2020. Volume 7

NATIONAL MEDICAL PRODUCTS NEWSLETTER

中国食品药品国际交流中心
SERVIER
施维雅(天津)制药有限公司

Center for Drug Evaluation issued 5 guidances including the *Technical Guidance for Research & Development of Prophylactic Vaccines for Novel Coronavirus (Interim)*

In order to guide the clinical research & development of COVID-19 vaccines in China and provide technical standards that can be used as references, upon the approval by the National Medical Products Administration (NMPA), CDE issued the *Technical Guidance for Research & Development of Prophylactic Vaccines for Novel Coronavirus (Interim), Technical Guidance for Pharmaceutical Studies of Prophylactic mRNA Vaccines for Novel Coronavirus (Interim), Technical Essentials for Non-Clinical Effectiveness Study and Evaluation of Prophylactic Vaccines for Novel Coronavirus (Interim), Technical Guidance for Clinical Studies of Prophylactic Vaccines for Novel Coronavirus (Interim)*, and *Guidance for Clinical Evaluation of Prophylactic Vaccines for Novel Coronavirus (Interim)*. The above Guidances shall come into effect as of the date of August 14, 2020.

(August 14, 2020)

《新型冠状病毒预防用疫苗研发技术指导原则（试行）》等5个指导原则发布

为指导我国新冠疫苗的临床研发，提供可参考的技术标准，经国家药品监督管理局审核同意，2020年8月14日，药品审评中心发布了《新型冠状病毒预防用疫苗研发技术指导原则（试行）》《新型冠状病毒预防用mRNA疫苗药学研究技术指导原则（试行）》《新型冠状病毒预防用疫苗非临床有效性研究与评价技术要点（试行）》《新型冠状病毒预防用疫苗临床研究技术指导原则（试行）》《新型冠状病毒预防用疫苗临床评价指导原则（试行）》。上述指导原则自2020年8月14日起施行。（2020-08-14）

Center for Drug Evaluation issued the *Technical Guidance for Real-World Study Supporting Research & Development and Evaluation of Pediatric Drugs (Interim)*

Considering the actual needs in research & development and registration of pediatric drugs, to help enterprises better understand the application of the *Guidance for Real-World Evidences Supporting Research & Development and Evaluation of Drugs (Interim)* in research & development of pediatric drugs, upon the approval by the NMPA, CDE issued the *Technical Guidance for Real-World Study Supporting Research & Development and Evaluation of Pediatric Drugs (Interim)* on August 27, 2020, which shall come into force as of the date of issuance.

(September 1, 2020)

《真实世界研究支持儿童药物研发与审评的技术指导原则（试行）》发布

考虑到我国儿童药物研发及药品注册中的实际需要，帮助企业更好地理解《真实世界证据支持药物研发与审评的指导原则（试行）》在儿童药物研发中的应用，经国家药品监督管理局审核同意，2020年8月27日，药审中心发布《真实世界研究支持儿童药物研发与审评的技术指导原则（试行）》，自发布之日起施行。（2020-09-01）

NMPA and General Administration of Customs issued the Announcement on the Setting up of Wuxi Airport and Jiangyin Port as Drug Import Ports

On September 2, 2020, NMPA and General Administration of Customs issued the following announcement:

According to the *Drug Administration Law of the People's Republic of China*, upon the approval of the State Council, it is agreed to set up Wuxi Airport and Jiangyin Port as drug import ports. The relevant matters are announced as follows:

I. As of the date of issuance of this Announcement, except for the drugs specified in Article 10 of the Provisions for Import Drugs (hereinafter referred to as the Provisions), other import drugs (including narcotic drugs and psychotropic drugs) may be imported

国家药监局 海关总署发布关于增设无锡航空口岸、江阴港口岸为药品进口口岸的公告

2020年9月2日，国家药监局、海关总署发布如下公告：

根据《中华人民共和国药品管理法》，经国务院批准，同意增设无锡航空口岸、江阴港口岸为药品进口口岸。现将有关事宜公告如下：

一、自本公告发布之日起，除《药品进口管理办法》（以下简称《办法》）第十条规定的药品外，其他进口药品（包括麻醉药品、精神药品）可经由无锡航空口岸、江阴港口岸进口。

Published by
China Center for Food and Drug International Exchange
Servier (Tianjin) Pharmaceutical Co., Ltd.

through Wuxi Airport and Jiangyin Port.

II. Wuxi Administration of Market Regulation is added as the port drug regulatory authority, which shall undertake the specific drug import filing at Wuxi Airport and Jiangyin Port.

III. Wuxi Center for Drug Safety Inspection and Testing is added as the port drug inspection agency. As of the date of issuance of this Announcement, Wuxi Center for Drug Safety Inspection and Testing starts to undertake the drug port inspection at Wuxi Airport and Jiangyin Port.

(September 14, 2020)

二、增加无锡市市场监督管理局为口岸药品监督管理部门，由其承担无锡航空口岸、江阴港口岸药品进口备案的具体工作。

三、增加无锡市药品安全检验检测中心为口岸药品检验机构。自本公告发布之日起，无锡市药品安全检验检测中心开始承担无锡航空口岸、江阴港口岸的药品口岸检验工作。 (2020-09-14)

NMPA issued *the* Announcement on Matters Concerning the Production of Imported Medical Devices in Domestic Enterprises in China

In order to further implement the *Opinions on the Reform of Review and Approval System for Drugs and Medical Devices* issued by the State Council and the *Opinions on Deepening the Reform of Review and Approval System to Encourage Innovation of Drugs and Medical Devices* issued by the General Office of the CPC Central Committee and the General Office of the State Council as well as the reform of "Streamline Administration, Delegate Power, Strengthen Regulation and Improve Services", and optimize business environment requirements, comprehensively deepen reform of the review and approval system for medical devices, promote high-quality development of the medical device industry, and better meet public health needs, on September 18, 2020, NMPA announced the following matters concerning the production of products with imported medical device registration certificates in domestic enterprises in China:

I. Scope of application

This Announcement is applicable to the matters concerning the production of Class II and Class III medical devices with imported medical device registration certificates in China by the imported medical device registrants through their foreign-invested enterprises established in China.

II. Registration requirements

(I) The foreign-invested enterprise established by an imported medical device registrant in China shall, as the registration applicant, submit the application for medical device registration in China to the corresponding drug regulatory authority. The content of the registration application, except the name, domicile and production address of the registrant, shall, in principle, be consistent with relevant items specified in the corresponding imported medical device registration certificate and its attachments.

(II) The registration applicant shall submit the registration application dossiers according to the requirements of *Announcement on the Requirements for Registration Application Dossiers of Medical Devices and the Format of Approval Documents* (CFDA Announcement [2014] No.43) and *Announcement on the Requirements for Registration Application Dossiers of In Vitro Diagnostic Reagents and the Format of Approval Documents* (CFDA Announcement [2014] No.44). For the summary data, study data, clinical evaluation data, product risk analysis data of medical devices, and the summary data, study data of main raw materials (if applicable), study data of main production process and reaction system (if applicable), analysis performance evaluation data, positive cut-off value or reference interval determination data, stability study data, clinical evaluation data, product risk analysis data etc. of in vitro diagnostic reagents, the original registration application dossiers for the imported medical devices can be submitted. The import registrant and

国家药监局发布关于进口医疗器械产品在中国境内企业生产有关事项的公告

为进一步贯彻落实国务院《关于改革药品医疗器械审评审批制度的意见》和中共中央办公厅、国务院办公厅印发的《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》，落实“放管服”改革和优化营商环境要求，全面深化医疗器械审评审批制度改革，推动医疗器械产业高质量发展，更好地满足公众健康需求，2020年9月18日，国家药品监督管理局就已获进口医疗器械注册证产品在中国境内企业生产的有关事项公告如下：

一、适用范围

进口医疗器械注册人通过其在境内设立的外商投资企业在境内生产第二类、第三类已获进口医疗器械注册证产品的有关事项，适用本公告。

二、注册要求

（一）进口医疗器械注册人在中国境内设立的外商投资企业作为注册申请人，向药品监督管理部门提交境内医疗器械注册申请。注册申请内容，除注册人名称、住所、生产地址外，原则上应当与所对应的进口医疗器械注册证及其附件载明的相关事项保持一致。

（二）注册申请人按照《医疗器械注册申报资料要求和批准证明文件格式的公告》（国家食品药品监督管理总局2014年第43号公告）、《体外诊断试剂注册申报资料要求和批准证明文件格式的公告》（国家食品药品监督管理总局2014年第44号公告）等要求提交注册申报资料。其中，医疗器械产品的综述资料、研究资料、临床评价资料、产品风险分析资料，体外诊断试剂产品的综述资料、主要原材料的研究资料（适用时）、主要生产工艺及反应体系的研究资料（适用时）、分析性能评估资料、阳性判断值或参考区间确定资料、稳定性研究资料、临床评价资料、产品风险分析资料，可提交进口医

domestic registration applicant shall ensure that the above materials are relevant to and supportive for this registration application.

(III) The registration and application procedures are implemented in accordance with the *Provisions for Medical Device Registration*, the Provisions for In Vitro Diagnostic Reagent Registration and relevant provisions for electronic Regulated Product Submission (eRPS).

(IV) Where an application for registration is submitted and approved in accordance with the requirements of this Announcement, the column of Remark shall indicate the medical device registration certificate number of the imported product that has been approved for registration.

III. Registration system verification requirements

Registration applicants shall ensure that the main production process of the product is included in the domestic production, commit that there will be no change in main raw materials and production processes, and provide the self-inspection report that the domestic production quality management system of the product complies with the *Good Manufacturing Practice for Medical Devices* and equivalence comparison report of overseas and domestic quality management systems. According to the working procedure for the verification of quality management system for medical device registration, drug regulatory authorities shall conduct comprehensive verification for domestic registration applicants, focusing on the equivalence and traceability of domestic and foreign quality management systems, as well as whether changes in the system caused by changes in the production processes will generate new risks and cause changes in the registered items.

IV. Post-marketing surveillance requirements

Domestic registrants shall apply for the production licenses of medical devices in accordance with the *Measures for Supervision and Administration of Medical Device Production,* strictly implement the principal responsibility of quality safety, and strengthen the quality management of medical devices throughout their life cycle; and establish and improve the quality management system and ensure its effective operation according to the requirements of the *Good Manufacturing Practice for Medical Devices*.

V. Other aspects

The production of Class II and Class III medical devices with imported medical device registration certificates in China by overseas registrants invested by domestic enterprises in China can be implemented with reference to this Announcement. The domestic enterprises in China that invest the overseas registrants should apply for product registration as the registration applicants.

The matters related to the products with medical device registration certificates obtained in Hong Kong, Macao and Taiwan can be implemented with reference to this Announcement.

This Announcement shall be implemented as of the date of issuance.

(September 25, 2020)

疗器械的原注册申报资料。进口注册人和境内注册申请人应当确保上述资料与本次注册申请的相关性和支持性。

（三）注册申报程序按照《医疗器械注册管理办法》《体外诊断试剂注册管理办法》以及医疗器械电子申报相关规定执行。

（四）按照本公告要求提交注册申请并获得批准的，注册证备注栏中应当载明相关已获准注册的进口产品的医疗器械注册证号。

三、注册体系核查要求

注册申请人应当确保境内生产包含产品的主要生产工艺，并承诺主要原材料和生产工艺不发生改变，提供产品在境内生产质量管理体系符合我国《医疗器械生产质量管理规范》的自查报告和境内外质量管理体系等同性对比报告。药品监管部门按照医疗器械注册质量管理体系核查工作程序，对境内注册申请人开展全面核查，重点关注境内外质量管理体系的等同性、溯源性，以及变更生产过程带来的体系变化是否会产生新的风险，引起注册事项的变更。

四、上市后监管要求

境内注册人应当按照《医疗器械生产监督管理办法》办理医疗器械生产许可证，严格落实质量安全主体责任，加强医疗器械全生命周期质量管理；按照《医疗器械生产质量管理规范》要求，建立健全质量管理体系并保证有效运行。

五、其他方面

中国境内企业投资的境外注册人在境内生产已获进口医疗器械注册证的第二类、第三类医疗器械产品的，参照本公告执行，由投资境外注册人的中国境内企业作为注册申请人申请该产品注册。

香港、澳门、台湾地区已获医疗器械注册证的产品有关事项参照本公告执行。

本公告自公告之日起施行。

（2020-09-25）

NMPA issued *the Announcement on Provisions for the Filing of Medical Representatives (Interim)*

In order to regulate the academic promotion of medical representatives and promote the healthy and orderly development of the pharmaceutical industry, NMPA has organized to formulate the *Provisions for the Filing of Medical Representatives (Interim)*, which was issued on September 22, 2020.

(September 30, 2020)

国家药监局发布关于医药代表备案管理办法（试行）的公告

为规范医药代表学术推广行为，促进医药产业健康有序发展，国家药监局组织制定了《医药代表备案管理办法（试行）》，于2020年9月22日发布。

（2020-09-30）

Center for Drug Evaluation, NMPA issued *the Clinical Technical Requirements for Drugs Marketed Overseas but Not Marketed in China*

The marketing or imitation of overseas marketed drugs is an important means to solve the availability and accessibility of drugs in urgent clinical needs of patients in China. In order to speed up the research & development and marketing processes of such drugs, strengthen the scientific regulation, according to the *Provisions for Drug Registration* (SAMR Order No.27) and supporting documents thereof, upon the approval by NMPA, CDE issued the *Clinical Technical Requirements for Drugs Marketed Overseas but Not Marketed in China* on October 9, 2020, which shall come into force as of the date of issuance.

(October 16, 2020)

国家药监局药审中心发布《境外已上市境内未上市药品临床技术要求》

境外已上市药品境内上市或仿制，是解决我国患者对临床迫切需求领域药品的可获得性和可及性的重要手段。为加快此类药品研发上市进程，加强科学监管，依据《药品注册管理办法》（总局令第27号）及其配套文件，经国家药品监督管理局审核同意，2020年10月9日，药审中心发布了《境外已上市境内未上市药品临床技术要求》，自发布之日起施行。（2020-10-16）

Clinical Technical Requirements for Drugs Marketed Overseas but Not Marketed in China

I. Background

The marketing or imitation of overseas marketed drugs is an important means to solve the availability and accessibility of drugs in urgent clinical needs of patients in China. In order to speed up the research & development and marketing processes of the originator drugs and generic drugs marketed overseas but not marketed in China, according to the *Provisions for Drug Registration* (SAMR Order No.27) and supporting documents thereof, and in combination with the *Technical Guidance for Accepting Overseas Clinical Trial Data* ([2018] No.52), the technical requirements for clinical study and evaluation of such drugs have been formulated to provide technical reference for the industry, academia and regulatory authorities.

II. Scope of application

The Technical Requirements are applicable to the drugs marketed overseas but not marketed in China, mainly including two types of cases: (1) Originator chemicals and therapeutic biological products marketed overseas; (2) Generic chemicals at home and abroad.

III. General considerations

For drugs marketed overseas but not marketed in China, technical requirements for clinical trials to support its marketing in China should be established in compliance with the basic logic of clinical evaluation and on the basis of full evaluation of clinical demand of Chinese patients, clinical safety and effectiveness of overseas originator drugs, influences of racial factors as well as the need of benefit/risk evaluation in Chinese patients.

IV. Basic logic for clinical evaluation

(I) Clinical demand evaluation

The epidemiological status and severity of diseases and prognosis of the proposed indications in China as well as the existing treatment means and the limitations thereof should be analyzed, and advantages of the drug compared with existing domestic treatment means should be clarified, so as to make a judgment on the degree of clinical demand of Chinese patients.

For the drugs for the treatment of critical diseases and rare diseases for which there is no effective treatment means in clinical practice, regulatory authorities should take an encouraging attitude to conduct review and approval on the premise that the availability of drugs to the public is the first priority.

(II) Effectiveness and safety evaluation

First of all, scientific evaluation on the

境外已上市境内未上市药品临床技术要求

一、背景

境外已上市药品境内上市或仿制，是解决我国患者对临床迫切需求领域药品的可获得性和可及性的重要手段。为加快境外已上市境内未上市原研药品及仿制药品研发上市进程，依据《药品注册管理办法》（总局令第27号）及其配套文件，结合《接受境外临床试验数据的技术指导原则》（2018年52号文），制定对此类药品临床研究和评价的技术要求，为工业界、学术界和监管机构提供技术参考。

二、适用范围

本技术要求适用于境外已上市境内未上市的药品，主要包括两类情形：（1）境外已上市的原研化学药品和治疗用生物制品；（2）境内外化学药品仿制药。

三、基本考虑

境外已上市境内未上市药品的临床技术要求，应遵循临床评价基本逻辑，在充分评价中国患者临床需求、境外原研药品临床安全性和有效性、以及种族因素影响的基础上，基于中国患者获益/风险评估的需要，确定其在境内上市需开展的临床试验技术要求。

四、临床评价基本逻辑

（一）临床需求评估

应分析拟申报适应症在我国的疾病流行病学现状、疾病严重程度和预后，现有治疗手段及其局限性，明确该药品与国内现有治疗手段的比较优势，进而对中国患者临床需求的程度做出判断。

对用于临床缺乏有效治疗手段的危重疾病和罕见病治疗药品等，监管机构持鼓励态

effectiveness and safety of drugs should be performed according to relevant Chinese technical requirements and based on the clinical study data of the originator drug. The evaluation steps are as follows:

1. Clarify the source of clinical data

It mainly includes two parts of data. One is clinical trial data used for registration, and the other is post-marketing clinical data. At the same time, the dynamic evaluation of the originator drug by foreign regulatory authorities should be concerned.

2. Evaluate the quality of overseas clinical trial data

The premise of scientific evaluation of clinical trial data is that clinical trials are carried out in accordance with the internationally accepted GCP and the clinical trial data shall be authentic, accurate, complete and traceable. The applicant can provide the drug evaluation authority with relevant documents or materials that prove the quality of clinical trial data for supporting marketing application. Verification results and conclusions of regulatory authorities of foreign countries with management practice can be taken as the references for quality evaluation of clinical trial data. China's drug regulatory authorities should conduct necessary verification of the clinical trial data for supporting marketing registration in China based on risks.

3. Understand the characteristics of biopharmaceutics and clinical pharmacology

In terms of biopharmaceutics, attention should be paid to the data of bioavailability/bioequivalence (BA/BE) of dosage form, food influence and in vitro dissolution curve.

In terms of clinical pharmacology, attention should be paid to pharmacokinetics (PK), pharmacodynamics (PD), PK/PD correlation and drug interaction, providing basis for safe and effective clinical application. Possible racial differences in PK and/or PD between Chinese patient populations and foreign study populations should be evaluated by referencing ICH E5 and E17 guidelines, etc.

4. Evaluate the overall effectiveness and safety

Overseas clinical trial data and post-marketing data for registration should be systematically evaluated according to the current criteria for effectiveness and safety evaluation, so as to determine the overall effectiveness and safety of the investigational drug and assess whether the overall benefits outweigh the risks for patients.

(III) Racial sensitivity analysis

Racial sensitivity analysis should focus on possible influences from differences in PK and/or PD between Chinese patient population and foreign population on the safety and effectiveness. Such analysis should be performed on existing overseas clinical trial data to assess the racial sensitivity in accordance with the requirements in ICH E5 guidelines under the premise that it is firstly determined that the overall population benefits of the drug outweigh the risks. Racial sensitivity analysis involves the overall evaluation related to in vitro and human PK, PD, effectiveness and safety, judgment on whether there is any racial sensitivity difference in therapeutic response between Chinese patients and foreign population, and analysis on regulatory measures taken by foreign regulatory authorities according to the evaluation of clinical trial data. For those with sufficient studies on racial sensitivity conducted overseas, applicants should also consider the actual situation in China when submitting application for marketing or imitation. Disease and medical practice are two major factors that may affect the therapeutic response, so they should also be analyzed and judged together.

度，以解决公众用药可获得性为首要前提进行审评审批。

（二）有效性和安全性评价

首先，应基于原研药品的临床研究数据，按照中国相关技术要求，对药品的有效性和安全性进行科学评价。评价步骤为：

1. 明确临床数据来源

主要包括两部分数据，一是用于注册的临床试验数据，二是上市后临床数据。同时要关注国外监管机构对原研药品的动态评估。

2. 评估境外临床试验数据质量

科学评价临床试验数据的前提是，临床试验按照国际通行GCP开展，临床试验数据应具有真实性、准确性、完整性和可溯源性。申请人可向药品审评部门提供证明支持其上市申请的临床试验数据质量的相关文件或资料。境外管理规范国家的监管机构核查结果和结论可作为临床试验数据质量评估的参考。中国药品监管机构基于风险对用于支持在中国境内注册上市的临床试验数据进行必要的核查。

3. 了解生物药剂学与临床药理学特征

生物药剂学，应关注剂型生物利用度/生物等效性（BA/BE）、食物影响和体外溶出曲线数据。临床药理学，应关注药代动力学（PK）、药效动力学（PD）、药代动力学/药效动力学（PK/PD）相关性、药物相互作用等，为临床安全有效应用提供依据。应参考ICH E5和E17等指导原则，对中国患者人群与境外研究人群可能存在的PK和/或PD种族差异进行评估。

4. 评估总体有效性和安全性

按照现行的有效性和安全性评价标准，对境外注册临床试验数据和上市后数据进行系统评价，确定研究药物的总体有效性和安全性，并评估总体人群用药的获益是否大于风险。

（三）种族敏感性分析

种族敏感性分析，应重点关注中国患者人群与境外人群PK和/或PD差异可能带来的安全性和有效性影响。该分析应在首先确定药品总体人群获益大于风险的前提下，遵循ICH E5指导原则要求，对已有境外临床试验数据进行种族敏感性分析。种族敏感性分析的内容涉及相关体外、人体PK、PD、有效性和安全性等进行整体评价，判断中国患者人群在治疗反应方面与境外人群是否存在种族敏感性差异，并分析境外监管机构根据临床试验数据审评情况采取的监管措施。对于境外已经开展过充分的种族敏感性研究的，申请人在递交上市或仿制申请时还应考虑中国的实际情况，疾病和医疗实践是可能影响

(IV) Decision-making based on benefit-risk assessment of Chinese patients

On the basis that the clinical study data of the originator drug is sufficient to support that the overall population benefits of the drug outweigh the risks, the evaluation decision should be made based on data analysis on the influence of racial factors in Chinese patients and foreign population. If the analysis data shows that the therapeutic response of Chinese patients is consistent with the results of overall population, the marketing of the drug can be supported. If there is any difference, it is necessary to evaluate whether the difference can affect the safety and effectiveness of medication for Chinese patients based on relevant study data. For those that have impact, it is necessary to further evaluate whether the applicant has conducted the specific study and taken necessary measures, including adjusting dosage and usage, adding contraindications, precautions and other contents related to racial factors, to support that the drug can be used in Chinese patients. After conducting specific study and taking necessary measures, if the benefits of the drug for Chinese patients outweigh the risks, its marketing can be supported.

V. Requirements for clinical trials

For the drugs marketed overseas but not marketed in China, full evaluation should be performed for the clinical study data of the originator drugs according to the basic logic of clinical evaluation and in combination with the actual situation of the drugs, and the clinical trial requirements should be determined according to the evaluation results. For drugs with different R & D backgrounds, the clinical trials required to be carried out should be determined case by case.

(I) Overseas originator drugs

It is encouraged to conduct synchronous clinical trials of overseas originator drugs in the early clinical R & D stage in China, for example, in the form of international multi-center clinical study, conducting synchronous human PK and PD, PK/PD, effectiveness and safety and other clinical trials in Chinese patients and foreign patients in the form of international multi-center clinical study and under the same clinical trial design and implementation conditions. These systematic clinical trials will help obtain direct evidences of the complete chain of evidences related to racial factors, help conduct comparative analysis on whether there is any difference and how big the difference is in the dose-exposure-effect relationship, effectiveness and safety between Chinese patients and overall patients worldwide and how big the difference is on the basis of the overall population safety and effectiveness evaluation, and help conduct comprehensive evaluation when any difference is identified, to comprehensively weigh the clinical benefits/risks of the drug for Chinese patients, so as to support the marketing application. Study design should comply with recommendations of ICH guidelines (such as ICH E5 and ICH E17).

Different overseas applicants have different global clinical R & D strategies for originator drugs, resulting in differences in the contents and the degree of support of clinical trial data at the time of submitting application dossiers; therefore, the clinical trial requirements for overseas originator drugs should be determined according to the basic logic of clinical evaluation and based on the clinical needs of Chinese patients, study data of completed clinical trials and analysis results of the impact of racial factors.

The clinical trial requirements mainly include the following 3 conditions:

1. Safe, effective and racially insensitive

Where it is considered that a drug is safe, effective and racially insensitive upon evaluation, the exemption from clinical trials

治疗反应的两大因素，故也应一并进行分析研判。

（四）基于中国患者获益/风险评估进行决策

在原研药品的临床研究数据足以支持该药品用于总体人群的获益大于风险的基础上，应基于中国患者与境外人群种族因素影响的数据分析，做出审评决策。如分析数据显示，中国患者治疗反应与总体人群结果一致，则可支持其上市。如存在差异，则需基于相关研究数据评估差异对中国患者用药的安全性和有效性是否产生影响，产生影响的，应进一步评估申请人是否进行了针对性研究并采取了必要的措施，包括：种族因素相关的用法用量调整、禁忌或注意事项内容的增加等，以支持其用于中国患者。在进行了针对性研究并采取了必要的措施后，如该药用于中国患者的获益大于风险，则可支持其上市。

五、临床试验要求

对于境外已上市境内未上市的药品，需结合药品具体情况，按照临床评价的基本逻辑对原研药品的临床研究数据进行充分评价，根据评价结果确定临床试验要求。对于不同研发背景的药品，其所需开展的临床试验应具体问题具体分析。

（一）境外原研药品

鼓励境外原研药品自临床早期研发阶段即在中国同步开展临床试验，如以国际多中心临床研究的方式，在相同临床试验设计和实施条件下，对中国患者人群和境外患者人群同步开展人体PK、PD、PK/PD、有效性和安全性等系统临床试验。这些系统临床试验将有助于获得种族因素影响相关的完整证据链的直接证据，有助于在总体人群安全性和有效性评价的基础上，进一步比较分析中国患者人群与全球总体人群在剂量-暴露-效应关系、有效性和安全性等方面是否存在差异以及差异的大小，有助于在发现差异时进行综合评估，全面权衡药品用于中国患者临床获益/风险，进而支持其上市申请。研究设计应遵循ICH相关指导原则（如ICH E5和ICH E17）的建议。

不同境外申请人对于原研药品的全球临床研发策略不同，导致其在递交申报资料时临床试验数据的内容和支持性程度不同，故应按照临床评价的基本逻辑，根据中国患者临床需求、已完成临床试验的研究数据、种族因素影响分析结果等，确定对境外原研药品的临床试验要求。

临床试验要求主要包括以下3种情形：

1. 安全有效且无种族敏感性

in China may be considered.

Where there have been PK, and/or PD, effectiveness and safety data of Chinese population in global data, and the analysis shows that the benefits of the drug used for Chinese patients outweigh the risks, data from relevant domestic and overseas clinical trials can be directly used to support the marketing application.

For drugs with no relevant data of Chinese population in the global data, but there is relatively sufficient racial factor related study and analysis data and no significant impact of racial factors is identified, the analysis should be conducted on a case-by-case basis: (1) For a drug used for serious or life-threatening diseases and rare diseases for which there is no effective therapeutic means, or a drug with significantly improved effectiveness or safety and other advantages over existing therapeutic means when being used for such diseases, the approval for marketing can be considered on the premise of strict risk control, and post-marketing effectiveness and safety clinical trial should be conducted to support the whole life cycle benefit/risk evaluation of the drug. (2) For a drug without significant clinical advantages over existing therapeutic means, the clinical trial should be conducted with reference to the requirements of Section "V (I) 2".

For adding new dosage form (with clinical advantage), new administration route, new usage and dosage approved overseas but not in China for approved indications of drugs marketed in China, and each domestically marketed single drug in a new compound drug marketed overseas but not marketed in China, when the following conditions are met simultaneously, reduction or exemption of clinical trials can be considered according to the evaluation of overseas clinical trial data : ①Data of completed clinical trials of marketed originator drugs indicates that benefits of the drug for Chinese patients outweigh the risks, and there is no significant impact of racial factors compared with data in foreign populations; ②The overseas clinical trial data of new dosage form, new administration route, new usage and dosage or new compound of the drug can be used to

fully evaluate its safety and effectiveness.

If a new indication that has been approved overseas but not in China is added to drugs marketed domestically, besides complying with the above-mentioned basic logic of clinical evaluation and clinical trial requirements, analysis should be based on cases because multi-dimensional complicated factors of diseases and drugs are involved. It is suggested to communicate with regulatory authorities before application.

2. Safe and effective but lacking racial sensitivity data or racially sensitive

Where it is considered that the drug is safe and effective but there lacks racial sensitivity data upon evaluation, or the existing data suggest that the drug is racially sensitive, a bridging clinical trial should be considered.

In the absence of the study and data related to the impact of racial factors in global data, necessary PK, and/or PD, effectiveness and safety studies should be conducted to support the marketing application of the drug.

Global data indicated that racial factors had impacts on evaluation of safety and effectiveness, and necessary clinical trials (including dosage exploration) should be conducted to support marketing application of the drug.

3. Insufficient data of safety and effectiveness

Where it is considered that there is insufficient safety and effectiveness data of the drug upon evaluation, the R & D by applicants should be considered carefully; and if they intend to continue the R & D work, necessary exploratory and confirmatory clinical trials should be

经评估，该药品安全有效且无种族敏感性的，可考虑豁免境内临床试验。

对于全球数据中已有中国人群PK、和/或PD、有效性和安全性数据，经分析认为其用于中国患者的获益大于风险的，相关境内外临床试验数据可直接用于支持上市申请。

对于全球数据中没有中国人群相关数据，但有较充分的种族因素相关研究和分析数据且未见明显种族因素影响的药品，应具体问题具体分析：（1）用于严重或危及生命疾病、罕见病且无有效治疗手段的药品，或用于此类疾病且较现有治疗手段具有明显提高疗效或安全性等优势的药品，可考虑在严格风险控制的前提下批准上市，并应开展上市后有效性和安全性临床试验以支持药品全生命周期获益/风险评估。（2）对于较现有治疗手段未见明显临床优势的药品，应参考"五（一）2"项相关要求进行临床试验。

对于境内已上市药品增加境外已批准境内未批准的新剂型（有临床优势的）、新给药途径、新用法用量，用于境内已上市药品已批准适应症的情形，以及境外已上市境内未上市新复方药品中各单药均已在境内上市的情形，在同时满足以下条件时，可考虑基于境外临床试验数据评价情况，减或免临床试验：①已上市原研药品完成的临床试验数据显示，该药品用于中国患者的获益大于风险，且与境外人群数据相比未见明显种族因素的影响；②递交的该药物新剂型、新给药途径、新用法用量，或新复方的境外临床试验数据可用于充分评价其安全性和有效性。

对于境内已上市药品增加境外已批准境内未批准的新适应症的情形，除应遵循上述临床评价基本逻辑和临床试验要求外，因涉及疾病和药物等多维度复杂因素，应具体问题具体分析，建议申报前与监管机构进行沟通。

2. 安全有效但缺乏种族敏感性数据或存在种族敏感性

经评估，该药品安全有效但缺乏种族敏感性数据或已有数据提示存在种族敏感性的，应开展相关桥接性临床试验。

全球数据缺乏种族因素影响相关研究和数据的，应开展必要的PK，和/或PD，有效性和安全性研究，以支持该药品上市申请。

全球数据显示种族因素对安全有效性评价存在影响的，应开展必要的临床试验（包括剂量探索等），以支持该药品的上市申请。

3. 安全有效性数据不充分

经评估，该药品安全有效性数据不充分的，申请人应慎重研发，如拟继续研发，应按新药要求开展必要的探索性和确证性临床试验。

conducted according to the requirements for new drugs.

4. The clinical data show ineffectiveness, or there are safety problems

Where there is sufficient evidence for ineffectiveness of the drug or serious safety problems, the clinical trial in China is not recommended.

(II) Domestic and overseas generic drugs

As for the requirements for clinical trials of generic drugs marketed overseas but not marketed in China, they should be determined after comprehensive consideration of two factors including clinical evaluation results and pharmaceutics of originator drugs.

1. Considerations based on clinical evaluation results

The requirements for conducting necessary clinical trials in Chinese patients based on the results of clinical evaluation of originator drugs should be consistent with those of clinical trials of originator drugs (see V (I) for details). Because it is difficult to obtain complete clinical trial data of originator drugs, there may be influences on the full clinical evaluation. Therefore, necessary clinical trials should be conducted to support evaluation of safety and effectiveness of generic drugs in Chinese patients.

2. Considerations based on pharmaceutics factors

For pharmaceutical evaluation of generic drugs, analysis should be based on cases according to drug characteristics. The details are as follows:

The reference preparation should be determined first. In general, the originator products with sufficient effectiveness and safety data should be selected, which are mainly approved by EU EMA, US FDA and Japan PMDA and marketed as reference preparations. At the same time, the selected reference preparation should be identified in accordance with the requirements in the Announcement on Issuing the Procedures for Selection and Determination of Reference Preparations for Generic Chemicals ([2019] No.25).

Secondly, the consistency of quality and effectiveness of generic drugs with originator products should be proved through studies according to pharmaceutical and biopharmaceutical characteristics. For example, for oral solid preparations, in addition to the comparison with pharmaceutical study of originator products, bioequivalence study should be conducted with reference to the issued technical requirements. For complex dosage forms (liposomes, microemulsions, external preparations, etc.), necessary clinical trials should be considered based on pharmaceutics and non-clinical comparative studies and evaluations and in combination with the characteristics of drugs and indications, so as to support the comparable evaluation of effectiveness and safety between generic drugs and originator drugs.

4. 临床数据显示无效或存在安全性问题

如有充分证据证明该药品无效或存在严重安全性问题的，则不建议其在中国开展临床试验。

（二）境内外仿制药品

对于境外已上市境内未上市药品的仿制药的临床试验要求，需结合原研药品临床评价结果及制剂学两个方面的因素综合考虑后确定。

1. 基于临床评价结果的考虑

基于原研药品临床评价结果，开展必要的中国患者人群临床试验的要求与原研药品一致（详见五（一））。由于难以获得原研药品完整临床试验数据，可能影响对原研药品进行充分临床评价，故通常需开展必要的临床试验以支持仿制药用于中国患者的安全性和有效性评价。

2. 基于制剂学因素的考虑

对于仿制药制剂学方面评估，需基于药品特点具体问题具体分析。具体如下：

首先，应确定参比制剂，通常应选择具有充分有效性和安全性数据的原研产品，且主要为欧盟EMA、美国FDA和日本PMDA批准上市并被列为参比制剂的药品。同时，应根据“关于发布化学仿制药参比制剂遴选与确定程序的公告（2019年第25号）”要求，对所选参比制剂进行认定。

其次，应根据药学和生物药剂学特征，通过研究证明仿制药品与原研产品质量与疗效一致性。如口服固体制剂，除进行与原研产品药学研究比较之外，还应参照已发布的技术要求，开展生物等效性研究等。对于复杂剂型（脂质体、微乳、外用制剂等），则尚需结合药物及适应症特点，在药学和非临床对比研究和评价的基础上，考虑必要的临床试验，以支持仿制药品与原研药品间疗效和安全的可比性评价。

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