To: Chinese Food and Drug Administration (CFDA)
From: Initiative for Medicines, Access and Knowledge (I-MAK)
Re: Submission regarding 'Measures of Implementing Test Data Protection on Pharmaceuticals'
Date: May 30, 2018

The Initiative for Medicines, Access and Knowledge (I-MAK) is a team of lawyers, pharmaceutical scientists and health experts who are working to ensure people get the lifesaving medicine they need to survive and lead healthy lives. We founded I-MAK in 2006 to prevent unmerited pharmaceutical patents from blocking affordable access to lifesaving medicines. We believe that unmerited patents should not be permitted to prevent legitimate competition.

Over the past decade, we have successfully challenged unmerited patents in several countries around the world. We currently work with a local law firm in China to file third-party observations and invalidation actions against unmerited patents on hepatitis C drugs in China. Our patent challenges in China have helped to remove patents that could prevent local generic companies from manufacturing medicines.

We welcome the opportunity to provide our perspectives and analysis on the proposed changes to China's data protection law, as well as some suggestions in light of our analysis for the Chinese Food and Drug Administration's consideration.

I. The impact of data exclusivity upon access to affordable medicines and economic development

The original negotiations of the World Trade Organization's TRIPS Agreement specifically did not mandate exclusive rights over test data. In particular, Article 39.3 of TRIPS provides countries with the flexibility to not provide exclusive rights over test data, and instead only requires countries to protect data from unauthorized disclosure as well as avoiding fraudulent use of test data.

Nevertheless, multinational pharmaceutical companies have focused on introducing or expanding data exclusivity regimes because it confers a guaranteed monopoly when a company registers a new drug, whether or not the drug meets minimum patentability criteria in a particular jurisdiction. Multinational drug companies not only seek to introduce such rules, but also aggressively enforce data exclusivity to prevent governments from taking steps to induce competition when needed to ensure affordability. Competition is one proven method to reduce medicine prices in a sustainable manner. Monopolies, whether backed by patent protection or through enforcement of data exclusivity, prevents competition and thus affordable medicine prices. Moreover, where a medicine may not deserve patent protection, allowing data exclusivity could unnecessarily block generic competition.

By aggressively seeking to enforce data exclusivity, pharmaceutical companies prevent drug regulatory authorities from approving low-cost generic versions of medicines until data exclusivity expires. Such rules convert drug regulatory authorities from focusing upon ensuring the safety and efficacy of new medicines to enforcing monopolies on behalf of drug companies. These rules also enable companies to hold governments liable if such companies assert that data exclusivity is not being fully enforced.

As an example, in 2017, Gilead Sciences, a U.S. pharmaceutical company, threatened a lawsuit (through an investor-state dispute settlement procedure) against the Government of Ukraine for over 800 million US dollars because the company believed the government was not enforcing its 'right' to data exclusivity. In particular, the company disagreed with a court decision in Ukraine to uphold the registration of a generic

version of the drug sofosbuvir – which is used to treat Hepatitis C.[1] Due to concerns with the lawsuit, the Government withdrew the generic registration of sofosbuvir, despite the high burden of Hepatitis C in the country and the high prices charged for the medicine, and despite the fact that the patent applications filed by Gilead Sciences for sofosbuvir were rejected for not meeting patentability standards for novelty and inventiveness. Ultimately, Gilead used data exclusivity as a means to assert control over the market when otherwise it would not have had legal cause to do so.

Enforcement of data exclusivity can exert a tremendous financial burden on governments, other payers, and upon households. A prior study in Jordan, looking at only a very small subset of medicines, found in 2006, less than 5 years after Jordan introduced data exclusivity under the US-Jordan free trade agreement, that the additional cost of just data exclusivity (upon examination of 80 medicines) was over 20 million USD, with particular medicines needed to provide treatment for cardiovascular disease and diabetes costing anywhere from two to six times more in Jordan than in neighboring countries due solely to data exclusivity.[2] In other countries, such as Guatemala, data exclusivity rules, introduced through the US-Central American Free Trade Agreement, resulted in significant delays that prevented entry of generic medicines into Guatemala. In fact, the delay in generic entry was so lengthy that low-cost versions of the medicines entered the US pharmaceutical market before generic entry in Guatemala.[3]

Does data exclusivity spur economic development?

One purported rationale for introducing data exclusivity, despite its harmful impact on medicine prices, is that data exclusivity can encourage additional foreign (and domestic) investment, which ultimately can contribute to economic development. Yet a statistical analysis of the relationship between levels of data exclusivity and investment found that 'there is no relationship between whether or not a country has data exclusivity, and the amount of investment in the country by the pharmaceutical industry.'[4]

Specific case studies have also borne out this finding. In Jordan, according to the aforementioned study, the introduction of data exclusivity in 2001 (as well as the prior introduction of TRIPS in 1995) did not result in additional foreign direct investment into Jordan except for companies expanding their 'scientific offices', which only engage in aggressive marketing of medicines and do nothing to contribute to economic development – whether to enhance research and development or manufacturing. By contrast Egypt, which did not introduce any intellectual property rules for medicines until 2005, attracted 223 million USD of investment (in particular for expanding the manufacturing of medicines) between 1995 and 2005. This was most likely due to the attractiveness of the domestic market which foreign investors wanted to exploit.[5] This may also be the case as it relates to China, where the willingness of multinational pharmaceutical companies to enter into licensing and technology transfer arrangements 'may be due to the very large scale of the Chinese market.'[6]

Canada, which has steadily expanded monopoly protections for medicines since 1988, including eight years of data exclusivity, has witnessed a decline in investments into research and development, especially by multinational drug companies. According to data from the Organization for Economic Co-operation and

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[1] https://www.kyivpost.com/business/company-sues-ukraine-bid-corner-hepatitis-c-drug-market.html
[2] https://policy-practice.oxfam.org.uk/publications/all-costs-no-benefits-how-trips-plus-intellectual-property-rules-in-the-us-jord-114080
[3] https://www.healthaffairs.org/doi/abs/10.1377/hlthaff.28.5.w957
[4] https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2259797
[5] https://policy-practice.oxfam.org.uk/publications/all-costs-no-benefits-how-trips-plus-intellectual-property-rules-in-the-us-jord-114080
[6] http://www.who.int/phi/publications/china_policies_promote_local_production_pharm/en/

Development, pharmaceutical research and development in Canada was slashed almost in half between 2000 and 2013, from approximately 620 million USD to 320 million USD.[7] This is in spite of the fact that previously, multinational pharmaceutical companies had promised to eventually invest the equivalent of 10 percent of pharmaceutical sales in Canada. Such a figure has not been achieved even once.

Finally, since data exclusivity prevents regulatory approval of a generic competitor, it is likely that local industry will delay investing in manufacturing, packaging and marketing of new drugs until the term of data exclusivity expires. This undermines the development of the local pharmaceutical industry, and puts the local industry at a disadvantage to regional or global competitors who have not introduced data exclusivity.

II. Analysis and of the proposed Regulation

I-MAK respectfully advises that countries are not legally required to introduce a data exclusivity regime – whether as a means to protect clinical trial data, or to provide an incentive for R&D investments. Nevertheless, our analysis below looks at measures that can be taken to minimize the negative public health impact of a data exclusivity regime (based upon the additional rules that the CFDA is proposing to introduce), and in particular to avoid providing multinational drug companies with excessive monopoly protection.

1. Types of products included in the data exclusivity framework

Article 3 (Subject matter) of Chapter II (Subject of the Protection) of the Draft Measures includes five different types of products for which a drug regulatory authority will be required to enforce data exclusivity on behalf of the originator company. The following looks at each category of medicines included in this Article:

- Innovative pharmaceutical products: The draft regulation includes 'innovative' pharmaceutical products without any additional definition of what such products includes or excludes. Most pharmaceutical companies define 'innovative' to include any modification to an existing product, no matter how trivial the actual modification or change. Preferably, an 'innovative' product, as defined under a data exclusivity regime, would require such a product to only include new chemical entities. Such a definition ensures that pharmaceutical companies do not use a data exclusivity regime to engage in the practice of 'ever-greening', or to seek to prolong the exclusivity period for an existing drug by making minor modifications, combining the drug (with another molecule) or changing the formulation or mode of delivery.

- Innovative biologic products for therapeutic use: Similarly, the draft regulation includes 'innovative' biologic products, without defining 'innovative' for the purposes of the draft measures. By failing to define 'innovative' as products that only contain 'new protein sequences or DNA that is not naturally occurring", such a measure invites pharmaceutical companies to utilize the proposed measure as a means to engage in 'ever-greening' practices by changing formulations and delivery mechanisms for an existing product to obtain further data exclusivity.

- Medicines for the treatment of orphan diseases: Orphan diseases are defined in the United States as those that affect fewer than 200,000 people. Orphan diseases, due to the small market size, may not necessarily be targeted by pharmaceutical companies since the potential returns are insufficient. Yet a range of incentives, in particular in the United States and Europe, have emerged to encourage investment in orphan disease research. I-MAK agrees that new incentives are needed to encourage investment in orphan disease

[7] https://secure.globeadvisor.com/servlet/ArticleNews/story/gam/20151030/RBMWHITECOATS

research, and also registration and production of such drugs. Yet providing an additional exclusivity for a multinational company is unlikely to encourage additional investment, since the market size will remain too small, while at the same time keeping such medicines out of reach of patients due to the high prices which emerge due to the monopoly period. Instead, I-MAK recommends that the government consider other measures, including up front push investments, tax credits, or other pull incentives that do not rely upon an additional exclusivity grant.

- Pediatric medicines: As with orphan diseases, pediatric medical needs are not targeted by pharmaceutical companies due to the lack of potential commercial returns. Providing an additional exclusivity for such medicines is also unlikely to encourage additional investment by pharmaceutical companies because of the lack of commercial potential. In fact, over the last fifteen years, other approaches have been introduced to encourage investment in pediatric medicines. In particular, companies have worked with public research agencies and donors, in particular through push incentives, to develop child-friendly formulations of needed medicines (for example to develop pediatric versions of HIV and AIDS medicines). Such efforts are often the basis for continuing improvements by other companies or research collaborations to make such medicines palatable and effective for children. Introducing an additional exclusive right for a pediatric medicine may discourage other research entities, whether companies or partnerships, to improve upon existing pediatric formulations. If such an exclusive right is to be introduced, it should only be granted if and when the company actually markets the pediatric version in China, and such additional term of exclusivity should be shortened due to company delays in registering and marketing the pediatric version.

- Medicine (generic medicines) of which (originator's patent) has been successfully challenged: Finally, the regulation provides data exclusivity to a generic competitor that has successfully challenged patent protection of the originator company. While I-MAK agrees with providing incentives for patent challenges, the use of data exclusivity as a reward for successfully challenging patents is both difficult to implement and unlikely to encourage patent challenges. Such a measure is difficult to introduce in part because there are often multiple challenges by third parties to patent exclusivity. Secondly, assuming a court agrees with such patent challenges, it will be difficult to award any one generic company with the right to exclusivity (since multiple companies may file a patent challenge). And rewarding the first company to file a challenge, as is the case in the United States, can be counterproductive since it can create a duopoly, with the branded and generic company seeking to limit competition through a negotiated settlement. Thirdly, data exclusivity is not necessarily relevant for generics companies unless such a company decides to fully repeat clinical trials, which is unethical since the results of such trials are already known. It is most likely, as has been the case historically, that such companies are likely to wait until such term of data exclusivity expires. Thus, while I-MAK believes that the government should introduce measures to both simplify and encourage patent oppositions, we do not think introduction of a term of data exclusivity is neither appropriate, sufficient nor necessary. Such measures could include ensuring the standard for patents is more stringent so that generics are encouraged to challenge patents. Additionally, a robust pre-grant patent opposition mechanism would incentivize generics as currently it is only an observation mechanism that vests too much discretion with the patent examiner. Finally, speedier approval of generic versions of medicine would both incentivize challenges and market competition, whereas data exclusivity will have the opposite effect.

2. *Duration of data exclusivity*:

   The duration of data exclusivity can have a significant impact upon the affordability of medicines. Irrespective of when the term of data exclusivity begins – for example whether at first registration worldwide or upon registration in the relevant country, it can create barriers to generic competition since it can create a monopoly even when a company fails to secure a patent, it can block the use of

compulsory licensing (during the patent term), or it run past the end of the patent term, thereby acting as a type of monopoly extension in addition to the term of patent protection.

The following is feedback on the term of data exclusivity provided under the proposed measures.

- Twelve year term of data exclusivity for biological medicines: The proposed term of data exclusivity for biologics medicine is extremely long, and would provide multinational patent holders with an 'effective monopoly period' that is longer than the average effective monopoly period under patent protection. While the United States currently provides twelve years of data exclusivity for biologics, the Obama Administration tried repeatedly to modify the twelve year term of protection to seven years, as such a modification, even though it leaves in place a seven year term of data exclusivity, would have saved the US billions of dollars over the ensuing decade.[8] In fact, another US government agency, the Federal Trade Commission, has previously recommended that the US provide zero years of data exclusivity for biological medicines[9].

- Terms of data exclusivity for pediatric drugs or orphan drugs: Article 6 proposes to provide six years of data exclusivity for pediatric drugs or orphan drugs. Article 7 allows for such data exclusivity to be applied independent of and in addition to other terms of data exclusivity for the same product. The term of data exclusivity for a pediatric drug is extremely lengthy and will be in addition to the original term provided for a new product, which a company could thereby manage to enable twelve or eighteen years of data exclusivity for the product. Similarly, the provision of six years of data exclusivity for an orphan drug is also lengthy and will arrest generic competition, and in the same manner as a pediatric formulation, could extend the overall term of protection to eighteen years or even twenty four years depending on the strategy employed by a pharmaceutical company.

  In the European Union and the United States, the current term of pediatric exclusivity is six months (or one year under certain conditions). The European Union is also conducting a year-long review to ascertain whether incentives provided to drug makers for orphan drugs are excessive (and in particular since such incentives enable drug makers to charge high prices).

- Incentives or restrictions that affect the term of data exclusivity: The proposed regulation introduces specific rules that can abridge or negate the term of data exclusivity. The following is an analysis of each of the proposed rules:

  - Start date of a term of data exclusivity in China: Under Article 5, the CFDA applies minimal requirements to encourage pharmaceutical firms to register their drugs in China after the first worldwide registration. To ensure drugs are registered as soon as possible in China, and to limit the duration of data exclusivity, the term of data exclusivity in China should begin on the date of the first registration worldwide, both to limit the impact of data exclusivity on competition, and also to ensure that firms register their drugs in China as soon as possible after the drug is first registered worldwide.

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[8] http://www.pewtrusts.org/en/research-and-analysis/fact-sheets/2017/09/policy-proposal-reducing-the-exclusivity-period-for-biological-products

[9] https://www.ftc.gov/sites/default/files/documents/reports/emerging-health-care-issues-follow-biologic-drug-competition-federal-trade-commission-report/p083901biologicsreport.pdf

- Performance of clinical trials in China: The proposed measures include the laudable goal of encouraging firms to conduct clinical trials in China, and to use such data when applying for regulatory approval. While I-MAK agrees with the goal, we do not think that a term of data exclusivity needs to be provided to ensure firms conduct clinical trials in China, especially since such a provision is enormously costly for payers and households if and when such a drug is approved. Instead, I-MAK encourages the government to provide particular incentives, through well targeted push funding, to ensure pharmaceutical firms conduct clinical trials in China, and to ensure that in exchange for such support, firms apply for regulatory approval with such data to the CDA within a short period of the first worldwide application for regulatory approval.

3. Safeguards related to provision of a term of data exclusivity:

Given the considerable negative impacts that a term of data exclusivity may have upon public health and the economic development of local manufacturers, it is critical that any provision of data exclusivity can be managed to avoid abuse or undermining the public interest. Below is an analysis of the safeguards included in the proposed measures:

- Publication and challenges to a term of data exclusivity: It is welcome under Article 9 that after a registration application is registered with the CFDA, the agency publishes the application for 30 days. Under Article 15, the 'right holder' of the test data is allowed to appeal a decision made by the CFDA through relevant legal measures. Yet under both Article 9 and Article 15, the CFDA does not introduce any opportunity for a petitioner, whether a competitor or a public interest party, to submit an application to either avoid or shorten a term of data exclusivity (although we acknowledge there is at least a procedure for revocation of data exclusivity). An opposition procedure would ensure the CFDA, to the extent that it must provide a term of data exclusivity, is able to take into account all legal and public interest arguments before issuing a final decision.

- Exceptions to data exclusivity: Article 12 creates exceptions to the issuance of a term of data exclusivity, and in particular Article 12 (a) includes a 'public interest' ground. Yet Article 12 does not enable the CFDA to rely upon the relevant clinical trial data to approve a generic version of a medicine. Instead the proposed measure only concerns disclosure of the data by the CFDA, which is not relevant to introducing a generic version of a pharmaceutical product on the market. It would be preferred for any exceptions included under Article 12 to permit the CFDA to approve a generic version of a medicine, and to include explicit grounds under which a public interest exception could be applied (while leaving room for unforeseen circumstances), including in particular an exception to address unaffordable medicine prices.

- Revocation of data exclusivity: Articles 17 and 18 provide limited grounds for revocation of data exclusivity, and enable competitors to register their produce. While I-MAK welcomes measures that can enable revocation of a term of data exclusivity, we do not agree with limiting revocation to only one ground (namely that the relevant medicine is not marketed within one year of registration in China). I-MAK would encourage the CFDA to consider additional grounds for revocation, including evidence that the prices charges for the originator product lead to little or no consumption of the medicine. Even though such a medicine may be registered on the market locally, high prices that leave people unable to gain access to the medicine. I-MAK would recommend expanding the grounds for revocation under the proposed Articles.

III. Conclusion and Recommendations

Finding an appropriate balance between promoting research and development and ensuring access to the end result of such research and development is difficult. We support rewarding companies for developing novel products, but are concerned that the proposed measures included in the draft regulation provides excessive incentives to pharmaceutical companies, unnecessarily extends monopolies, delay generic competition and ultimately reduce access to affordable medicines. The Chinese government has recently signaled an interest in promoting competition in the pharmaceutical sector, including a joint request with the South African government to discuss competition law and policy as it relates to the pharmaceutical sector at the WTO TRIPS Council.[10] Yet data exclusivity enables pharmaceutical companies to engage in practices that not only delay competition but can also enable anti-competitive conduct through ever-greening practices.

Data exclusivity is not mandated under the WTO TRIPS Agreement. We believe China has no legal obligation to introduce additional data exclusivity protections. Not only would such an additional term of data exclusivity harm consumers, it would have a detrimental impact on the growth of local manufacturing capability, do nothing to encourage additional foreign direct investment or to spur innovation for pediatrics or orphan drugs. If the CFDA does move ahead with the proposed regulation and does choose to introduce additional data exclusivity protections, I-MAK recommends the following as it relates to the proposed regulation:

1. The proposed term of data exclusivity for biologics is excessive. No term of data exclusivity should be provided for biologics, or such term should be shortened as much as possible and should not exceed the six year term currently provided under China's existing regulations.

2. Data exclusivity should be provided for small molecule products which only include a new chemical entity. For biological products, it should only be provided for products that are based on new protein sequences or DNA that are not naturally occurring. Formulations and other changes to the core ingredient or biologic should not warrant further exclusivity.

3. The CFDA should provide no term of data exclusivity for orphan drugs or pediatric formulations of products. No such term of data exclusivity that may be provided for such products should be in addition to the original grant of data exclusivity for a product. CFDA should define a maximum term of data exclusivity to avoid companies from seeking consecutive terms of data exclusivity under multiple grounds.

4. Generics companies that successfully challenge patents that block generic competition should not be rewarded with a term of data exclusivity. However, I-MAK does support other measures that can encourage oppositions to patents, including a more robust pre-grant opposition. Such a mechanism should allow the patent challenger a full hearing with the patent examiner rather than the current observation practice which leaves the final decision at the Examiner's discretion.

5. The term of data exclusivity in China should commence at the same time as the first worldwide registration of the relevant product.

6. Companies should be provided no benefit (for data exclusivity) for having conducted clinical trials in China. I-MAK does recognize that encouraging clinical trials in China is an important policy objective,

[10] http://www.keionline.org/wp-content/uploads/2018/05/W643.pdf

but would suggest that other incentives, such as public funding of trials, would be preferable to providing companies with additional monopoly protection for new medicines.

7. The CFDA should provide a mechanism to challenge a grant of data exclusivity during the thirty day period after a new drug application is submitted to the CFDA and published. In particular, public interest grounds should be available to oppose a grant of data exclusivity.

8. I-MAK supports a public interest exception to a grant of data exclusivity, yet would recommend that any such application of a public interest exception should allow the CFDA to rely upon such data to approve a generic version of the relevant product. In addition, the CFDA should provide concrete grounds to use the public interest exception, while not limiting the actual grounds that a petitioner my employ.

9. I-MAK welcomes the revocation mechanism for data exclusivity, yet would recommend that additional grounds for revocation, including unaffordability of the end product, should be available to any third party petitioner.