Global Harmonization Working Party
GHWP Towards Medical Device Harmonization

Regulatory science practice

——Research and Practice in Supporting Medical Device Evaluation with RWE

Liu Yinghui

Center for Medical Device Evaluation, NMPA

01 Real World Evidence --- a New Tool for Regulatory Science

02 Chinese Practice of RWE for Medical Devices Clinical Evaluation

03 Prospect of RWE in modern medical device review system

01 Real World Evidence --- a New Tool for Regulatory Science

I. Evolution of RWE research in medical device clinical evaluation

Global Harmonization Working Party
GHWP Towards Medical Device Harmonization

The policy of using imported drugs and devices in the Pilot zone provides clinical data for the registration of related products in China, which enable the RWE research in China.

-- April 2018

Methodological research on RWE used in clinical evaluation of medical devices

— July 2019 to December 2021

Methodological research on the application of RWE in clinical evaluation of innovative and urgently needed medical devices

— December 2021 to December 2023

Study on the key technologies of real-world database construction and governance as well as RWD supported clinical evaluation of heart failure treatment and management related medical devices

— 2024-2027

II. Progresses in the methodological study on RWE supporting medical devices clinical evaluation

Global Harmonization Working Party
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国家药品监督管理局
National Medical Products Administration

中国药品监管 中国药闻 中国药监APP 邮箱 政务信息报送

请输入关键字

国家药监局启动中国药品监管科学行动计划

2019年04月30日 发布

细胞和基因治疗产品、药械组合产品、人工智能医疗器械、中药安全评价研究等首批立项

为全面贯彻落实习近平总书记有关药品安全“四个最严”要求，围绕“创新、质量、效率、体系、能力”主题，推动监管理念制度机制创新，加快推进我国从制药大国向制药强国迈进，国家药品监督管理局今日发布通知，决定开展药品、医疗器械、化妆品监管科学研究，启动实施中国药品监管科学行动计划，并确定首批九个重点研究项目。

通知指出，立足我国药品监管工作实际，围绕药品审评审批制度改革创新，密切跟踪国际监管发展前沿，拟通过监管工具、标准、方法等系列创新，经过3-5年的努力，制定一批监管政策、审评技术规范指南、检查检验评价技术、技术标准等，有效解决影响和制约药品创新、质量、效率的突出性问题，加快实现药品治理体系和治理能力现代化。

01 IMDRF MDCE WG/N65FINAL:2021 Post-Market Clinical Follow-Up Studies

02 Technical guideline for the Use of Real-World Data in the Clinical Evaluation of Medical Devices

03 Collection principle for the Clinical Use Data of Imported Medical Devices for Clinical Urgently-needed in the Hainan Boao Lecheng International Medical Tourism Pilot Zone

04 Research Report on Common Design and Statistical Analysis of Real-World Studies

05 Research Report on Common Types, Sources, and Quality Evaluation of Real-World Data of Medical Devices

06 Pilot Practice for the Application of Real-World Data in Hainan Boao Lecheng International Medical Tourism (First Batch)

III. Progresses in the methodological research on RWE supporting the clinical evaluation of innovative and clinical urgently-needed medical devices

国家药品监督管理局
National Medical Products Administration

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索引号	XZXK-2021-204	主题分类	工作动态
标题	中国药品监管科学行动计划第二批重点项目发布		
发布日期	2021-06-28		

中国药品监管科学行动计划第二批重点项目发布

文章来源：发布时间：2021-06-28

为全面贯彻落实《国务院办公厅关于全面加强药品监管能力建设的实施意见》（国办发〔2021〕16号）要求，国家药监局在全面总结中国药品监管科学行动计划首批重点项目实施情况的基础上，确定并发布了第二批10个重点项目。

10个重点项目分别为中药有效性安全性评价及全过程质量控制研究，干细胞和基因治疗产品评价体系及方法研究，真实世界数据支持中药、罕见病治疗药物、创新和临床急需医疗器械评价方法研究，新发突发传染病诊断及治疗产品评价研究，纳米类创新药物、医疗器械安全性有效性和质量控制评价研究，基于远程传输、柔性电子技术及医用机器人的创新医疗器械评价研究，新型生物材料安全性有效性评价研究，化妆品新原料技术指南研究和化妆品安全监测与分析预警方法研究，恶性肿瘤等常见病、多发病诊疗产品评价新工具、新标准和新方法研究，药品、医疗器械警戒技术和方法研究。

本批重点项目执行周期原则上为2年。各项目由国家药监局相关司局牵头，相关直属单位实施，合作单位原则上依托国家药监局监管科学研究基地和重点实验室。国家药监局要求各牵头单位、实施单位按照聚焦前沿、突出重点、强化实效、稳步推进的原则，抓紧研究制定项目实施方案，明确研究计划，细化研究目标和任务，落实合作单位，加快创新监管工具、标准和方法，进一步提升药品监管能力和水平，加快创新产品上市步伐，更好满足公众健康需要。

中国药品监管科学行动计划自2019年4月启动，同步确定了首批9个重点研究项目。经过2年努力，首批重点项目取得重要成果，已研究制定监管新工具、新方法、新标准103项，其中31项已发布。

01 Technical Guideline for Real-World Study Design and Statistical Analysis of Medical Devices. (Draft)

02 Key Points for Technical Evaluation of Real-World Data as External Control Arms in Clinical Trials of Medical Devices. (Draft)

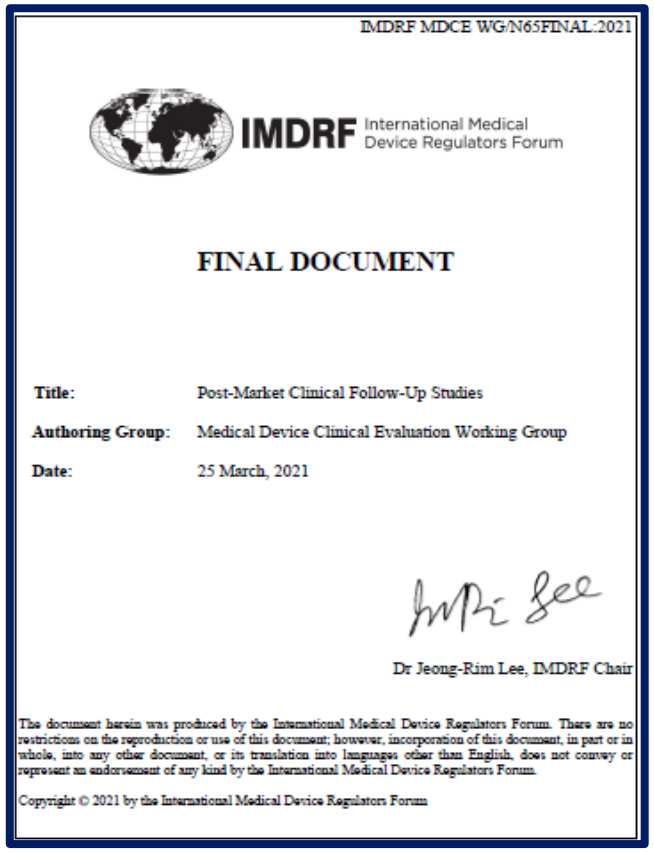
03 Key Points for Technical Evaluation of Real-World Data in Post-Marketing Clinical Follow-up Studies for Innovative and Clinical Urgently-needed Medical Devices. (Draft)

04 Methodological Research Report on Setting Single-arm Target Values for Innovative and Clinical Urgently-needed Medical Devices Using Real-World Data.

05 Methodological Research Report on Using Real-World Data to Support Medical Device Evaluation for Clinical Rare Situations.

06 Pilot Practice for the Application of Real-World Data in Hainan Boao Lecheng International Medical Tourism (Second Batch, Normalization)

IV. First to introduce RWD into IMDRF harmonization documents



IMDRF MDCE WG/N65FINAL:2021

IMDRF International Medical Device Regulators Forum

FINAL DOCUMENT

Title: Post-Market Clinical Follow-Up Studies

Authoring Group: Medical Device Clinical Evaluation Working Group

Date: 25 March, 2021

Dr Jeong-Rim Lee, IMDRF Chair

- **RWD was introduced for post-marketing clinical follow-up (PMCF) studies**
- **Considerations for RWS**
- **RWD sources for PMCF**
- **Potential bias and control methods of RWS**

IMDRF MDCE WG/N65FINAL:2021 Post-Market Clinical Follow-Up Studies

V. Integration of RWE into the Clinical Evidence System of Medical Devices

Global Harmonization Working Party
GHWP Towards Medical Device Harmonization

Exempt from Clinical Evaluation (Medical Devices)

- Technical Guidelines for Product Comparison Explanations in the List of Medical Devices Exempt from Clinical Evaluation
- List of Medical Devices Exempt from Clinical Evaluation

Clinical Evaluation

- Technical Guidelines for Clinical Evaluation of Medical Devices
- Technical Guidelines for Writing Clinical Evaluation Reports of Medical Devices
- Guidelines for the Use of Real World Data in the Clinical Evaluation of Medical Devices
- Guidelines for the Registration Review of Study Design and Statistical Analysis of Real World Studies for Medical Devices

Exempt from Clinical Trials (IVD)

- Technical Guidelines for Product Comparison Explanations in the List of Medical Devices Exempt from Clinical Evaluation
- Technical Guidelines for the Clinical Evaluation of *In Vitro* Diagnostic Reagents Exempt from Clinical Trials

Clinical Trials

- Technical Guidelines for Decision-Making on the Conduct of Clinical Trials for Medical Devices
- Guidelines for the Design of Clinical Trials for Medical Devices
- Guidelines for Clinical Trials of *In Vitro* Diagnostic Reagents
- Technical Guidelines for Accepting Overseas Clinical Trial Data of Medical Devices
- Technical Guidelines for Data Submission Requirements on Clinical Trials for Medical Devices
- Technical Guidelines for Data Submission Requirements on Clinical Trials for *In Vitro* Diagnostic Reagents

Comparison with predicate medical device (Medical Device)

- Technical Guidelines for the Substantial Equivalence Demonstration of Medical Devices

Urgently- Needed Clinical Practice & Rare Diseases

- Basic Principles for the Conditional Approval of Urgently Needed Medical Devices in Clinical Practice
- Guidelines for the Registration Review of Medical Devices for Prevention and Treatment of Rare Disease
- Notice on Matters Concerning the Registration Declaration of Urgently Needed Medical Devices in Clinical Practice

V. Integration of RWE into the clinical evidence system of medical devices

Conduct regulatory scientific research on utilizing RWE to support clinical evaluations and establish relevant technical review standards:

- ✓ **Research methodologies for transforming RWD into RWE, Propose methods and standards for assessing the quality of RWD, methods and standards for designing, implementing and analyzing RWE to generate clinical evidence that can be used for product safety and efficacy ;**
- ✓ **study the methodologies for the clinical evaluation of RWE-assisted products as valid scientific evidence for regulatory decision-making.**

The system of general guiding principles for clinical evaluation of medical devices has been preliminarily completed, covering 8 guiding principles issued in the form of department notices and 3 recommended clinical evaluation paths issued in the form of CMDE notices. Comprehensive coverage of various key issues in the field of clinical evaluation, including the application of RWD in the clinical evaluation of medical devices, a rapidly evolving issue of great interest in the industry

02 Chinese Practice of RWD for Medical Devices Clinical Evaluation

I. Role of RWE in Product Evaluation

Global Harmonization Working Party
GHWP Towards Medical Device Harmonization

Pre-marketing

01. To provide supplement clinical evidence for substantial equivalent Demostration

02. To provide supplement evidence for registration

03. RWE generated during domestic use of imported devices in clinical urgently-needed can be used as supplement evidence for registration

04. As the external control arm of single-arm trials

05. To provide clinical data for setting single-arm target values

Post-marketing

01. To support the modification of the intended use

02. To support the modification of the labelling / instuction for use

03. To support post-marketing clinical follow-up study with conditional approval

04. To be used for long-term safety and effectiveness evaluation of medical devices such as high-risk implants

05. To be used for clinical evaluation of medical devices for rare diseases

06. Post-marketing surveillance

II Explore the use of Boao RWD for product registration

Global Harmonization Working Party
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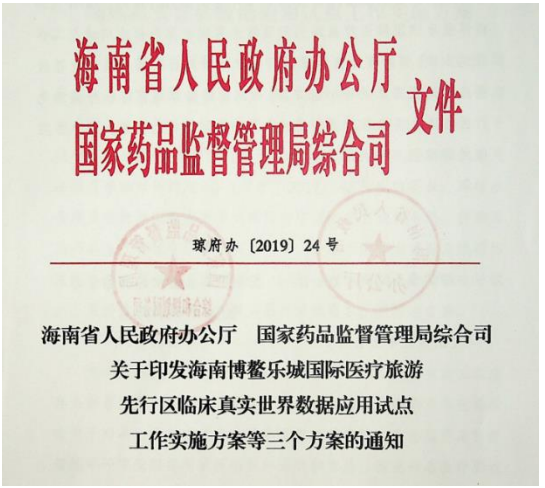
海南省人民政府办公厅
国家药品监督管理局综合司 文件

琼府办〔2019〕24号

海南省人民政府办公厅 国家药品监督管理局综合司
关于印发海南博鳌乐城国际医疗旅游
先行区临床真实世界数据应用试点
工作实施方案等三个方案的通知

国家药品监督管理局
National Medical Products Administration

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索引号	XZXK-2020-1061	主题分类	工作动态
标题	国家药品监督管理局 海南省人民政府进一步研究落实《中共中央 国务院关于支持海南全面深化改革开放的指导意见》相关举措		
发布日期	2018-04-25		

国家药品监督管理局 海南省人民政府进一步研究落实《中共中央 国务院关于支持海南全面深化改革开放的指导意见》相关举措

发布时间：2018-04-25

4月24日，国家药品监督管理局深入贯彻落实习近平总书记在庆祝海南建省办经济特区30周年大会和在海南博鳌乐城国际医疗旅游先行区考察时的重要讲话精神，会同海南省人民政府就共同贯彻《中共中央 国务院关于支持海南全面深化改革开放的指导意见》，研究提出具体落实措施。

近日，国家药品监督管理局按照《国务院关于在海南博鳌乐城国际医疗旅游先行区暂停实施〈医疗器械监督管理条例〉有关规定的决定》（以下简称《决定》），在征求有关部门意见的基础上，制定了《海南博鳌乐城国际医疗旅游先行区临床急需进口医疗器械管理暂行规定》，明确了临床急需医疗器械批准进口的范围、使用条件、办理程序及有关职责等，将《决定》落地落实。与此同时，国家药品监督管理局正在研究先行区医疗机构因临床急需进口少量药品的问题，予以简化程序。

双方一致认为，在先行区先行先试，有助于进一步积累经验，对于深入落实中办、国办《关于深化审评审批制度改革鼓励药品医疗器械创新的意见》（厅字〔2017〕42号）文件具有重要意义。先行区指定医疗机构因临床急需使用进口药品、医疗器械在满足特殊人群诊断和治疗的同时，可为相关产品在我国注册提供临床数据。先行区在探索积累经验、打造医药产业创新平台的同时，要进一步强化监管，落实各方责任，探索建立职业化检查员队伍，加强能力建设，严格落实“四个最严”的要求。下一步，国家药品监督管理局将会同海南省人民政府积极稳妥推动实施先行区有关政策，加强沟通，及时总结，把控风险，把各项工作落到实处。

- **The document issued in April, 2018 stated that designated medical institutions in the pilot zone, while using imported drugs and medical devices to meet the clinical urgent needs of certain populations, can provide clinical data for the registration of the said medical products in China**

- **In September 2019, the General Office of the Hainan Provincial People’s Government and the Department of Comprehensive Affairs of National Medical Products Administration issued the *Implementation Plan for the Pilot of Clinical Real-World Data Application in the Boao Lecheng International Medical Tourism Pilot Zone***

II Explore the use of RWD for product registration

Global Harmonization Working Party
GHWP Towards Medical Device Harmonization

国家药品监督管理局
National Medical Products Administration

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索引号	XZXK-2020-1401	主题分类	
标题	我国首个使用境内真实世界数据的医疗器械产品获批上市		
发布日期	2020-03-26		

我国首个使用境内真实世界数据的医疗器械产品获批上市

发布时间：2020-03-26

3月26日，国家药监局经审查，批准了美国艾尔建公司“青光眼引流管”注册。

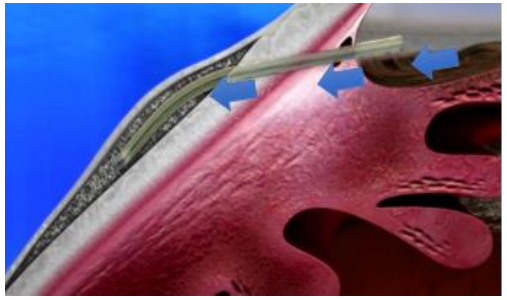
为推进我国医疗器械审评审批制度改革，探索将临床真实世界数据用于医疗器械产品注册，2019年6月，国家药监局与海南省政府联合启动了海南临床真实世界数据应用试点工作。该产品是试点的第一个产品，在注册中使用了在海南博鳌乐城先行区收集的临床真实世界证据进行人种差异评价，为国内首个通过该途径获批的产品。

该产品由引流管及注射器两部分组成，引流管由猪皮明胶及戊二醛制成，并预装于注射器内，适用于同时满足以下4个条件的开角型青光眼：1.房角入口较宽；2.单纯用药效果不佳或不能用药；3.房角激光治疗不能控制病情进展，或医生判断不宜开展或无法开展房角激光治疗；4.传统滤过性手术效果不佳或不能耐受。

药品监督管理部门将加强该产品上市后监管，切实保护患者用械安全。

The first batch

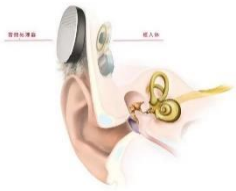
Product name	Approval time	Evaluation pathway
Glaucoma drainage implant tube	March 2020	Clinical trial +RWE
Femtosecond laser for cataract surgery	January 2021	Comparison with predicate device + clinical trial +RWE
Cochlear implant	October 2023	Comparison with predicate device + RWE

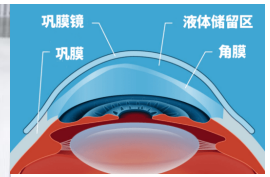


March 2020 marked a milestone for using RWD for medical device clinical evaluation: the first medical device using domestic RWD was approved for marketing in China.

III Promote the use of RWE for product registration

- Up to now, a total of 9 products in 7 varieties have been registered and approved for marketing using RWE generated in Boao
- RWE supplements existing clinical evidence in the clinical evaluation of medical devices
- RWE has played an important role in clinical evaluation of medium-risk products and high-risk products design change.





The second batch

Global Harmonization Working Party
GHWP Towards Medical Device Harmonization

Product name	Approval time	Evaluation pathway
Single-use water vapour therapy device	March 2022	Clinical trial +RWE
Cochlear implant	June, July 2022	Comparison with predicate device + RWE
Scleral contact lens (Capricornia)	June 2023	Comparison with predicate device + RWE
Scleral contact lens (Valley Contax)	October 2023	Comparison with predicate device + clinical trial +RWE
Spacer hydrogel	Technical review	Clinical trial +RWE
Renal artery ablation system	Technical review	Clinical trial +RWE
Scleral contact lens (Menicon)	RWS	
Artificial iris	RWS	
Growth differentiation factor -15 assay kit	Voluntary withdrawal	
Electronic duodenal imaging catheter Digital imaging controller	Voluntary withdrawal	

IV. Policy support - More communication and exchanges

国家药品监督管理局
医疗器械技术审评中心
海南省药品监督管理局

通　告

2022年 第16号

关于发布海南博鳌乐城国际医疗旅游先行区医疗器械临床真实世界数据应用试点品种沟通交流程序（试行）的通告

为有序推进海南博鳌乐城国际医疗旅游先行区医疗器械临床真实世界数据应用试点工作，促进海南博鳌乐城国际医疗旅游先行区更快更好发展，加强对医疗器械试点品种的早期介入和全程指导，进一步提高医疗器械试点品种沟通交流的质量和

—1—

First meeting

The working group of the Center for Medical Device Evaluation (CMDE), NMPA and the taskforce of the Hainan Provincial Medical Products Administration participate in the first meeting and discuss the reports and presentations of the applicant

Complex issues

For complex issues, the Provincial Medical Products Administration escalates them to CMDE, and CMDE will promptly dwell on the issues and provide its opinions on reply to the Provincial Medical Products Administration. Upon receiving the opinions, the Provincial Medical Products Administration will timely give its reply to the applicant

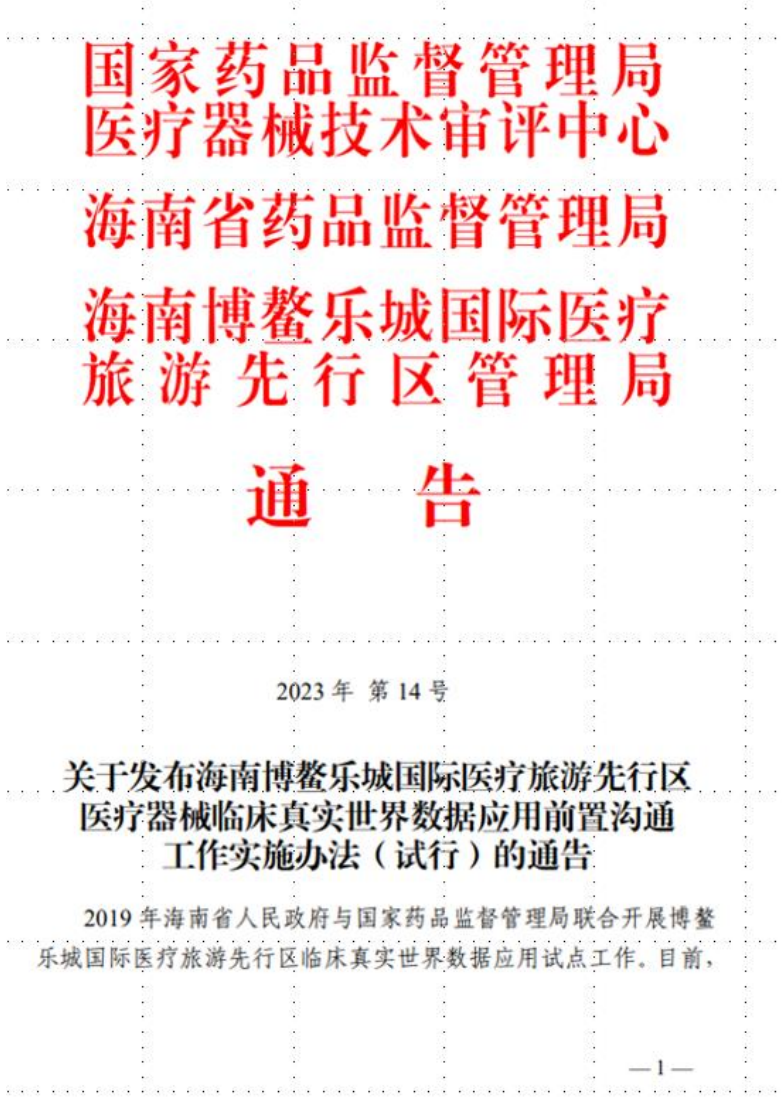
Simple issues

For simple issues or issues that have already been addressed in previous communications, the Provincial Medical Products Administration may directly respond to the applicant

Last meeting

Before the submission, the Provincial Medical Products Administration organizes a final meeting. The CMDE working group and the taskforce of the Provincial Medical Products Administration will attend the meeting and provide opinions and suggestions on key issues. Based on the opinions and suggestions, the applicant may improve the registration application materials and then submit them

V Explore the normalization of RWD application



国家药品监督管理局
医疗器械技术审评中心
海南省药品监督管理局
海南博鳌乐城国际医疗
旅游先行区管理局

通　告

2023年 第14号

关于发布海南博鳌乐城国际医疗旅游先行区
医疗器械临床真实世界数据应用前置沟通
工作实施办法（试行）的通告

2019年海南省人民政府与国家药品监督管理局联合开展博鳌乐城国际医疗旅游先行区临床真实世界数据应用试点工作。目前，

—1—

- **A standardized system, smooth operational mechanisms, and communication platforms have been put in place through pilot programs. the application of real-world data is now being carried out on a regular basis**

- **In April 2023, the *Implementation Measures for Early Communication Concerning the Application of Clinical Real-World Data of Medical Devices in the Hainan Boao Lecheng International Medical Tourism Pilot Zone (Trial)* was issued**

- **The above-mentioned document was jointly formulated by the Center for Medical Device Evaluation, NMPA, the Hainan Provincial Medical Products Administration and the Administration Bureau of the Lecheng Pilot Zone**

V Explore the normalization of RWD application

- **CMDE, NMPA**
- **Hainan Provincial Medical Products Administration**
- **The Lecheng Administration**

01

First meeting

For applicants that qualify for preliminary communication, a first meeting will be organized to have exchanges with them face to face

02

Mid-term guidance

Upon application filed by the applicant and response of the Hainan Provincial Medical Products Administration, CMDE will accordingly offer guidance and review

03

Last meeting

A last meeting for communication will be organized before the applicant's registration submission

Early intervention, whole-process guidance and timely communication

A ministerial-provincial coordinated work mechanism

Institutional arrangements for informing registration decision-making with RWE on a regular basis

03

Prospect of RWE in modern medical device review system

I. RWE is an important part of modern medical device review systems

Modern review system 1.0

—— Established the principles of scientific review, built a guidance system, clarified evidence standards for safety and effectiveness evaluation, pioneered electronic submission, optimized the evaluation process, established smooth communication, and took the lead in implementing an effective quality management system for evaluations

—— Coordinated and planned the establishment of two sub-centers, established two innovation cooperation platforms, set up nine provincial-level innovation service stations, promoted research in regulatory science, supported the establishment of a regulatory science research base and a key laboratory, and conducted multidimensional cooperation; accelerated the marketing process of a number of internationally advanced medical devices that fill domestic gaps and meet clinical urgent needs

Modern review system 2.0

—— Ensuring leading or sufficient technological mastery in all fields of regulatory science

- Promoting the utilization of real-world data
- Making efforts to bring into play research-oriented clinical institutions

—— Embarking on the construction of a clinical-oriented evaluation system

—— Making efforts to improve information services for the public

II. Improve the role of RWE in the evaluation of medical devices

1. Current situation

At the current stage of development, real-world evidence is more of a supplement to existing clinical evidence than a complete replacement of existing clinical evaluation pathways in the clinical evaluation of medical devices

--- Interpretation of *the Technical Guidelines of Using Real-world Data for Clinical Evaluation of Medical Devices (Trial)*

High-risk products

Clinical trial (primary evidence) +RWE (complementary evidence)

Medium and low risk products

Same-variety comparison/non-clinical (primary evidence) +RWE (complementary evidence)

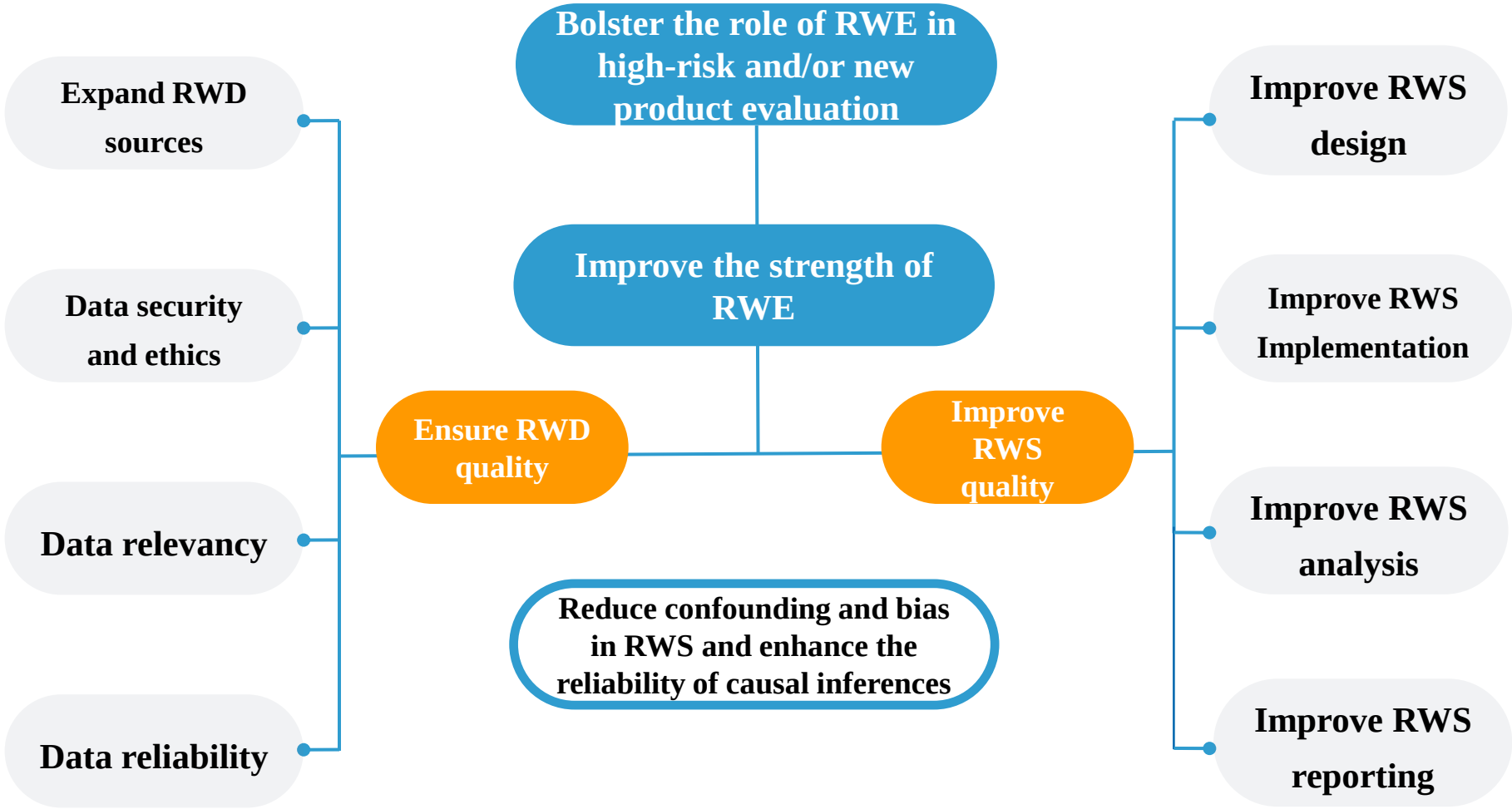
Product iteration

Non-clinical +RWE

II Bolster the role of RWE in the evaluation of medical devices

Global Harmonization Working Party
GHWP Towards Medical Device Harmonization

2. In the Future



II Bolster the role of RWE in the evaluation of medical devices

Global Harmonization Working Party
GHWP Towards Medical Device Harmonization

3. Suggestions

Identify the clinical evidence required for design confirmation based on the compliance with fundamental principles of product safety and performance, product risk-benefit analysis and evaluation.

Plan the overall clinical evaluation and identify the ways to generate clinical evidence. The cumulative clinical evidence generated through RWE and other ways shall meet the clinical evidence requirements for design confirmation.

Determine the research objective of RWS based on the issues to be addressed with RWE and develop RWS protocols following the relevant technical guidelines.

With an international perspective and a scientific attitude, we aim to expand the application scenarios of RWE under the prerequisite of compliance. This helps satisfy the need for diverse forms of evidence in reviews of new technologies, ultimately ensuring patients' early access to safe and effective medical devices and contributing more to public health

Thank you!