August 31, 2018)

NMPA Issued the Announcement on Revising the Requirements for Application Dossiers of Medical Device Registration Renewal and Others

To implement the policies set forth in the Opinions of the General Office of the CPC Central Committee and the General Office of the State Council on Deepening the Reform of Review & Approval System to Encourage Innovation in Drugs and Medical Devices (General Office [2017] No. 42), and the State Council's requirements for deepening the reform of "Streamlining Administration, Delegating More Powers to Lower-level Governments and Society, Improving Regulation and Optimizing Services", further simplify and optimize the registration renewal for medical devices and review and approval of clinical trials, improve the review & approval efficiency, NMPA has organized revisions of the requirements for application dossiers of medical device registration renewal, etc., and issued an Announcement on August 23, 2018, which shall be implemented as from the date of issuance. (August 23, 2018)

NMPA Office Issued the *Notice on Strengthening the Management of Medical Device Production & Distribution Licensing (Record-filling) Information*

To continuously improve the medical device production & distribution licensing (record-filling), strengthen the management of information thereof, and facilitate regulatory authorities and enterprises to use the “Medical Device Production & Distribution Licensing (Record-filling) Information System”, so as to adapt to the provisions for medical device administration, on August 2, 2018, NMPA Office issued the above Notice, requiring the food and drug administrations of all provinces, autonomous regions and municipalities directly under the Central Government, the Xinjiang Production and Construction Corps to effectively adjust, disclose and upload the information of medical device production & distribution (record-filling). (August 2, 2018)

CNDA Issued the Guidelines for Compiling Application Dossiers for Review & Approval of Clinical Trials for Passive Implantable Medical Devices

As per the *Opinions on Deepening the Review and Approval System Reform and Encouraging the Drug and Medical Device Innovation* issued by the General Office of the CPC Central Committee and the General Office of the State Council (CPCCC & SC General Office [2017] No. 42), to strengthen the supervision and management of medical device clinical trials, and further improve the quality of registration review, according to the *Announcement on Issuing the Requirements for Medical Device Registration Application Dossiers and the Format of Approval Documents* (CFDA Announcement [2014] No. 43), CNDA organized to formulate the *Guidelines for Compiling Application Dossiers for Review & Approval of Clinical Trials for Passive Implantable Medical Devices* which was released on June 4, 2018. (June 7, 2018)

CNDA General Office Issued the *Notice on the Management Specifications for the Development and Revision of the Guidelines for Technical Review of Medical Device Registration*

To strengthen the standardized management of medical device registration and the development and revision of the guidelines for technical review of medical device registration, CNDA organized to formulate the *Management Specifications for the Development and Revision of the Guidelines for*

Technical Review of Medical Device Registration which was released on May 28, 2018 and effective thenceforward.

(May 28, 2018)

National Drug Administration Issued Four Guidelines for Technical Review of Registration Including the Guidelines for Technical Review of Surgical Microscope Registration

To strengthen the supervision and guidance over the medical device registration and further improve the registration review quality, National Drug Administration has formulated the *Guidelines for Technical Review of Surgical Microscope Registration*, the *Guidelines for Technical Review of Medical Clean Bench Registration*, the *Guidelines for Technical Review of Ophthalmotonometry Registration*, and the *Guidelines for Technical Review of Pulse Wave Velocity and Ankle-brachial Index Testing Product Registration* which were released on May 18, 2018.

(May 18, 2018)

National Drug Administration Issued Two Guidelines for Preclinical Study and Clinical Trials of Coronary Drug-eluting Stents

To strengthen the supervision and guidance over the medical device registration and further improve the registration review quality, National Drug Administration organized to formulate the *Guidelines for Preclinical Study of Coronary Drug-eluting Stents* and the *Guidelines for Clinical Trials of Coronary Drug-eluting Stents* which were released on May 11, 2018.

(May 11, 2018)

National Drug Administration Issued Four Guidelines for Technical Review of Registration Including the Guidelines for Technical Review of Insufflator Registration

To strengthen the supervision and guidance over the medical device registration and further improve the registration review quality, National Drug Administration organized to formulate the *Guidelines for Technical Review of Insufflator Registration*, the *Guidelines for Technical Review of Medical Cryopreservation Box Registration*, the *Guidelines for Technical Review of Electronic Urinary Volume Meter Registration*, and the *Guidelines for Technical Review of Electronic Colpomicroscope Registration* which were released on April 24, 2018.

(April 24, 2018)

Annual Report for National Medical Device Adverse Event Monitoring (2017) Released

On May 23, 2018, National Drug Administration issued the Annual Report for National Medical Device Adverse Event Monitoring (2017), which covers the progress of medical device adverse event (MDAE) monitoring, the overall status of MDAE reporting, statistical analysis of MDAE reports, the 2017 key MDAE monitoring, the release of MDAE Vigilance Express, and the quality assessment of MDAE reports. The Report presents a rather full-fledged reflection of China's MDAE monitoring in 2017.

By and large, in 2017, the national MDAE reporting showed a good development trend. The number of reports continued to grow and topped 370,000. The average number of reports per million population has reached 282. Among them, 326,622 reports were from user units, accounting for 86.83% of the total number of reports; and 8,655 (2.30%) were from manufacturers; 40,754 (10.83%) were from distributors; and 120 (0.03%) were from individuals. The reports involving Class III medical devices amounted to 154,192, accounting for 40.99% of the total; and 181,175 (48.16%), 25,555 (6.79%) and 15,235 (4.05%) reports were related to Class II medical devices, Class I medical devices and unknown categories of medical devices, respectively.

In 2017, a total of 1,431 key monitoring sentinel points were set up across the country; 990 investigations in various forms, 143 training sessions, and 97 expert consultation meetings were conducted; and 2.29 million monitoring data were actively collected. Furthermore, the National Center for Adverse Drug Reaction Monitoring released a total of six issues of Medical Device Vigilance Express, covering safety information of 32 products such as bioabsorbable intravascular stents and implantable cardioverter defibrillator.

Figure 1. Numbers of National Medical Device Adverse Event Reports from 2013 to 2017

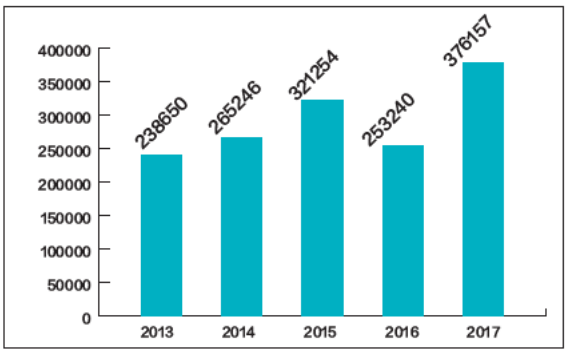
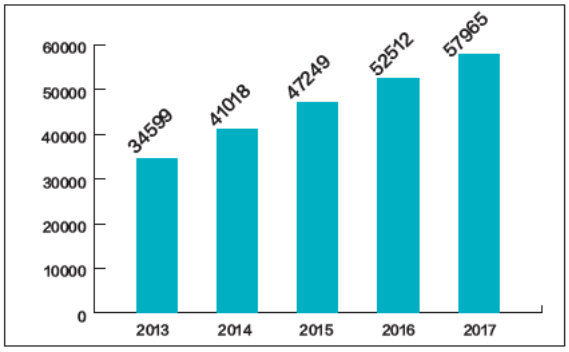


Figure 2. A Comparison of Numbers of Reports on Suspected Adverse Events Resulting in Death and Serious Injuries in China from 2013 to 2017



(May 23, 2018)

Notes: • All Chinese information in the Newsletter is extracted from newspapers and the Internet. All English articles are translations from the Chinese version.

• For electronic version of the Newsletter please visit http://www.ccfdie.org

National Drug Administration Issued the Guidelines for *Technical Review of Oral Pantomography X-Ray Machine Registration*

To strengthen the supervision and guidance over medical device registration, and further improve the quality of registration review, National Drug Administration organized the formulation of the *Guidelines for Technical Review of Oral Pantomography X-Ray Machine Registration*, which has been released on April 16, 2018.

(April 16, 2018)

Guidelines for Technical Review of Rigid Optical Endoscope (Invasive) Registration Released

To strengthen the supervision and guidance over medical device registration, and further improve the quality of registration review, CFDA organized the formulation of the *Guidelines for Technical Review of Rigid Optical Endoscope (Invasive) Registration*, which has been released on March 27, 2018.

(March 27, 2018)

Guidelines for Technical Review of Continuous Glucose Monitoring System Registration Released

To strengthen the supervision and guidance over medical device registration, and further improve the quality of registration review, CFDA organized the formulation of the *Guidelines for Technical Review of Continuous Glucose Monitoring System Registration*, which has been released on March 21, 2018.

(March 21, 2018)

Guidelines for Technical Review of Mycobacterium Tuberculosis Specific Cellular Immune Response Reagent Registration Released

To strengthen the supervision and guidance over medical device registration, and further improve the quality of registration review, CFDA organized the formulation of the *Guidelines for Technical Review of Mycobacterium Tuberculosis Specific Cellular Immune Response Reagent Registration*, which has been released on March 21, 2018.

(March 21, 2018)

2017 Annual Report for Medical Device Registration Released

On March 27, 2018, CFDA issued the 2017 *Annual Report for Medical Device Registration*, which is excerpted as follows:

Medical device registration applications

In 2017, CFDA has, according to its powers and duties, accepted a total of 6,834 applications for initial registration, registration renewal, and registration change of medical devices. Compared with 2016, the number of accepted registration applications decreased by 23.4%.

Review & approval of medical device registration

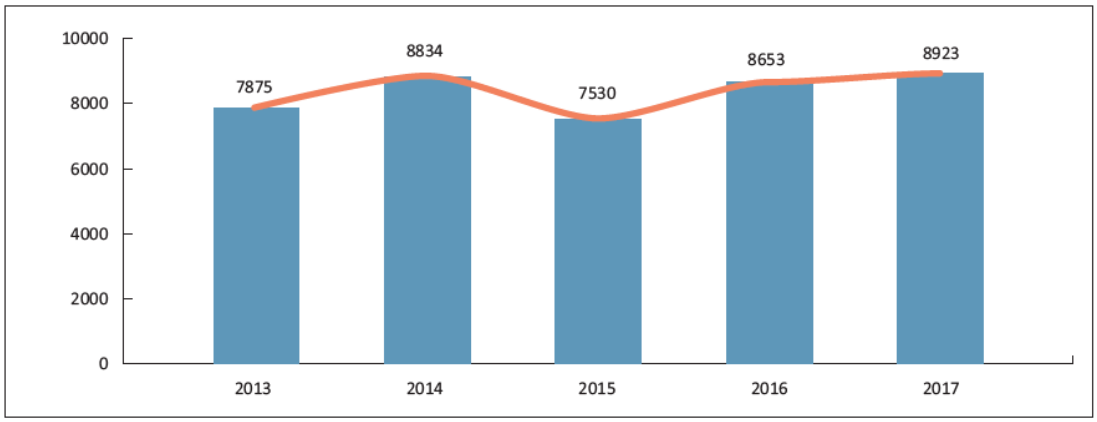
In 2017, CFDA completed technical review of a total of 8,579 medical device registration applications, down by 8.1% compared to 2016. Of these, 1,507 were for initial registration, 5,218 were for registration renewal, and 1,854 were for registration change.

In 2017, CFDA approved 8,923 applications for initial registration, registration renewal and registration change of medical devices. Compared with 2016, the total number of registration applications approved

increased by 3.1%.

In 2017, CFDA has rejected a total of 223 medical device registration applications, 331 of which were voluntarily withdrawn by the enterprises.

Figure. Review & approval of medical device registration in 2013-2017



Review & approval of innovative medical devices and other products

In 2017, CFDA sought furtherance and betterment of reviewing innovative medical devices as per the *Special Review & Approval Procedure for Innovative Medical Devices (Interim)*, and approved the marketing for some of them.

In 2017, CFDA received a total of 273 applications for special review & approval for innovative medical devices, completed review of 323 applications (including those in 2016), and determined that 63 products entered the Special Review & Approval Procedure for Innovative Medical Devices. Twelve innovative products such as branch-type aortic stent graft and delivery systems were approved for marketing. Among them, there were 4 active medical devices and 8 passive medical devices, outnumbering those of 2016 by 2 products.

Notes: The statistics period of this report is from January 1, 2017 to December 31, 2017.

(March 28, 2018)

CFDA Issued the *Guidelines for Technical Review of Ophthalmic Optical Coherence Tomography Scanner Registration*

To strengthen the supervision and guidance of the registration of medical devices and further improve the quality of registration review, CFDA organized the formulation of the *Guidelines for Technical Review of Ophthalmic Optical Coherence Tomography Scanner Registration* which was promulgated on March 2, 2018.

(March 2, 2018)

CFDA General Office Issues *the Notice on Implementing the Provisions for the Supervision and Administration of Network Sales of Medical Devices*

The *Provisions for the Supervision and Administration of Network Sales of Medical Devices* (CFDA Order No. 38) (hereinafter referred to as the Provisions) have been issued and shall be put into effect as from March 1, 2018. For effective implementation of the Provisions, on February 27, 2018, the General Office of CFDA issued the Notice on Implementing the *Provisions for the Supervision and Administration of Network Sales of Medical Devices*. The Notice requires more input into the publicity and implementation of the Provisions and relevant training for effectively supervision and management

of medical device network sales, and clarifies the filing work for medical device network sales and third-party platforms for network trading service. (February 27, 2018)

CFDA Issued the *Guidelines for Technical Review of Ultrasonic Soft Tissue Cutting and Hemostatic System Registration*

To strengthen the supervision and guidance of the registration of medical devices and further improve the quality of registration review, CFDA organized the formulation of the *Guidelines for Technical Review of Ultrasonic Soft Tissue Cutting and Hemostatic System Registration* which was promulgated on February 24, 2018.
(February 24, 2018)

CFDA Issued Four Guidelines for Technical Review of Registration Incl. Guidelines for Technical Review of Human Epidermal Growth Factor Receptor (EGFR) Mutation Gene Detection Reagent Registration

To strengthen the supervision and guidance of the registration of medical devices and further improve the quality of registration review, CFDA organized the formulation of the *Guidelines for Technical Review of Human Epidermal Growth Factor Receptor (EGFR) Mutation Gene Detection Reagent Registration (PCR Method)*, the *Guidelines for Technical Review of Helicobacter Pylori Antigen/Antibody Detection Reagent Registration*, the *Guidelines for Technical Review of Anti-human Globulin Detection Reagent Registration*, and the *Guidelines for Technical Review of Intestinal Virus Nucleic Acid Detection Reagent Registration*, which were promulgated on February 24, 2018.
(February 24, 2018)

CFDA Issued the *Planning for the Development of Medical Device Standards (2018-2020)*

Pursuant to the *Guiding Opinions of the CPC Central Committee and the State Council on Carrying out Quality Improvement Actions* (CPC Central Committee [2017] No. 24) and the *Opinions on Deepening the Review & Approval System Reform and Encouraging the Drug and Medical Device Innovation* (CPC Central Committee & SC [2017] No. 42) issued by the General Office of the CPC Central Committee and the General Office of the State Council, as well as the relevant requirements set forth in the *Provisions for Medical Device Standards and the Management Practice for the Development and Revision of Medical Device Standards, CFDA organized the formulation of the Planning for the Development of Medical Device Standards* (2018-2020), which has been issued on January 29, 2018, with a view to improving the levels of medical device standards, strengthening the supervisory inspection on the implementation of standards, and promoting the innovative development of medical devices.
(January 29, 2018)

CFDA Issued Three Guidelines for Technical Review of Registration Incl. Guidelines for Technical Review of Apolipoprotein A1 Assay Reagent Registration

To strengthen the supervision and guidance of the registration of medical devices and further improve the quality of registration review, CFDA organized to formulate the *Guidelines for Technical Review of Apolipoprotein A1 Assay Reagent Registration*, the *Guidelines for Technical Review of Apolipoprotein*

B Assay Reagent Registration, and the *Guidelines for Technical Review of D-Dimer Assay Reagent (Immunoturbidimetry) Registration*, which were promulgated on January 16, 2018. (January 16, 2018)

CFDA Issued Five Guidelines for Technical Review of Registration Incl. Guidelines for Technical Review of Alanine Aminotransferase Assay Reagent Registration

To strengthen the supervision and guidance of the registration of medical devices and further improve the quality of registration review, CFDA organized the formulation of the *Guidelines for Technical Review of Alanine Aminotransferase Assay Reagent Registration*, the *Guidelines for Technical Review of Urinalysis Test Strip Registration*, the *Guidelines for Technical Review of Homocysteine Assay Reagent Registration*, the *Guidelines for Technical Review of Insulin Assay Reagent Registration*, and the *Guidelines for Technical Review of C-Peptide Assay Reagent Registration*, which were promulgated on January 16, 2018. (January 16, 2018)