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Re: Comments of PhRMA, BIO, EFPIA, JPMA, IFPMA and INTERPAT on the Four Announcements of China Food and Drug Administration on Relevant Policies for Encouraging Innovation in Drugs and Medical Devices (for public comment) (2017, Nos. 52, 53, 54, 55)

关于：美国药品研究与制造企业协会、生物技术创新协会、欧洲制药工业协会联合会、日本制药工业协会、国际制药商协会联合会和国际药企联盟关于食品药品监督管理总局发布的征求关于鼓励药品医疗器械创新意见等四项（2017 年第 52、53、54、55 号）公告的意见

To Whom It May Concern:
敬启者：

The Pharmaceutical Research and Manufacturers of America ("PhRMA"), European Federation of Pharmaceutical Industries and Associations ("EFPIA"), Biotechnology Innovation Organization ("BIO"), and Japan Pharmaceutical Manufacturers Association ("JPMA"), the International Federation of Pharmaceutical Manufacturers and Associations ("IFPMA") and INTERPAT (collectively "the Associations") appreciate the opportunity to submit these comments representing our collective views on the China Food and Drug Administration's ("CFDA's") Relevant Policies on Accelerating the Review and Approval for New Drugs and Medical Devices to Encourage New Drug and Medical Device Innovation ("Circular 52"), Relevant Policies on Reforming Clinical Trial Management to Encourage New Drug and Medical Device Innovation ("Circular 53"), Relevant Policies on Implementing Life-cycle Management for New Drugs and Medical Devices to Encourage New Drug and Medical Device Innovation ("Circular 54"), and Relevant Policies on Protecting Innovators' Rights to Encourage New Drug and Medical Device Innovation ("Circular 55") (collectively "the Draft Policies").

美国□品研究与制造企□□会(PhRMA)、欧洲制□工□□会□合会(EFPIA)、生物技□□新协会（BIO）、日本制□工□□会(JPMA)、国际制药商协会联合会(IFPMA)和国际药企联盟(INTERPAT)（合称“□会”） 感□有机会就国家食品□品□督管理□局（“食品□品□管□局”或“□局”）的下列公告向贵局提交我们的集体意见：关于征求《关于鼓励药品医疗器械创新加快新药医疗器械上市审评审批的相关政策》（征求意见稿）意见的公告（“第 52 号公告”）、关于征求《关于鼓励药品医疗器械创新改革临床试验管理的相关政策》（征求意见稿）意见的公告（“第 53 号公告”）、关于征求《关于鼓励药品医疗器械创新实施药品医疗器械全生命周期管理的相关政策》（征求意见稿）意见的公告（“第 54 号公告”）以及关于征求《关于鼓励药品医疗器械创新保护创新者权益的相关政策（征求意见稿）》意见的公告（“第 55 号公告”）（合称“政策草案”）。

Our shared mission is to support government policies that encourage the discovery and clinical development of innovative medicines for patients around the world. Our Associations are strong supporters of China’s goals for development of sustainable and innovation-driven pharmaceutical and biotechnology industries. As an expression of our support, our Associations and members have partnered with several Chinese domestic industry groups and national academic institutions to advance biopharmaceutical research and share international experience in key areas, such as drug registration and clinical trials.

我们协会的共同使命是向鼓励为世界各地患者发现创新药品及其临床研究的公共政策提供支持。我们协会鼎力支持中国可持续、创新驱动的制药和生物技术行业发展目标。作为表达上述支持的一项实际行动，我们协会及会员已与数家中国国内行业团体和国家级学术机构开展合作，推进生物制药研究并分享药物注册和临床试验等重要领域的国际经验。

I. General Comments on the Draft Policies
关于政策草案的总体意见

The Associations applaud CFDA for taking a significant and historic step forward with the Draft Policies. Among other achievements, these policies once implemented have the potential to remove significant obstacles for innovators and improve safety and quality of biopharmaceuticals, reduce delays, and facilitate the initiation of clinical trials in China. The Draft Policies also create important incentives for life saving innovative drugs to reach Chinese patients faster and set the stage for approval of a larger pool of innovative drugs that may serve as reference products for higher quality generics.

协会高度赞赏贵局以政策草案的出台迈出了具有重大历史性意义的一步。这些政策如果得以切实执行，将有可能为创新者扫除了重大的障碍，而且将提高生物药品的安全性和质量、减少上市延迟并促进临床试验在中国的启动。政策草案还为中国患者更快地获得治疗危及生命疾病的创新药品提供了重要的激励措施，并为更大范围的可用作较高质量仿制药参比制剂的创新药品的批准做好了准备。

We are particularly encouraged to see China establishing a patent linkage system and a concrete mechanism for providing applicants with regulatory data protection (“RDP”) and

address that Circular first before providing some comments and suggestions on the implementation of other points in Circulars 52, 53, and 54.

特别令我们感到鼓舞的是，中国拟建立专利链接制度以及向申请人提供监管数据保护的具体机制。接下来我们将就该公告提出意见，然后就第 52、53 和 54 号公告中的其他要点的执行提供一些意见和建议。

II. Comments on Circular 55: Encouraging Drug and Medical Device Innovations and Protecting the Interests of Innovators
关于《第 55 号公告：鼓励药品和医疗器械创新保护创新者权益》的意见

A. Patent Linkage Proposal
专利链接提议

i. Mechanics of Patent Listing
专利登记机制

The Associations are greatly encouraged to see that CFDA is proposing a patent linkage system with the critical components of notice to innovators of potentially infringing applications prior to approval of subsequent applications referencing the original application, and a stay of marketing approval pending the resolution of disputes concerning those patents.

协会倍受鼓舞地看到，贵局提出了一项专利链接制度，其关键要素包括：在参照原始申请的后续药品申请获取批准前，创新者得以被告知存在潜在专利侵权的申请情形，以及在申请所涉及的专利争议尚待解决期间设置一项上市批准等待期。

The Associations generally support the establishment of systems that permit the listing of patents as a mechanism to provide notice to future drug applicants. A system for listing patents is particularly suitable for patents that cover an approved product (e.g., patents claiming the active ingredient(s) or formulations of the drug product), as well as approved uses of the drug product. Mechanisms for identifying other types of patents that are relevant to biological products also should be considered.

协会大力支持该制度的设立，其允许通过专利登记机制告知后续药品申请者。该专利登记制度特别适用于那些已获批产品（如宣称药品活性成分及配方的专利）以及药品批准用途的专利。同时还应当考虑建立其他与生物制品相关的专利类型的机制。

We encourage CFDA to provide more guidance on the listing process, including the information must be provided to list patents, when patents must be identified, and the process for providing and posting patent information. In particular, we recommend that the guidance specify where and how submitted information will be posted publicly. CFDA should consider how these listing procedures will compare with those in other similar systems, such as the Orange Book in the United States and the Green List in South Korea. We also suggest that CFDA create a transitional mechanism through which patent information for currently approved innovative drugs can be listed under this system.

我们希望贵局就登记程序提供更多指导，包括专利登记应当提交的信息、专利应当登记的时间以及提供和发布专利信息的程序。具体而言，我们建议该指导明确提交的信息在哪里公布及如何公布。贵局应当考虑如何将该登记制度与其他国家的类似制度（如美国的橘皮书和韩国的绿色清单）相比照。我们还建议贵局建立一个过渡机制允许在该机制下，当前已获批准的创新药的专利信息得以登记。

For example, in Canada, the applicant submits patent information to the Patent Register, which is publicly available during government business hours and available online. In South Korea, the innovator files a patent listing application ("PLA") within 30 days of receipt of marketing approval from the Ministry of Food and Drug Safety ("MFDS"). As mentioned, MFDS publishes patent listings in the Green List, which is publicly available and online.

例如，在加拿大，申请人向专利登记簿（Patent Register）提交专利信息，该登记簿在政府办公时间内可公开查询也可在线访问。在韩国，创新者在从食品药品安全部获得上市批准后 30 天内提交专利披露申请。如上所述，韩国食品药品安全部在绿色清单中公布专利披露内容，绿色清单可公开查询也可在线访问。

We believe that it is important that this listed patent information be readily accessible to all applicants. The listed information should be available in an online database that is easily searchable by different criteria (for example, proprietary name, active ingredient, applicant, dosage form, route of administration, and patent number).

我们认为已登记专利信息可供所有申请人随时查询很重要。登记信息应当存放于易于通过不同关键字（如专有名称、活性成分、申请人、剂型、给药途径和专利号）搜索的在线数据库。

ii. Content of the Statement of Relevant Patents
相关专利声明的内容

We suggest that CFDA require that generic applicants submit a statement for each relevant patent and address the necessary content to give both the agency and the innovator notice of the generic manufacturer's basis for seeking marketing approval. For example, we urge CFDA to provide a standard form and require the generic applicant to provide some detail for the reason that it believes that there is no patent bar to marketing its product. This might include a statement that there is no patent, that the patent is expired, that the patent will expire, or that the patent is invalid or will not be infringed by the marketing of the proposed product.

我们建议贵局要求仿制药申请人为每项相关的专利提交一份声明，并提供必要资料，以告知贵局和创新者仿制药厂商提出上市申请的依据。例如，我们恳请贵局提供一项标准格式，并要求仿制药申请人较为详细地阐述其认为产品上市没有专利阻碍的理由。这可以包括关于不存在任何专利、专利期满、专利将期满或该专利无效或不会因申请药品上市而被侵犯的声明。

For example, in Canada, the generic manufacturer must provide information for each patent listed on the Patent Register for the comparator drug. Also, it must either agree to wait

until patent expiration before obtaining regulatory approval **or** provide one of the following statements in its application: (1) the innovator falsely claimed to have owned, had an exclusive license to, or had obtained consent of the patent owner to list the patent; (2) the patent has expired; (3) the patent is not valid; or (4) the patent would not be infringed by the construction, use, or sale of the proposed generic drug. As in Circular 55, the applicant must give the innovator notice if it raises any of these challenges.

例如，在加拿大，仿制药厂商须为专利登记簿上列出的比照药物的每项专利提供信息。同时，其须同意在取得监管部门批准之前等待至专利期满，**或者**在其申请中提供下列任一声明：(1)创新者虚假地声称拥有或曾拥有该专利的排他性许可，或在声明该专利前取得了专利权人的同意；(2)该专利已期满；(3)该专利无效；或(4)该专利不会因申请上市仿制药的制造、使用或销售而遭到侵犯。如果申请人提出这些挑战中的任何一条，如第 55 号公告所述，申请人必须告知创新者。

iii. Initiation of the Stay
批准等待期的启动

To implement the stay and patent infringement lawsuit, we recommend that CFDA ensure, likely in collaboration with the State Intellectual Property Office, that the appropriate patent suit can be initiated under China's Patent Law in time to permit the required notices to trigger a stay. For example, the act of filing an abbreviated new drug application with a Paragraph IV certification in the United States constitutes an act of infringement that allows the innovator to file suit.[1] Similarly, as anticipated in Circular 55, it would be necessary to ensure that the Patent Law permits a patent holder to file a suit for infringement in those instances where a generic applicant does not appropriately declare its position relative to a listed patent.

为执行批准等待期和专利侵权诉讼，我们建议贵局在有可能与国家知识产权局合作的情况下确保相关专利诉讼可根据中国《专利法》及时得以提起，以便发出启动等待期所需的告知。例如，在美国以第四段证明提交简化新药申请的行为构成允许创新者提起诉讼的侵权行为。[2] 同样地，如第 55 号公告预期，如果申请人未适当地声明相关专利，则有必要确保《专利法》允许专利持有人在仿制药申请人未适当声明其相对于已登记专利的立场的情况下提起侵权诉讼。

The Associations also urge CFDA to ensure that the proposed time periods are realistic for the parties to accomplish the procedural steps envisioned in the Draft Policies to resolve their dispute in the most efficient manner. Specifically, the period for initiating suit, proposed as 20 days[3] from receipt of the applicant's notice, should be based on data from the Chinese court system regarding the time that it would take to prepare and file a patent infringement suit and receive and file with CFDA the necessary documentation from the judicial authority. Applicants

[1] *See* 35 U.S.C. § 271(e)(2). Pursuant to a paragraph IV certification, a generic manufacturer alleges that the listed patent is invalid or will not be infringed by the manufacture, use, or sale of its proposed generic drug. 21 U.S.C. § 355(b)(2)(A)(iv).

[2] 参见《联邦法规汇编》第 35 篇第 271(e)(2)条。根据第四段证明，仿制药厂商声称所声明专利无效或不会因申请上市仿制药的制造、使用或销售而遭到侵犯。参见《联邦法规汇编》，第 355(b)(2)(A)(iv)条。

[3] We would suggest clarifying whether this is business days or calendar days.

seeking similar stays in the United States, South Korea, and Canada have 45 days to prepare and file their suits. We would strongly encourage CFDA to provide the same 45 days for an applicant to secure a stay in China.

协会还恳请贵局确保，提议的时间段对于完成政策草案中预期的程序性步骤具有现实可操作性。具体而言，提起诉讼的期限（提议为自收到申请人告知之日起 20 天[4]）应当基于中国法院系统提供的关于准备和提起专利侵权案件、及收到并向贵局提交司法机关必要文件所需的时间期限。在美国、韩国和加拿大申请类似批准等待期的申请人有 45 天的时间准备和提起诉讼。我们强烈建议贵局为中国申请批准等待期的申请人同样提供 45 天的期限。

In addition, we would propose that once the stay mechanism is implemented, CFDA work with the Courts to monitor how long it takes for patent lawsuits generally to be resolved to ensure that the 24-month stay period is sufficient.

此外，我们还建议一旦等待期机制得以实施，贵局可与法院共同监测专利诉讼得以解决通常所需的时间，以确保 24 个月的批准等待期足够长。

There should also be clear instructions, including forms as appropriate, on CFDA's website addressing how the patent owner can inform CFDA and the Center for Drug Evaluation of the basis for a stay once the patent suit is filed.[5] This website should include instructions as to precisely what court documentation must be submitted (whether originals or copies) as evidence of the commencement of litigation. Parties should be able to readily communicate with a relevant office to obtain confirmation as to whether the documentation has been accepted and the stay is in place.

一旦发生专利诉讼，专利权人如何能告知贵局和药品审评中心设置批准等待期的依据，对此，贵局网站上也应当有明确的说明（视情形包括范本）。[6] 该网站应当包含关于须提交具体哪些法院文件（无论是原件或复印件）作为诉讼启动之证明的说明。当事方应当能够随时与相关办事机构沟通，以获得关于文件是否被接受以及批准等待期是否已被设置的确认。

[4] 我们建议澄清这指的是工作日或是公历日。

[5] In the United States, the generic manufacturer must notify FDA immediately of any legal action. This notification must include: the generic application number, the name of the generic applicant, the established name of the drug product, and a certification that an action for patent infringement (identified by number) has been filed with an appropriate court on a certain date. A patent owner or its representative may also submit a similar notification to FDA. 21 C.F.R. § 314.107(f)(2). In Canada, the patent owner or its representative must provide the Minister of Health with proof that a court application has been made.

[6] 在美国，仿制药厂商若有任何法律诉讼须立即通知美国食品药品监督管理局。该通知须包括：仿制药申请编号、仿制药申请人名称、药品的确定名称以及关于专利侵权诉讼（注明编号）已于特定日期向适当法院提交的证明。专利所有人及其代表也可向美国食品药品监督管理局提交类似通知。（《联邦法规汇编》第 21 篇第 314.107(f)(2)条。在加拿大，专利所有人或其代表须向卫生部提供已提出法院申请的证明。

B. Regulatory Data Protection ("RDP")
监管数据保护

The Associations applaud CFDA for working to establish a concrete structure to provide meaningful RDP. RDP is a critical incentive in encouraging more innovation in China. We are very supportive of CFDA's foundational efforts in Circular 55.

协会大力赞赏贵局建立具体框架提供监管数据保护的努力。监管数据保护是促进中国产生更多创新的重要激励措施。我们十分支持贵局在第 55 号公告中的基本努力。

i. Scope of RDP
监管数据保护的范围

Our comments on the proposal relate primarily to better understanding the specifics of the operation of the proposed RDP system. In that respect, we seek clarification that innovative drugs, new orphan and pediatric drugs,[7] and innovative biologics that receive six, ten, and ten years of data protection, respectively, include those products that are approved for marketing elsewhere, but are new to China and have been approved based on a full safety and effectiveness package being submitted in China. In other words, this would include both categories 1 and 5 for small molecule drugs[8] and category 7 for therapeutic biologics under the current Drug Registration Regulation.[9] We believe this approach is consistent with China's aspirations to promote local innovation and the intent of Circular 55, which mentions "a new drug for which the data has been submitted in China within one year after it has been approved for marketing by the European Medicines Agency, by the U.S., or by Japan shall have *the corresponding type of data protection.*" We urge CFDA to expressly clarify that is the case for ease of implementation.

我们对此提议的意见主要涉及对提议的监管数据保护体系运行细节加以更好理解。在此方面，我们请求贵局澄清，分别获得六年、十年和十年的数据保护期的创新药、新的罕见病药和儿童专用药[10]以及创新生物制品包括在中国境外获准上市但尚未在中国境内上市且已基于在中国提交的关于安全性和有效性的全套资料获得批准的产品。换言之，受该数据保护期保护的产品将包括 1 类和 5 类小分子药[11]以及现行《药品注册管理办法》下的 7 类治疗用生物制品。[12] 我们认为此方法符合中国促进国内创新的宏愿和第 55 号公告的意图，该公告提到，"欧洲药品管理局、美国和日本获准上市后 1 年内在中国提出上市申请和数据保护的新药，给予*相应类别数据保护期。*"我们恳请贵局明确澄清，这是为了易于执行而作出的规定。

[7] It will also be important to clearly define "orphan" and "pediatric" drugs so that innovators and follow-on applicants have a clear understanding of those products eligible for the longer RDP term proposed by CFDA.
[8] Reform Plan for the Classification of Small Molecule Drugs (CFDA No. 51, 2016).
[9] Drug Registration Regulation, Appendix 3.
[10] 明确定义"罕见病"和"儿童专用"药也十分重要，以便创新者和后续申请人清楚地了解贵局提议的有资格享受较长监管数据保护期的产品。
[11] 《化学药品注册分类改革工作方案》（食品药品监管总局 2016 年第 51 号公告）
[12] 《药品注册管理办法》附件 3。

We also urge CFDA to consider providing RDP to all improved drugs—not just improved orphan and pediatric drugs.[13] Incremental improvements to existing drugs, such as new dosage forms and dosing regimens, can create substantial benefits for patients regardless of whether they treat an orphan or pediatric disease. RDP is an important incentive to encourage studies supporting such changes.

我们还恳请贵局考虑向所有改良型药品提供监管数据保护，而不仅仅是改良型罕见病药和儿童专用药。[14] 对现有药品的增量改良，如新的剂型和给药方案，可为患者带来很大的益处，而无论其是否治疗罕见病和儿童疾病。监管数据保护是鼓励支持这些变更的研究的重要激励措施。

It is also unclear whether CFDA plans to provide a guaranteed minimum period of time before a follow-on applicant can seek marketing approval based on (or relying on) the original applicant's data. For example, in the United States, a generic applicant cannot file an abbreviated new drug application until after four years of the RDP term has expired, thereby providing a period of certainty to the innovator, as well as administrative predictability for the regulator.

同样不明确的还有，贵局是否计划在后续申请人基于（或依赖于）原申请人数据申请上市批准之前提供一个可保证的最短期限。例如，在美国，仿制药申请人须等到监管数据保护期期满四年后方可提交简化新药申请，因而给创新者提供了一个明确的期限以及行政机关的程序可预见性。

We would also like to clarify that when CFDA indicates that it will provide first to launch generics with RDP that in fact means marketing exclusivity. It is also not clear why this protection is proposed for generics that have been initially launched abroad. We suggest that this protection be provided to generic applicants that successfully challenge a patent in China and obtain approval in China based on a reference product that CFDA has evaluated for safety and effectiveness based on a full package of preclinical and clinical data.

我们恳请贵局澄清，当贵局指出将为首次上市的仿制药提供监管数据保护时，其实是指上市专属权。而且也不清楚为何提议为首先在国外上市的仿制药提供此项保护。我们建议，此项保护应给予在中国成功挑战专利并在中国获得基于贵局根据充分完整的非临床试验及临床试验数据已综合考量安全性和有效性的参照药品批准的仿制药申请人。

Finally, we would like to clarify the meaning of the exemption for an applicant that obtains the data on its own. We suggest that CFDA refer here to an applicant that *generates* its own data and clarify that an applicant's reliance on others' protected data would not enable that applicant to circumvent RDP, even if the applicant somehow "obtains" the data. Circular 55

[13] Consistent with the use of this term in other contexts in China, CFDA should clarify that "improved drugs" refers to a new dosage form, drug delivery system, change to the manufacturing process, route of administration, indication, or compound preparation, as well as certain changes to the formulation, of an existing active ingredient.
[14] 根据中国其他语境下此术语的用法，贵局应当澄清"改良型药品"指的是在已知活性成分的基础上的新剂型、给药系统、工艺变更、给药途径、适应症或复方制剂以及现有配方的某些变更。

should also clarify that RDP does not apply to a follow-on applicant who obtains express, written consent from the owner of protected data to use those data.

最后，我们恳请贵局澄清关于自行取得数据的申请人的豁免规定的含义。我们建议贵局在此处指明*生成*自己数据的申请人，并澄清依赖他人受保护数据的申请人不得使该申请人规避监管数据保护，即使该申请人以任何方式“取得”数据。第 55 号公告还应当澄清，监管数据保护不适用于从受保护数据所有人获得使用该等数据的明确书面同意的后续申请人。

ii. RDP Window
监管数据保护申请期

The Associations offer several suggestions regarding the discussion of the “RDP Window” in Circular 55 requiring companies to initiate a marketing approval application process in China within one year of approval in the U.S., EU or Japan to benefit from the full RDP terms.

55 号公告要求企业于新药在美国、欧洲或日本获准上市后 1 年内在中国提出上市申请以获得完整的监管数据保护期，关于其中涉及“监管数据保护申请期”的讨论，协会提出几项建议。

We recognize that at first blush, a phased-in approach to RDP in which this type of a mechanism is used may appear attractive to encourage a greater number of innovators to bring their medicines to China in a short period of time. However, as the second largest pharmaceutical market in the world, companies already are incentivized to seek marketing approval promptly in China without using this type of mechanism, and these incentives will only grow as China reforms its regulatory system and improves other aspects of the policy ecosystem. Moreover, imposing an arbitrary time limit for seeking marketing approval in order to qualify for full RDP could have negative effects. For example, some companies may have an important reason for delaying entry into the China market, such as safety concerns because of an adverse event in another market. Meanwhile smaller and medium-sized enterprises may not have either the resources or the expertise in global marketing of products to meet the RDP Window. In such instances, a time-sensitive window to qualify for RDP could potentially discourage these companies from later bringing their medicines to China.

我们认为，乍看起来，应用此机制，对监管数据保护进行分阶段对待，看似可能鼓励更多的创新者在短期内将其药品引入中国。但是，中国作为全世界第二大医药市场这一因素已足以激励企业及时寻求在中国获得上市批准，而无需采用该类机制，且只有中国改革其监管体制并改善政策生态系统的其他方面才能进一步增强此类激励因素的效果。另外，在寻求上市批准以获得完整监管数据保护期方面实施任意期限规定，可能产生不利影响。例如，某些企业可能出于重要原因推迟进入中国市场，例如其他市场的不良事件引起的安全顾虑。与此同时，中小企业或许没有在全球上市药品的资源和技能以满足监管数据保护申请期。在该等情况下，若以时间紧迫的申请期来衡量是否符合监管数据保护，可能使这些公司失去之后将其药品引入中国的信心。

Furthermore, the RDP Window raises a number of technical questions concerning how this would be determined and its feasibility under China's current and anticipated regulatory process. For example, it would be important to know what event/submission will fulfill the requirement for submission of an application within the proposed one-year window. Indeed, even if the policy is referring to a clinical trial application (CTA), there are multiple pre-requisites that must be met in China before an applicant can file a CTA, including ethics committee review (as proposed in Circular 53), sample testing, human genetic resources review, and any good clinical practice inspection. As such, CFDA should elaborate on how an applicant would be assured that it could meet any proposed window without jeopardizing a reduction of the applicable RDP term.

进而，监管数据保护申请期的提议还将引发一些技术问题，包括如何认定该申请期以及其在中国目前和预期监管程序下的可行性。例如，重要的是应知道哪些活动/材料能够满足在所提议之一年申请期内提交申请的要求。事实上，即使该政策是针对临床试验申请，申请人在中国也必须满足许多先决条件方可提交临床试验申请，包括伦理审查（见53 号公告）、样品检验、人类遗传资源审批和关于药物临床试验质量管理规范的任何检查。同样地，贵局应详细说明如何向申请人确保其能满足任何提议的申请期而不会导致缩减相应类别的监管数据保护期。

Furthermore, it needs to be made clear that the date of submission rather than the date that CFDA accepts the application will be used to determine whether the window has been met. It should also be clarified that the RDP period runs from the date of approval for marketing (i.e., the date on the license) in China.

此外，需要明确，用于确定申请期是否满足的是提交之日而非贵局受理申请之日。还应阐明监管数据保护期从在中国上市批准之日（即许可证上的日期）开始计算。

III. Comments on Circular 52: Relevant Policies on Accelerating the Review and Approval for New Drugs and Medical Devices to Encourage New Drug and Medical Device Innovation
关于第 52 号公告《关于鼓励药品医疗器械创新加快新药医疗器械上市审评审批的相关政策》的意见

A. Expedited Regulatory Pathways and Orphan Drug System
加快审评审批和罕见病用药制度

We strongly agree with the establishment of expedited pathways for drugs that treat serious and life threatening illnesses. This approach is a sign of a strong and flexible regulatory system that increases access for those patients with the greatest need. We also agree that granting a conditional approval, based on an earlier established positive risk-benefit assessment prior to a confirmatory study, is a critical regulatory pathway to achieve this goal. We suggest that in implementing the conditional approval mechanism, it is important to put in place measures to ensure that all stakeholders in the biopharmaceutical ecosystem understand the meaning of this status, including payers (government and private insurance companies), public and private medical institutions, and the physicians themselves.

我们强烈赞同为用于治疗严重危及生命疾病的药品建立快速审评审批通道。这标志着一项强大且灵活的监管制度从而增加最急需患者获取药物的机会。我们也赞同，基于确证性研究之前建立的积极风险-效益评估授予有条件的批准是实现此目标的关键监管途径。我们建议，在实施有条件批准机制时，重要的是实施适当措施以确保生物制药生态系统的所有利益相关人理解其含义，包括支付人（政府和私人保险公司）、公共和私人医疗机构以及医生。

Additionally, it is important to grant priority review of the registration application for all products that receive conditional approval, and include specified timelines compared to standard review times, e.g., six months for priority review and 12 months for standard review. Limiting priority review to innovative drugs that were funded by the National Science and Technology Major Project and the National Key Research and Development plan will limit access for those patients with the greatest medical needs.

此外，对于获得有条件批准的所有产品的注册申请务必要给予优先审评，并包括与普通审评时间相对照的具体时间表，如优先审评为六个月，普通审评为 12 个月。仅对列入国家科技重大专项和国家重点研发计划支持的创新药物给予优先审评可将受益人限制为那些有最大临床需要的患者。

Patients with rare diseases will truly benefit from CFDA forming an orphan drug registration pathway, particularly one that includes an option to rely on data evaluated and approved by another established health authority, such as the U.S. FDA or the European Medicines Agency ("EMA"). We look forward to the opportunity to understand and comment on the criteria according to which the National Health and Family Planning Commission ("NHFPC") will establish the orphan drug disease list. Chinese patients may benefit from aligning this list with international standards related to patient population thresholds. The possibility to reduce subject numbers should also be available for products not officially listed on the rare disease list but still being developed for a small population. We also look forward to the opportunity to provide comments on the expectations for the confirmatory clinical trial conducted pursuant to a conditional orphan drug approval. Additionally, we support mechanisms to align the expectations of the sponsor and the CDE, including related to the application of CFDA's draft policy on accepting overseas clinical data, according to Circular 53, and whether overseas clinical data can satisfy post-approval clinical data requirements.

罕见病患者将真正受益于食品药品监管总局建立的罕见病用药注册途径，尤其是其能够选择依赖其他已设立的卫生部门（如美国食品药品管理局或者欧洲药品管理局）评估批准的数据。我们期待有机会理解并探讨国家卫生和计划生育委员会（"**国家卫生计生委**"）建立罕见病用药目录所依据的标准。将此目录与关于患者人数门槛的国际标准接轨可使中国患者受益。对于未正式列入罕见病清单但仍在为小众患者开发的产品，也应当允许减少受试者人数，我们还期待有机会就按照有条件批准罕见病用药开展的确证性临床试验之期望提供意见。此外，我们支持旨在协调申办者与药品审评中心期望的机制，包括关于适用食品药品监管总局关于接受境外临床试验数据的政策草案（见 53 号公告），以及境外临床数据是否能满足批准后的临床数据要求。

B. Mechanisms for Stakeholder-CFDA Communications
利益相关人-食品药品监管总局沟通制度

Building a formal agency consultation and structured communication system between CDE (the technical review institution) and the applicant during the product review will be a valuable reform for all parties and increase stakeholder alignment and efficiency throughout the entire development and registration process. Circular 52 appears to call for mandatory meetings before Phase I, after Phase II, and before the NDA filing. As a matter of international practice, regulatory agency consultation and discussion meetings are optional for sponsors, although they are used very frequently in practice. These meetings are typically requested when there is a true technical question on the complexities of drug development that warrants further scientific discussions to ensure full alignment of expectations. Therefore, we urge CFDA to create flexibility in this respect so that it can focus its resources on the most pressing questions.

建立项目审评过程中药品审评中心（技术审评机构）与申请人正式的机构咨询和结构化沟通制度，对于各方而言将是极有价值的改革，且将提高利益相关人在整个开发和注册过程中的一致性和效率。52 号公告似乎强制要求在 I 期临床试验前、II 期临床试验后和新药申请提交前必须进行会议沟通。虽然会议沟通确实在实践中经常用到，但实际上国际惯例是，与监管机构间的咨询讨论会议对申办者而言是选择性的。通常召开该等会议的情况是，确实出现关于药品开发复杂性的技术问题而需要进行进一步的科学讨论以确保各方期望得到充分协调。因此，我们强烈希望食品药品监管总局就此建立灵活机制以便将其资源集中用于解决最紧迫的问题。

C. Management model of drug substances, excipients and packaging materials
药用原辅料和包装材料的管理模式

To avoid unintended consequences, such as disrupting product supply/delaying patient access, it is critical that changes to the filing measures for drug substances and excipients and packaging materials are consistent with globally harmonized standards, particularly for imported drugs that are typically supplied globally and subject to requirements across multiple jurisdictions. For example, international GMP standards, such as those developed by the International Council on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), require the responsible MAH to have proper quality agreements in place with contract manufacturers of API and to provide information regarding the excipients and primary packaging materials as part of the regulatory file.

为避免诸如中断产品供应及延迟患者使用等非预期的后果，关于药用原辅料和包装材料的备案措施须符合全球统一的标准，对于通常全球供应且受多个辖区要求限制的进口药尤为如此。例如，国际药品生产质量管理规范（GMP）标准（譬如人用药品注册技术国际协调会议（ICH）制订的标准），要求负责的上市许可持有人与活性成分的合同生产商签订适当的质量协议，并在监管文件中提供关于辅料和主要包装材料的信息。

D. Priority Procurement Status
优先采购

We urge CFDA and other agencies to provide additional details regarding the criteria necessary to show the "clear efficacy" to qualify for priority procurement status for new innovative drugs. In order for this priority status to function effectively, it is important that stakeholders understand when their drugs would qualify, including whether this standard is similar to that for the priority status that CFDA grants for marketing approval. This priority status should be granted to drugs regardless of whether they are new to China or new to the world.

我们强烈希望食品药品监管总局和其他部门就优先采购创新药要求的"疗效明确"适用的必要认定标准提供详细说明。为使该等优先制度有效运作，重要的是使利益相关人理解他们的药品何时符合所需要求，包括该等标准是否类似于食品药品监管总局授予上市批准应用的优先制度所依据的标准。该等优先制度应当可适用于无论在中国或世界是否属于新药的药品。

E. Priority Review System for Drugs Granted a Compulsory License
针对获得强制许可之药品的优先审评审批制度

The Associations commend CFDA for appropriately indicating that compulsory licenses should be used only in the case of public security or a major public health threat. As a policy matter, the Associations believe that compulsory licensing is not an effective or sustainable way to improve patient access to medicines and that better alternatives exist, including voluntary licensing, to address true health emergencies. Compulsory licenses are a limited exception to patent rights that should be granted in accordance with international rules, and even then only as a last resort. As such, we would appreciate the opportunity to understand and comment on any proposed definition by the NHFPC of those limited circumstances in which a compulsory license may be granted in China.

贵局恰当地表示强制许可应仅被用于为维护公共健康、在公共安全受到重大威胁情况下，协会表示赞同。作为一个政策问题，协会认为强制许可并非一项提高患者获得药物机会的有效或可持续方式，而且有其他解决实际发生的突发性卫生问题的更好方法，如自愿许可。对于按照国际规则应当授予的专利权，强制许可则是一项有限的例外，且即使那样，也仅作为最后对策。同样地，若能够理解国家卫生计生委对在中国可能授予强制许可的该等有限情况的任何提议定义并进行探讨，我们将深表感谢。

IV. Comments on Circular 53: Relevant Policies on Reforming Clinical Trial Management to Encourage New Drug and Medical Device Innovation
关于第 53 号公告《关于鼓励药品医疗器械创新改革临床试验管理的相关政策》的意见

A. Facilitating the Process for Initiating Clinical Trials
简化开展临床试验的流程

We strongly support abolishing the existing clinical trial site accreditation system and converting it to a filing system open to all public and private institutions. This reform will expand the number of sites available to conduct innovative biopharmaceutical research and afford Chinese patients more opportunities to enroll in clinical studies. We urge CFDA to provide instructions and guidance on the standards and processes necessary to submit these filings.

我们大力支持取消现有的临床试验机构资格认定制度，将其改为面向所有公共和私人机构的备案管理制度。该等改革将扩大可用于开展创新生物制药研究的机构数量并向中国患者提供更多机会加入临床研究。我们强烈建议贵局就提交该等备案申请所适用的标准和流程提供指导和说明。

We urge CFDA to consider permitting the ethics committee review of the protocol and CFDA review of clinical trial applications to proceed at the same time. We support CFDA's goal of building efficiency into the clinical trial application process. These reforms are critical to facilitating simultaneous global development and greater enrollment of Chinese patients in multiregional clinical trials. Parallel review is important in this respect. Such an approach would not interfere with CFDA's ability to intervene if concerns with the human subject protections were to arise before or during the trial.

我们建议食品药品监管总局考虑允许伦理委员会对试验方案的审查以及食品药品监管总局对临床试验申请的审评审批二者同时进行。我们支持贵局将效率纳入临床试验申请流程的目标。这些改革对于促进全球同步开发和允许中国患者更多参与多地区临床试验极其关键。并行审查在这方面相当重要。该等做法不会干涉在试验前或试验过程中出现任何关于保护人类受试者的问题时食品药品监管总局的介入能力。

Similarly, we also request that CFDA work with the Ministry of Science and Technology to permit the review of human genetic resource ("HGR") applications to proceed in parallel with the clinical trial application review. If this does not occur, review of the HGR applications can delay the start of trials and impede CFDA's important goals.

类似地，我们还请求贵局与科学技术部合作以允许临床试验申请的审评审批的同时并行开展人类遗传资源申请的审评审批。如果无法实现，对人类遗传资源申请的审评审批可能推迟试验的开始并阻碍食品药品监管总局的重要目标。

B. Acceptance of Foreign Data
接受境外数据

We applaud CFDA for permitting acceptance of overseas clinical data to support registration in China. This reform is another great example of a measure that will achieve global regulatory harmonization and accelerate innovative drug development and registration. In order to implement this provision, we urge CFDA to provide guidance and instructions on precisely what requirements such data will need to meet and what type of site inspection will be required, including whether there will be onsite inspection of the clinical sites or inspection of data on sponsor's site. For example, further clarification is required regarding the purpose of the "after on-site inspection" in order to accept foreign clinical data, and whether such site inspections are required prior to submitting the China registration application or prior to approval (the latter avoids unnecessary delay in CFDA beginning its review). Additionally, to further streamline regulatory review, CFDA could consider a risk-based approach to conducting such overseas inspections depending on the inspection history of the site and inspection reports from other established regulatory agencies.

食品药品监管总局允许接受境外临床试验数据以支持在中国的注册，对此我们深表赞赏。该项改革代表了旨在实现全球监管协调统一和加快创新药物开发与注册的又一重要举措。为实施此规定，我们强烈建议食品药品监管总局就该等数据需要满足的确切要求以及需要进行的现场检查类型，如是否包括临床试验地点的现场检查或申请者现场数据的检查，提供指南和说明。例如，关于经"现场检查后"接受境外临床试验数据的目的需要进一步澄清，以及在提交中国注册申请或批准（后者避免了贵局开始审评的不必要延迟）之前是否要求该等现场检查。此外，为进一步简化审评，根据现场的检查历史以及来自其他常设监管机构的检查报告，贵局可考虑在进行这些境外检查时采用基于风险的方法。

Moreover, specific guidance is needed on whether global and/or Asian data is acceptable to demonstrate the ethnic insensitivity requirement (e.g., following ICH bridging standards) or whether Chinse patient data is required. This guidance will be critical to ensure full alignment between CFDA and sponsors regarding the required study population to secure registration in China.

而且，关于全球和/或亚洲数据是否可接受用于证明符合不存在种族差异要求（如遵循 ICH 衔接标准）或是否要求提供中国患者数据，需提供具体指导。该指导对于确保贵局与申办者在获得中国注册所需的研究人群方面保持充分一致而言极其关键。

C. Facilitating Protocol Amendments
促进试验方案修改

We also support CFDA's efforts to create a mechanism to amend clinical trial applications and protocols once the trial has begun. We agree that non-safety related changes should not disrupt the course of a trial that may be providing important, and possibly lifesaving, treatment to the enrolled subjects. This approach is consistent with accepted global clinical trial best practices and is important to facilitate China's seamless participation in multiregional trials. We look forward to more guidance and instructions from CFDA on how this amendment process

will work, including how it will account for the dynamics of maintaining the conduct of the clinical study. For example, CFDA will need to establish criteria for changes that require pre-approval prior to being implemented (and the associated workable review timeline, in line with international standards such as 60 day IND review) and for changes that require notification only.

我们还支持食品药品监管总局为建立在试验开始后修改临床试验申请和试验方案的机制所作出的努力。我们同意，非安全性问题相关的变更不应中断可能向登记受试者提供重要且可能拯救生命之治疗的试验过程。该做法符合公认的全球临床试验最佳实践且对促进中国无缝参与多地区试验相当重要。我们期待食品药品监管总局就如何实施该等修改程序包括其如何解释维持开展临床研究的机制提供更多指南和指导。例如，贵局需要就执行前要求事先批准的变更（以及与譬如 60 天临床试验用药物（IND）审评等国际标准相接轨的相关可行审评时间表）以及仅需通知的变更制定标准。

D. Encourage the Extended Access Clinical Program
支持拓展性临床试验

Expanding patient access to treat serious, life-threatening illnesses with no effective treatments is a mutual goal of both regulators and industry. CFDA's approach seems consistent with this goal in calling for expanded drug utilization in the clinical trial setting. However, it is important to separate the mechanisms by which patients have access to such experimental treatments to ensure the integrity of the clinical trial and the proper regulatory oversight of all patients. Under CFDA's current framework, patients may obtain access to unapproved experimental medicines by participating in clinical trials under the oversight of CFDA and EC. For patients with a serious or life-threatening disease who are ineligible or unable to participate in a clinical trial, use of an unapproved investigational medicine via a separate CFDA expanded access program could provide another option for patients. Expanded access, including treatment use in individual patients, is the use of an unapproved investigational drug outside of a clinical trial to treat a patient with a serious or life-threatening disease or condition, when there are no other comparable or satisfactory alternative treatment options. For example, under the U.S. FDA's regulatory framework, patients can obtain unapproved experimental medicines through a separate expanded access program subject to an expedited FDA review.

让治疗严重危及生命且尚无有效治疗手段疾病的产品惠及更多患者是监管机构和医药行业的共同目标。贵局的方法符合这一目标，即要求扩大处于临床试验阶段的药物的使用范围。但是，需注意的是要务必区分患者获得此类试验性疗法的机制以确保临床试验的可信度以及监管机构对所有患者安全的适当监督。根据贵局目前的框架，患者可通过参与受国家食品药品监督管理总局及伦理委员会监督的临床试验获得未经批准的试验性药物。对于不具备资格或不能参加临床试验的患有严重危及生命疾病的患者，通过贵局另外一项扩展使用计划使用未经批准的研究用药物可为患者提供另一选项。扩展使用，包括对个别患者的治疗性使用，是指在没有其他任何类似或令人满意的替代治疗选项的情况下，在临床试验之外将未经批准的研究性药物用于治疗严重危及生命的疾病或症状。例如，根据美国食品药品监督管理局的监管框架，患者可通过受限于食品药品监督管理局优先审核的另一项扩展使用计划获得未经批准的试验性药物。

V. Comments on Circular 54: Relevant Policies on Implementing Life-cycle Management for New Drugs and Medical Devices to Encourage New Drug and Medical Device Innovation
关于第 54 号公告《关于鼓励药品医疗器械创新实施药品医疗器械全生命周期管理的相关政策》的意见

A. Expanding the Marketing Authorization Holder Program
扩大上市许可持有人项目

We support expanding the pilot program and establishing a marketing authorization holder ("MAH") system for all applicants. This reform will support a framework under which the legal roles and responsibilities of the sponsor (or MAH holder) are clearly documented regardless of the geographical manufacturing location. We request that CFDA clarify that "universally implemented" means that the expanded MAH system will apply to both Chinese- and foreign-based applicants and that the expanded system can be implemented prior to a revision to the Drug Administration Law of People's Republic of China, which is cited in Circular 54. It is also important to clarify that once the MAH receives the drug license approval for all products (domestic/imported; biologics, vaccines and small molecules), the MAH is permitted to immediately market the drug in China.

我们支持扩大试点项目并针对所有申请人建立上市许可持有人制度。该项改革支持的框架是，申办者（或上市许可持有人）的法律角色和职责被清晰记录，无论其生产地点位于何处。我们请求贵局阐明“普遍实行”指的是扩大的上市许可持有人制度将同时适用于中国和外国申请人，且扩大的制度可在修订《中华人民共和国药品管理法》之前落实，参见 54 号公告。同样需要澄清的是，一旦上市许可持有人为所有产品（包括国产/进口药；生物制品、疫苗及小分子药）获得药物许可批准，则上市许可持有人获准立即在中国上市药物。

B. Adoption of the Electronic Common Technical Document
采用电子通用技术文档

We strongly support what appears to be a proposal for CFDA's adoption of the electronic common technical document (eCTD) format, per ICH guidelines. This approach will increase the efficiency of reviews for both CFDA and sponsors. Based on experience from other regulatory authorities, full implementation takes time, and we suggest setting a clear, phased-in approach, e.g., start with a pilot on Chinese eCTD before its full implementation. This method has benefited both regulators and sponsors in the past because it avoids any unintended inefficiencies or disruption of the drug approval process, which can lead to delays in patient access. Another consideration is to clarify that the eCTD requirement would not apply retrospectively once fully implemented, and thereby avoid requiring modifications to ongoing applications, which can unnecessarily delay patient access.

我们强烈支持贵局按照 ICH 指南相关规定采用电子通用技术文档格式（eCTD）的提议。该做法将提高贵局及申办者的审查效率。基于其他国家监管机构的经验，充分落实需要时间，我们建议设置清晰的分阶段实施办法，如在全面实施前先开展中国通用技术文

档格式（eCTD）试点项目。该方法在过去已经使监管机构和申办者受益，原因是其能够避免药品审批流程中出现的意料之外的无效率或者中断进而导致延迟患者获得药品。另一项考量是澄清，通用技术文档格式（eCTD）要求一旦全面实施则不作追溯性地适用，因而可避免对进行中的申请作出修改的需要（这会不必要地延迟产品上市）。

C. Facilitating Sample Testing
促进样品检验

Reforming the clinical trial sample testing system of drugs is another key step to harmonizing CFDA practices with international standards and increasing efficiency in the CTA review process. Testing of biologic clinical trial samples by CFDA and its affiliated institutions has put a strain on resources and added complexity and time to the overall process. Therefore, we agree that creating flexibility to use the sponsor's validated testing of the submitted specifications (including biologic test samples) will significantly reduce the time to start patient enrollment in clinical trials.

改革药品临床试验样品检验制度是将贵局做法与国际标准协调统一并提高临床试验申请审查流程效率的又一关键步骤。由贵局及其附属机构检验生物临床试验样本造成了资源紧张并增加了整体流程的复杂性和所需时间。因此，我们同意建立灵活机制使用申办者对所提供规格项目（包括生物制品检验样本）的有效检验结果，将大幅缩短开始进行临床试验患者注册登记的时间。

D. Recognizing the Important Role of Medical Representatives
认可医药代表的重要作用

The innovative pharmaceutical industry strongly believes that a health care professional's care of patients should be based, and should be perceived as being based, solely on each patient's medical needs and the healthcare professional's medical knowledge and experience. As noted in Circular 54, Medical Representatives (MRs) play a critical role in providing information to physicians regarding new therapies and collecting real-world evidence of patient experiences using those medicines. As such, it is imperative that any new regulations concerning MRs do not stifle legitimate interactions between MRs and other health care professionals that serve to improve patient care.

创新医药行业坚信，医疗专业人员对患者的护理应当完全基于且应当被视为完全基于每名患者的医疗需要以及医疗专业人员的医学知识和经验。如第 54 号公告所述，医药代表的作用十分重要，他们负责向临床医生介绍新药知识，听取新药临床使用中的意见。因此，须确保关于医药代表的任何新法规不会阻碍医药代表与其他医疗专业人员之间旨在改善患者护理的正当互动。

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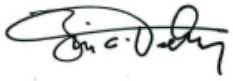
We are grateful for the opportunity to submit comments on these important policies. In light of the short comment period, we would propose that industry meet with CFDA and the other relevant Ministries to discuss these points and to address any questions that you may have.

我们非常感谢有此机会就该等重要政策提供意见。由于时间比较仓促，我们提议由行业机构与贵局及其他相关部委召开会议讨论该等事项及解决贵局可能提出的任何问题。



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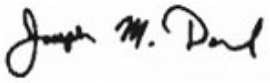

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