Responding to China's New Human Genetic Resource Regulation

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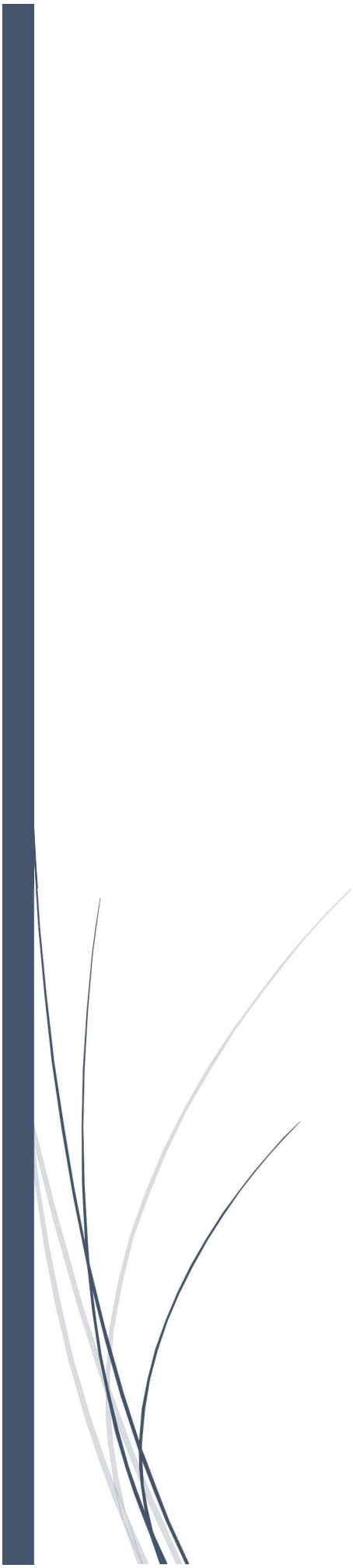

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Disclaimer

The author conducted this study as part of the program of professional education at the Frank Batten School of Leadership and Public Policy, University of Virginia. This paper is submitted in partial fulfillment of the course requirements for the Master of Public Policy degree. The judgments and conclusions are solely those of the author, and are not necessarily endorsed by the Batten School, by the University of Virginia, or by any other agency.

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Honor Statement

On my Honor as a student, I have neither given nor received unauthorized aid on this assignment.

Ruiling Tu

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Executive Summary

The Ministry of Science and Technology of China recently published a new regulation regarding foreign entities' access to Chinese human genetic resources (HGR). Similar to the interim regulation, the new rule requires foreign companies to establish international collaboration with a Chinese entity before accessing HGR. It further requires foreign entities to allow the Chinese party to become substantially involved with the project and to share its data and HGR informed result with the Chinese partner. The regulation established a record-filing system to reduce the approval time for companies accessing HGR for clinical trials. Nevertheless, the inability to develop an international partnership and potential IP security risks could prevent Biotechnology Innovation Organization members' research and development efforts in China.

In response, BIO should leverage its industry knowledge, research abilities, and representative power to lower the barrier to entry of the Chinese market for its members. This analysis examines five alternatives, including:

- Alternative I: The status quo
- Alternative II: Addressing the new regulation and strategic responses during BIO Conference's breakaway session
- Alternative III: Creating an ethics code and local BIO network in China to communicate the new regulation and ethical standards and facilitate behavioral changes
- Alternative IV: Establishing a partnership pool for BIO members
- Alternative V: Initiating partnership with China National Center for Biotechnology Development

Each alternative is assessed with five criteria: 1) the number of members affected by each option (membership reach), 2) monetary and non-monetary cost associated with each policy, 3) cost per number of new HGR access application (cost-effectiveness), 4) IP security, and 5) political feasibility.

As a result, this analysis recommends BIO to adopt Alternatives III and IV, given that they are highly complementary in nature. Both alternatives could reach a broad audience. In terms of cost-effectiveness, even though Alternative IV is less cost-effective than others, it is still under BIO's willingness to pay. The unique value it offers to biotechnology startups could also justify its adoption. Besides, Alternative IV alone could be politically unfeasible if the government officials in China perceive it as a way for foreign companies to bypass regulations and exploit Chinese HGR. Thus, by adopting Alternative III, BIO should incorporate certified Chinese partners to its local network, promoting collaboration for both Chinese and international companies.

For IP security, Alternative III provides an ethics code that members could always refer t. However, BIO members with limited business and legal resources could still find it hard to initiate collaboration. Therefore, BIO should conduct due diligence to help its members identify and screen potential Chinese associates. Startups could then reach out to those Chinese entities through BIO and utilize the collaborative framework that it has already initiated.

In light of the recent pandemic, BIO should prioritize its implementation on assisting members that are developing vaccines and medications for COVID-19, such as Inovio. It will be crucial for these companies to access blood samples from hospitals in China and begin clinical trials.

Problem Statement

In 2016, Wuxi PharmaTech exported 5156 blood samples labeled as "Canine blood" abroad. After investigation, the "Canine blood" turned out to be human blood samples collected from Chinese patients. Wuxi PharmaTech was later fined, required to destroy illegally obtained genetic samples, and demanded to halt all international collaboration and export pertaining human genetic resources (Ministry of Science and Technology of the PRC, 2016).

Recent illegal collection, transaction, and export of genetic resources in China violated the regulatory framework set by the Interim Measures for Management of Human Genetic Resources (HGR) since 1998. The sensitive U.S.- China relation and escalating controversy around data sharing facilitated the publication of Regulation on the Administration of Human Genetic Resources, which became effective on July 1st, 2019**.** However, **the lack of preparedness among U.S. pharmaceutical companies and research institutions poses new challenges to their ability to conduct clinical trials and protect intellectual property in China.**

Background

The New Regulatory Framework for Human Genetic Resources

Similar to the Interim Measures for Management of HGR in 1998, the new regulation pertains to sampling, collection, research, development, trading, export, and exit of HGR in China. It continues to restrict foreign entities from collecting or using HGR in China on their own unless they enter into an international collaboration with a Chinese entity (e.g., scientific institute, university, medical organization, or corporation). However, these requirements did not apply to drug and medical device regulation in China for many years. It was not until 2015, when China's Ministry of Science and Technology (MOST) issued a guideline on HGR, did that expanded the applicability of the Interim to cover clinical trials that support drug and medical device marketing applications. Since then, MOST's Office of Human Genetic Resources Administration (OHGRA) oversees HGR resources in China (State Council of PRC, 2019).

Expanded Definitions

The new regulation divides the definition of HGR into two components: the biological samples themselves (HGR Materials"), and the associated data (HGR Information). HGR Materials refer to genetic materials, such as organs, tissues, or cells, which contain the human genome, genes, and their products. HGR information refers to genetic information or data generated by using the HGR materials.

The regulation also expands the definition of "Foreign Parties" by incorporating OHGRA's broad interpretation that HGR requirements apply to both onshore and offshore entities established by foreign entities and individuals. Furthermore, the regulation adds the concept of "actual control" and deems foreign individuals and entities found or controlled by foreign entities or individuals to be "Foreign Parties." In other words, not only all foreign-invested enterprises in China but also domestic companies actually controlled by foreign shareholders could be considered "Foreign Parties" under the new regulation (State Council of PRC, 2019).

Broader Regulation of Sampling and Biobanking

The new regulation covers not only the use and provision of HGR to foreign parties through international collaboration but also specific requirements on the areas of sampling and biobanking. Foreign parties cannot independently sample or biobank any China HGR in China. Approvals from the OHGRA are required for similar activities conducted by Chinese parties. Although the new regulation emphasized informed consent by requiring the sampling party to obtain the written consent from the provider of HGR with a full, complete, and non-misleading notice (State Council of PRC, 2019).

New Record-filing Procedure for Clinical Trials in China

One of the most significant changes is the establishment of a record-filing procedure for international collaborations on clinical trials intended to support the marketing approval of drugs and devices in China that do not transfer HGR Materials abroad. The record-filling procedure could reduce the wait time for qualifying trials, permitting them to start after the filling is complete, instead of waiting for an affirmative approval from OHGRA. To comply, the parties must submit, to the OHGRA, information as to the types, quantities, and purposes of the HGR used prior to the commencement of the trials. However, the regulation does not appear to apply the record-filing procedure to investigator-led trials for research and development. It also requires that international collaborations receive ethics approvals from the respective country/region of both foreign and Chinese parties. This dual ethics committee approval requirement could cause a delay.

The provision of HGR Materials and HGR information to foreign parties is subject to different forms of review and pre-approval under the regulation. In addition to record filling, the provision of data to Foreign Parties or permitting uses of data by Foreign Parties requires submission of that corresponding data's copy to the OHGRA, and potentially a security assessment if such provision or permitting use could impact the public health, national security or public interest of China. The regulation did not specify how the requirement will work in practice. Furthermore, MOST requires an export certificate before any exportation of HGR materials, which is separate from the master approval for international collaborations. The regulation states that both parties may contractually agree on the rights to use, transfer and share results under international collaborations.

Expanded Enforcement Powers for MOST

Lastly, the regulation officially enhances the authority of MOST and its provincial counterparts to conduct on-site inspections, question individuals from companies and the institutions, review and copy the relevant documentation and seize HGR (whether data or samples). Increased penalties for non-compliance, including warnings, disgorgement of illegal gains, confiscation of illegal HGR, fines up to about 10 million RMB (about 1,450,000 USD) or even more (5-10 times of illegal gains), and temporary (1-5 years) or permanent debarment of companies, institutions and responsible persons from further HGR projects.

Importance of HGR in Clinical Researches

Human genetic resources are crucial to researchers and pharmaceutical companies. In new drug developments, variations in the human genome have meaningful implications on drug's efficacy and safety. Genetic differences can affect the rate of disease occurrence, the risk of disease progression, the drug most likely to provide benefit, and the likelihood of drug toxicity. Therefore, the study of drug exposure and response as related to variations in DNA and RNA characteristics depends on the collection and use of biological samples to generate data. An essential prerequisite to the successful use of genetic information in drug development is the appropriate collection and storage of DNA samples from a large enough number of participants in clinical trials (FDA, 2013). Some countries (UK, Spain, Estonia) establish national genomic biobanks (DNA banks) to research new methods of prevention, diagnosis, and treatment of genetic and lifestyle diseases and on pharmacogenetic research (Sak et al., 2012). Besides, many investigators, pharmaceutical companies, and institutions are collecting and storing biological specimens, clinical data, and genetic information in local and regional repositories.

While genetic information is crucial to research and development in health care, its usage generates ethical concerns. According to McGuire et al. (2011), most genetic and genomic research projects share several standard features that challenge the established norms of informed consent. Based on the ethical principle of respect for persons, the Belmont Report claims that the goal of informed consent is to ensure that subjects are aware of the risks and potential benefits and make a voluntary decision about participating in the research (The Belmont Report, 1979). Due to unspecified future use of genetic samples, participants are uncertain about what they have consented to. The stability of DNA information over time means that the privacy risk associated with the storage of genetic sample persist throughout the lifetime. Participants also have limited control over downstream access, use, and disclosure.

China's New HGR Regulation's Potential Impact on the U.S.

Because the regulation is relatively new, evidence-based analysis of its impact on the U.S. health care industry is lacking. However, this study offers four projections, given the results of previous regulations and similar policy implementation in other countries: a decline in approval rate for HGR access, a decrease in research innovation, an increase in intellectual property disputes, and challenges to public health.

Given the expanded definition for foreign parties, more researchers and pharmaceutical companies will be subjected to either international collaboration with Chinese parties or restriction on access to Chinese HGR. Requirements on ethics approval and punitive enforcement will increase the opportunity cost of obtaining drug marketing rights in China. The additional economic and legal effort of establishing a collaborative agreement with Chinese parties poses new burdens on U.S. researchers and companies. Despite these new barriers to the Chinese markets, it is unlikely for U.S. pharmaceutical companies to abandon the massive patient population in China to avoid complying with OHGRA. Of the 2385 projects approved by OHGRA in 2018, 85.7% and 7.8% were clinical trials intended to support the marketing approval of drugs and medical devices, respectively.

Nevertheless, the approval rate for HGR is expected to decline. Research suggests that the approval rate for HGR use declined from 70% in 2015 to 57% in 2017 after MOST tightened previous regulations on HCR (Cao et al., 2017). The new rule significantly expanded on its 2015 counterpart, raising the challenge for foreign parties to comply during a limited timeframe. Therefore, the approval rate for HCR usage should drop below 57% to approximately the 50% level.

Restrictions on collecting and storing HGR also inhibits innovation in drug developments. Limited access to HGR naturally reduces research opportunities that could shed light on variations in the human genome, which is central to modern pharmacokinetics. Information about the effect of medical compounds on biomarkers can provide proof-of-concept for drug development, improving the success rate of later trials (FDA, 2013). Thus, restricted usage of HGR also impedes innovation among pharmaceutical startups relying on best practices in R&D to reduce operating costs.

On the other hand, the creation of a record-filling system for clinical trials that do not involve exporting Chinese HGR will significantly reduce wait time for trial initiation. Companies and researchers no longer have to wait for government approval to begin clinical trials, as long as they can provide information on the category, amount, and usage of HGR. This advancement might not facilitate biotechnology innovation, but it will undoubtedly allow foreign companies to gain marketing rights more quickly in China.

Most importantly, because access to Chinese HGR resources is crucial to clinical trial research, the regulation, to some extent, forces foreign entities to collaborate with Chinese parties. This dynamic is the most concerning change rendered by this regulation. Apart from being required to ensure substantive involvement and full participation of Chinese parties, researchers and pharmaceutical companies should also share records and data with their partners. The new regulation allowed parties to contractually agree on their own as to how to dispose of their intellectual property rights provided under the Chinese Patent Law. However, the joint ownership requirement is still broad and unclear. The expected increase in collaboration with Chinese parties, coupled with China's problematic intellectual property records, would undoubtedly lead to more disputes over the usage of HGR informed results (Wright, 2018).

Lastly, restricting HGR sharing with foreign parties could pose challenges to global health. In February 2007, Indonesia stopped sharing avian influenza samples collected in its territory with the WHO. The moratorium rose from the Indonesian government's concern with how pharmaceutical companies in the developed world uses virus samples from India for vaccine development without compensation or any arrangement that would provide Indonesia affordable access to the vaccines developed. Thailand raised similar issues at the WHO's Executive Board meeting in January 2007 (American Society of International Law, 2007). Because Thailand did not gain access to developed vaccines after sharing genetic samples with the WHO, developed countries with vaccines access are better prepared for pandemics. If countries such as China poses stricter regulation on sharing valuable information with the international community to track virus development, it would be harder for researchers in the U.S. to combat global health challenges domestically. During the recent COVID-19 outbreak, hospitals in Shanghai have been utilizing blood samples of recovered patients to develop immune plasma therapy. While this method has attracted wide attention, including that of the WHO, sharing these valuable blood samples with the United States and other European countries may face new regulatory challenges.

Literature Review

Existing collaboration paradigm with Chinese entities

An accelerating shift in China's R&D landscape is already leading to increased R&D capabilities of local players, more competition for innovative programs, and larger uncertainties for the regulation of clinical studies of overseas compounds. They are collectively challenging multinational pharmaceutical companies' traditional, global-centric R&D models and creating a strong impetus for change. In response, multiple companies have established local research centers. Novo Nordisk occupies a $10 million research and development center at Shangdi Park in Beijing. Roche opened its fifth R&D center in China, stepping into traditional Chinese medicine research. The center website lists collaboration with Chinese academic institutes, biotech companies, and contract research organizations, claiming to be the *only* pharmaceutical company in China capable of designing, conducting, and analyzing clinical studies to meet the registration needs (Roche, 2019). This strategy would leverage increased local R&D capabilities to accelerate the development of therapies catered to Chinese patients, and in the longer-term, global products. However, this strategy requires significant investments and extended lengths of time to generate the desired impact.

In a report published by Deloitte (2016), authors encourage multinational companies to build alternate R&D models through partnership, which not only mitigate traditional development risk but can also leverage local efficiencies to add value. The document further identified three partnership models: co-development, in/out-licensing, and contract research organizations (CROs).

- Co-development: A co-development model is a major venue to realize benefits. It is frequently associated with the development of a particular therapeutic area portfolio that addresses a significant need in China. It also can be strategically developed to capitalize on local sales and other operational efficiencies. Despite the considerable upside, these partnerships tend to last the entire duration of the product lifecycle and require a substantial commitment from both parties in the face of uncertainties.
- In/out-licensing: To commercialize certain products locally, pharmaceutical companies can out-license new drugs to Chinese companies. This strategy is usually more suited for those with a lower expected value from a go-it-alone R&D and commercialization strategy.
- Contract research organizations: CROs provide the benefits of a local R&D partnership but cannot generally support commercialization. They are best suited for companies who see the benefits of a localized R&D process yet want to maintain control over their assets throughout the product lifecycle.

However, even with strategic collaboration, foreign entities' violation of China's regulatory framework suggests a lack of proper understanding and response to previous rules on HGR administration. A paper published in Nature was taken down after China claimed that the electronic genetic data was shared by Huashan Hospital illegally (Kretzschmar et al., 2015). Global pharmaceutical giant AstraZeneca, which has a research center in Shanghai, was caught transferring samples — used to create diagnostic tests for predisposition to breast cancer — to two smaller Chinese companies, Amoy Diagnostics in Xiamen and Kunhao Ruicheng in Beijing. AstraZeneca was authorized to collect the samples, but the company says it did not know that it needed permission to transfer the material to another party in China (Nature, 2018).

Figure 1: Local R&D partnership models comparison

Source: Monitor Deloitte Analysis (2016)

Intellectual property rights and ethics regarding HGR

Intellectual Property

Human genetic resources are increasingly considered as ordinary commercial goods, but their value and utility go beyond the immediate and straightforward private profit. Privacy and property rights over HGR makes them a sensitive subject for export and sharing. Typically, commercial use does not focus on the material itself but rather on the genetic information HGR contains. Informational goods are then usually subject to intellectual property rights. However, in the biological and life science domains, property rights can have a negative influence on commercializing genetic material and derivative products. Litigations in the United States and Europe reflect this dynamic. In particular, these lawsuits have revived the debate over private ownership and control over genes and genetic information.

Because the commercialization of biospecimens and HGR is still a legal grey area, the National Institute of Health shared best practices regarding intellectual property over biospecimens. Generally, biospecimen resource staff, as custodians of biospecimens, will not be considered a priori inventors under patent law for inventions made using materials distributed by the biospecimen resource. One whose sole contribution to an invention consists of the routine collection, handling, storage, and disbursement of biospecimens might not rise to the level of "inventor." Inventorship is determined by patent law and is considered on a case-by-case basis by legal personnel.

Furthermore, biospecimen resources have no inherent rights to the future intellectual property of end-users, such as reach-through rights to inventions made by investigators using samples obtained from the biospecimen resource. When IP resulting from biospecimen research is exclusively licensed, a research use license should be retained that allows nonprofit and Government research use and ensures access to resources and data for research and educational purposes. NIH

recommends that research data and research resources obtained using biospecimens should be made available to the research community to the greatest extent possible, consistent with, as applicable, the NIH Data Sharing Policy, the NIH Genomic Data Sharing Policy, other applicable NIH sharing policies, and the NIH Research Tools Policy. To promote future biomedical research, researchers should retain data and resources developed with biospecimens only as long as necessary for legitimate and imminent research purposes (National Institute of Health, 2016). These recommendations are in line with the new HGR regulation's requirement for foreign entities to disclose their data and findings with the Chinese party.

Ethics

The ethics committee overseeing the approval of HGR access application in China is governed by Human Ethics Review Methods for Biomedical Research (2016). The document indicates that essential criteria for approving a research project include 1) upholding the social value of bioethics, 2) scientific research proposal, 3) fair selection of subjects, 4) reasonable risk-benefit ratio, 5) informed consent, 6) respect for subjects' rights, and 7) compliance with scientific research integrity. These criteria are similar to bioethics standards in the United States and Europe, so foreign companies in China should not be surprised by these principles.

For privacy and confidentiality protections, NIH recommends researcher entities to establish clear policies for protecting the confidentiality of identifiable information. These policies may include data encryption, coding, developing limited access or varying levels of access to data by biospecimen resource employees, and the use of nondisclosure agreements. With regards to informed consent, NCI (National Cancer Institute) recommends seeking the informed consent of research participants who provide biospecimens and associated data whenever such consent is required by regulation, and also when consent is ethically appropriate and can practically be obtained. Respect for individuals who have provided data or biospecimens for research is of paramount importance; therefore, their preferences should be considered when deciding whether informed consent should be sought or waived. Some individuals may prefer to be actively engaged in future research, while others may be opposed to being re-contacted to consent for additional investigation or future uses. The biospecimen resource should have transparent policies concerning the informed consent process, including when consent is sought from human research participants or the next of kin of deceased biospecimen contributors. Electronic consent (e-consent) or mobile consent strategies may streamline the consent process and improve participant understanding of consent information.

Problems and Best Practices to Protect Intellectual Property Rights within China

IP enforcement, a significant concern for innovative pharmaceutical and biotech businesses, has improved profoundly, thanks in large part to the continued effort of China's central government to comply with its obligations as a member of the World Trade Organization (WTO). As Chinese pharmaceutical and biotech industries move up the value chain and begin to target higher-end drug products as well as more sophisticated and complex pharma and biotech contract research services, more effective IP protection and enforcement increase the competitiveness of these domestic industries. The general scope of patent protection offered under Chinese patent law is similar to what is typically provided under the United States or European patent law. Article 11 of the

Chinese Patent Law prohibits unauthorized making, use, offer for sale, sale, or import of a patented product. The provision also prohibits the unauthorized use of the patented process for production or business purposes.

There are, however, exemptions to the patent rights, some of which are more pertinent to biotech and drug patents. First, the Chinese patent law provides prior use rights. If one has already made an identical product, used an identical process or made necessary preparations for its making or using before the filing date of a patent, the person having such prior use may continue to make or use the patented invention, albeit such future use must be restricted to the scope of the prior use. Second, any person may use a patented invention solely for scientific research and experimentation. It is not entirely clear, however, what would constitute pure scientific research and experimentation under the Chinese patent law. The Supreme People's Court has interpreted Article 63(4) as providing exemption to research and experiments where the patented product or process is used to investigate, validate, or improve the patent itself. This exemption also applies to situations where one makes or uses the licensed product or process in clinical trials during drug regulatory approval. The Chinese courts will likely take into consideration these proposed interpretations to allow some level of exemption for clinical trial activities in connection with the regulatory approval of pharmaceutical products. Because the above arguments have not been formally approved, however, it remains to be seen whether protections comparable in scope to those offered by the United States and Europe will be provided. In the United States, an activity is exempt from infringement if it is reasonably related to the development and submission of information under a federal law regulating drugs or biological products. In Europe, a similar safe harbor is provided for activities such as clinical trials and other necessary studies, although the scope is less well defined.

Overseas pharmaceutical and biotech firms have a lot to gain or lose from the rapid growth and modernization of China's pharmaceutical and biotech industries and markets. Practical and effective IP protection and enforcement strategies should be an integrated part of the overall China strategy.

In a report presented to the U.S.- China Economic and Security Review Commission (Gryphon Scientific and Rhodium Group, 2019), the authors examined China's access to U.S.'s HGR resource and biotechnology innovations. They shared concerns about the Chinese government and companies' infringement on intellectual property rights. Apart from recommending federal actions such as reviewing inbound investments, the document urges companies to follow IPR guidance from NIH and BIS (Bureau of Industry and Security). Although these guidelines are still under development, The U.S. - China Business Council (2020) published best practices for IP protection in China, which include:

- Craft and Implement a Corporate IP Strategy in China

  Conduct an initial audit of the company's China operations to determine IP assets, IP risks, and assign appropriate levels of protection to those assets based on the risk of infringement. Review the company's internal IP controls to determine whether they provide sufficient protection. Classify IP-relevant information according to its level of sensitivity, and integrate that classification into information control and operational procedures. Make IP

protection a core responsibility of the entire China management team, not merely a function of the legal or brand protection teams, and adjust internal information flows and reporting structures to reflect those responsibilities. Take clear steps to document company IP protection policies and efforts as such documentation can play an important part in infringement disputes, particularly in areas like trade secrets.

- Understand the IP Legal Landscape

  Review not only China's core IP laws and regulations, such as the Patent, Trademark, Copyright, and Anti-Unfair Competition laws, but the growing body of other laws and regulations that impact China's IP environment, including (but not limited to) the Corporate Income Tax, Antimonopoly, and Labor Contract laws. Ensure that the legal protection the company is seeking for its IP in China is available. For example, many software products that are eligible for patent protection in other jurisdictions are not in China, and are more commonly protected as copyrighted products.

- Adopt Preventive Measures to Protect IP

  Negotiate clauses in technology transfer and licensing contracts to address company needs on royalty rates and ownership of improvements. Companies should recognize differences in how China's legal framework treats ownership of improvements and liability, and that negotiated royalty rates in China are frequently lower than in other markets. Compartmentalize critical steps in the design and production processes for IP-intensive products—and the equipment used to manufacture these products—to limit the likelihood that any one employee has access to all the information needed to copy IP. Consider tracking data flows and employee file transfers (both paper and electronic), engage internal stakeholders such as the human resources department in early conversations about developing and implementing policies that monitor employees in this manner. Run background checks on key hires to check for any IP-related "red flags," and include noncompete and nondisclosure agreements in employee contracts.

- Confront IP Infringement When Discovered

  Send cease-and-desist (C&D) letters to infringers. C&D letters can be a cost-effective way to stop infringement in some cases, especially those involving small infringers. Conduct a careful review of internal documents that can demonstrate infringement, including physical and electronic evidence. Companies should be aware that documentary evidence (as opposed to oral testimony or non-official documents such as marketing materials) carries more weight with Chinese officials.Weigh various channels available to halt infringement in China, including administrative, civil, and criminal channels. In determining a course of action, companies should consider company resources, timelines for action, and the strengths and weaknesses of each channel.

Solutions beyond bilateral relations: the possibility of an international body for HGR access

The sharing of biological samples and genetic data across countries is dependent on international agreements and specific national policies. The World Health Organization passed two resolutions to facilitate viral sample sharing of influenza strains to promote preparedness activities, development of vaccines, and surveillance efforts. The Convention on Biodiversity passed the Nagoya Protocol, which calls for the sharing of genetic data of organisms in a manner that promotes equitable and fair benefit-sharing.

Existing literature and data do not suggest that the Nagoya Protocol has led to a positive impact on sharing genetic resources with foreign parties. However, multiple studies have identified a central defect of the protocol. Even before the NP, some countries, such as Brazil, had a mechanism to permit the use of biological resources. After the NP came into force in 2014, sets of instructions were needed on how to comply with CBD requirements. Nations, whether they ratified the NP or not, needed legislation or regulations stipulating the conditions of access. Therefore, there could be 196 sets of different legislation, 1 for each NP-ratifying country, and a handful of best practices and codes of conduct. The unharmonized law created a severe burden for researchers to comply with different regulations in each country (Watanabe, 2017). Given these effects, many scholars argue against a multilateral platform for HGR sharing. Schroeder et al. (2006) argue that CBD should not include HGR to its scope because there are essential differences between human and non-human genetic resources. In the context of research on humans, a fundamentally fair exchange model is already available between the healthcare industry and research subjects. Those who contribute to research should receive benefits in the form of accessible new health care products and services, suitable for local health needs and linked to economic prosperity.

Evaluative Criteria

Membership reach (Unit: number of members)

The first criteria will examine the number of BIO members that could be reached by each alternative. As the literature review suggests, many companies in China are still unaware of the details of the new regulation, resulting in fines and confiscation of the genetic sample. To help members to adjust to the regulation, BIO must first inform. Therefore, how many members can each alternative reach out to is the first evaluative criteria. Even though it will be hard to find an exact number for each alternative, it is clear some will be less accessible to the members than others. For example, a keynote speech that is only open to some pharmaceutical companies (Alternative II) should bring the issue to more people's attention than maintaining the status quo (Alternative I). This criterion will assign "high," "medium," and "low" to each alternative with an estimated number, such as 100 out of a total of 1200 members.

Effectiveness (Unit: number of approved applications)

Since BIO's main objective is to promote access to HGR in China, effectiveness will be measured by the total number of approved HGR applications filed by BIO members each year. After being informed of the regulation, a typical pharmaceutical company has two options: 1) does nothing, or 2) adjusts its operations so that it complies with the new rule. If the company does not act on BIO's recommendation, then the alternative should be considered ineffective for that particular member. On the other hand, if the company responds to BIO's information, then there will be two types of positive outcomes: 1) obtaining access to HGR in China, and 2) avoiding potential fines and IP infringements. Even though the second outcome is a crucial objective for BIO, it could hardly be measured since MOST typically withhold this information. However, it does publish the number of companies applying for HGR access, the decision for each application, and a summary of the project.

It is important to note that the introduction of the record-filing system removed the prior requirement for government approval when foreign entities intend to use Chinese HGRs for clinical trials, as long as HGRs do not need to be exported. Therefore, BIO should expect a natural rise in the number of approved HGR access after it has been steadily declining since 2015. Even so, companies with fewer connections in China still cannot penetrate regulatory barriers. Thus, the baseline for effectiveness will be based on 2* the number of approvals for the 3rd and 4th quarter of 2019, after the regulation became effective, which is 140 (2*70).

Cost effectiveness (Unit: cost/additional approved application compared to the baseline)

Rather than listing cost as a separate criterion, this analysis decides to incorporate the cost into cost-effectiveness evaluation because each alternative would be affordable for BIO. The main objective is to promote access and generate behavioral changes among its members, so each option

does not rely heavily on funding. However, each alternative does generate operational costs. For example, establishing a pool of credible partners involves human capital, travel expenses, and legal consultation fees. Cost estimates and cost-effectiveness analysis is available in the appendix.

Benefit and benefit-cost analysis are not suitable for this project because BIO itself does not profit or benefit from increased access to HGR in China. Pharmaceutical companies will retain the revenue and intellectual property generated by HGR access. Furthermore, even though BIO is concerned about creativity and innovation in the biotechnology sector, the monetary value of incremental innovation can hardly be measured. The effectiveness criteria can roughly capture each alternative's potential to drive innovation.

IP security (Unit: Low, medium, high)

This criterion captures the effect of each alternative beyond accessing the HGR resource. Data sharing and IP co-ownership still pose challenges to BIO members since intellectual property rights could be contentious in this type of sensitive collaboration. There is no direct quantitative measurement for this criterion, so this evaluation will use a qualitative assessment based on whether the policy option 1) helps BIO members establish recommended IP protection infrastructure and 2) reduces IP risk for members that cannot afford to implement IP protection best practices.

Political feasibility (Unit: high, medium, low)

To some extent, the new rule was a product of intensified U.S. and China relations. As China recognizes the significance of HGR in precision medicine, vaccine development, and privacy, it begins to put a restraint on foreign entities' access to HGR in China (China Med Device, 2018). Thus, BIO might face political constraints when it tries to lower the barrier to entry for international companies. Each alternative will be assessed based on the level of interaction with Chinese companies and government agencies that it requires. Moreover, politically feasible options should not only promote BIO members' access to Chinese HGR and partners but also allow Chinese biotechnology companies to initiate joint ventures. Empowering international collaboration form both sides could legitimize BIO's stance as an independent organization. Avoiding the prominent "Eurocentric" or "Americentric" narrative will be crucial to BIO's success and standing in China.

Alternatives

Alternative I: Status Quo

Alternative one is based on the assumption that members operating in China can adjust to the regulation on their own. For companies who already have established partners such as Roche with Children's Hospital of Fudan University, and Merck with Jilin Province Tumor Hospital, they have the trust and ability to renegotiate terms for cooperation and data sharing. Given these existing relationships, BIO cannot effectively offer its members additional collaborative opportunities with new Chinese associates. Companies such as Roche have shown that even though new regulation raises the barrier for accessing HGR, foreign companies can still conduct a full range of R & D operations with oversight.

Admittedly, researchers and start-ups with less human resources and investment appeal will have a hard time obtaining access to Chinse HGR. Yet one could argue that some of those needs could be satisfied by studying domestic HGR. Furthermore, HGR is still a legal grey area in both China and the United States. The use of HGR often generates debates around ethics, privacy, and property right about commercialized derivative products. Therefore, while this regulation prevents certain access to Chinese HGR, foreign entities should also respect China MOST's intention to protect citizen privacy and security of the valuable genetic database.

Membership Reach*:* Low (0)

Under the status quo, BIO does not have to reach out to members and inform them about the recent changes made to HGR regulation. In the meantime, BIO would keep prioritizing its advocacy effort on sharing biotech innovation and promote collaboration within the industry.

Effectiveness*:* Low (0)

The effectiveness of non-intervention will be low even though, eventually, through trial and error, companies would adjust to the new regulation. However, by maintaining the status quo, BIO will miss the opportunity to help some of its members, such as start-ups with limited legal and political resources, to explore collaborative opportunities in China.

Cost-effectiveness*:* Medium (N/A)

The cost-effectiveness of this policy option is medium because the status quo does not require any operational cost. At the same time, it does not create new venues for researchers and companies interested in accessing biospecimens in China. Conducting clinical trials will continue to be challenging for American and European start-ups. Existing partnerships are also not shielded from the trade tensions and privacy concerns between the U.S. and China.

IP Security*:* Low

Maintaining the status quo will leave many companies unhedged against intellectual property theft and forced technology transfer. Companies with existing partnerships might face challenges in renegotiating terms for ownerships of IPR and guaranteeing substantial involvement of their

partners in the project. Companies looking forward to establishing new connections might be exposed to IP violation since they are unaware of the level of transparency demanded by the new rule. Furthermore, if startups cannot access the Chinese market and generate revenue, they might have to commercialize their product by licensing it to a Chinese firm or being acquired, limiting the company's ability to fund future R&D projects. Currently, investments from venture capital firms in China are flooding American biopharma startups (Financial Review, 2018). If the present trend continues, some BIO members will gradually lose its competitive position, market share, and even innovation to Chinese entities/competitors.

***Political Feasibility**:* High

The political feasibility of the status quo is high because BIO will not face opposition from the Chinese government, who has been wary of foreign exploitation of Chinese HGRs. Furthermore, it will also avoid challenges made by the FDA or BIS on the security of U.S. biotechnology innovation.

Alternative II: Invite scholars to present China's recent HGR regulation and recommend strategic responses during BIO's annual conferences

Existing literature suggests that the regulation poses challenges to biotechnology companies in China because they are unaware of the details of the rule, not because they lack the ability to adjust. Therefore, although BIO does not have to assist its members in developing strategies and establishing partnerships, it has to inform. As the largest biotechnology trade organization, BIO has multiple channels to reach out to its members, including web-based messages and newsletters. However, Santarossa et al. show that they are not the most effective tool for generating behavior changes and could often get lost in the flux of irrelevant information. A combination of face-to-face interaction and online engagement proves to be most effective.

Fortunately, well-attended annual conferences present an excellent opportunity for BIO to educate its members on the recent development of biotechnology innovation. With representatives from most pharmaceutical companies gathered in one setting, BIO could invite government representatives, scholars, and policy analysts to share their opinion on the HGR regulations. The content fits perfectly in the agenda for the intellectual property and regulatory innovation section. Before the conference, staffers could send out surveys to gather common concerns so experts can address them publicly and effectively. However, due to the recent COVID-19 outbreak, this alternative is under high uncertainty.

***Membership Reach**:* Medium (~ 300 members)

The membership reach of BIO International Convention is medium because a breakout session tailored to educating members on how to access HGR in China and protect derivative IPR might only be available to a portion of the attendees given the meeting room capacity. If conference staffers could share a video of the program online, or incorporate relevant materials to BIO's official website, membership reach could be higher.

***Effectiveness**:* Low (15 to 30 new applications)

The effectiveness of this alternative is projected to be low. It informs BIO members of the new regulatory updates and best practices on ethical compliance, and members that attend educational sessions tend to be those that have relatable concerns. However, this option does not create new channels for establishing cooperation. Some members might benefit from the program once they implement new strategies to reduce the risk of disapproval, but the primary barrier of building partnerships with a Chinese entity remains significant to other members.

***Cost-effectiveness**:* Medium ($1415 to $707 per additional application)

The cost-effectiveness of having a breakaway session is modest. It includes the cost of renting a conference room, inviting regulators and scholars to speak on the subject, staffers time, and company representative's time. However, its effect will also be modest, given that it has limited membership reach and lack of proactive measures to lower the barrier to entry for emerging pharmaceutical companies.

***IP Security**:* Medium

During the conference, speakers could introduce best practices mentioned in the literature review to help companies establish an IP protection strategy in China. However, merely conveying these doctrines might not necessarily lead to adoption, and companies might still miss the caveats in execution. Strategies that are applicable to established entities such as Roche, AstraZeneca, and Pfizer will not be appropriate for start-ups. The lack of due diligence capability will not prohibit BIO members from entering a partnership with concerning Chinese entities, and an educational program cannot adequately address this concern. Therefore, the IP security rating for this option is medium.

***Political Feasibility**:* High

Political feasibility is high because this alternative will not be challenged by Chinese officials and also encourage BIO members to adopt the best IP protection and ethical practices recommended by FDA and BIS.

Alternative III: Create ethics code to help BIO members adjust to the regulation and incentives to generate buy-in

Apart from simply informing members, BIO should also generate adaptive changes for its intervention to be effective. An overview of other trade organizations with members operating in China shows that creating an ethics code that not only informs members of Chinese regulation but also incentivizes adaptation is a common strategy.

The ethics code should have three sections. 1). The ethical standard for utilizing HGR in China. 2). The regulatory constraint for utilization. 3). Accountability. Section 1 should be based on existing bioethics research and past comments from China's HGR ethics committee. From this literature, BIO staffers should draft norms that follow the ethical principle and provide clear, both

negative and affirmative guidance for members' operations. Section 2 should be based on the new regulation and effectively inform members of compliance measures. Section 3 determines the accountability of members who abide by this ethics code. By signing on to the ethics code, members will be part of the network of pharmaceutical companies operating within China. The new organization naturally provides networking opportunities, but it will also examine the eligibility of its members annually. For those who violate the ethics code, they will no longer enjoy the backing of this network and other complimentary benefits.

Membership Reach*:* High (~ 1200 members)

The membership reach of this alternative is high because, with adequate promotion and communication, BIO should be able to broadcast this ethics code to all members who either have an operation in China or intend to access the Chinese pharmaceutical market. BIO could consider sending out an electronic version of the ethics code and publishing it on BIO's official website to solicit signatures.

Effectiveness*:* High (60 to 120 new applications)

If BIO could successfully come up with a non-monetary incentive, such as official backing or additional membership in a network of esteemed BIO members working in China, this alternative could generate concrete buy-in from companies and researchers. Because the ethics code offers members a guiding document that they can regularly refer to, with topics ranging from bioethics to IP protection best practices, it could effectively communicate the fundamental knowledge on dealing with HGR. As companies become more confident about their ability to manage partnerships with Chinese institutions, they should be more active in launching new initiatives and accessing HGRs to develop precision medicine and conducting clinical trials. Furthermore, a network of BIO members operating in China can also create an environment of support. A joint-pool by L.E.K and BIO (2018) suggests that three-quarters of biopharma firms are interested in China and do not want to enter the market alone. Apart from checking each member's compliance record, companies can share trustworthy partners with those in need and be reminded of regulatory updates during the annual meeting. This dynamic should also allow more companies to initiate international collaborations with a local hospital or CROs.

However, just like the status quo and the first alternative, this option does not lower the barrier to entry for a novel enterprise. The ethics code could effectively mitigate the operational cost associated with longer approval time and a lack of access to HGRs. However, these benefits are marginal for companies unable to establish a presence in China. Therefore, even though this option could potentially increase the number of approved HGR access above the baseline, it does not invite more parties to the world's fastest-growing biotechnology sector.

Cost-effectiveness*:* Medium ($1799 to $899 per additional application)

The cost of Alternative III includes the design cost and implementation cost. The design cost consists of the time of five staffers conducting comprehensive research on bioethics standards, legal framework, and IP protection best practices and drafting the ethics code for four weeks. The implementation leads to the cost of advertising the ethics code. It requires a new facilitator that

would communicate with the executive board of the BIO Chinese network and keep records of companies adopting or withdrawing from the ethics code. Furthermore, BIO should arrange a conference room for the network to holds its annual meeting. Lastly, a potential cost or benefit of this strategy is the goodwill of BIO. As the largest trade organization in the biotechnology industry, BIO's name carries weight among suppliers and policymakers. Its purchasing and negotiating power are crucial to members' interests. By backing the companies that abide by the ethics code, BIO associates its brand name with the behavior of those companies. If a member accidentally or intentionally violated the new HGR regulation and caused considerable media attention, BIO's goodwill might be affected. The cost-effectiveness of Alternative III is medium, since its effectiveness is high, and the cost is moderate.

***IP Security**:* Medium

While the ethics code can give members best practices on IP protection that they can always refer to, setting up an IP protection system is unique to each company. Advice for multi-national cooperation might not be realistic for companies with limited due-diligence abilities and no legal consultation. On the other hand, having a local network might be able to offset this effect. Similar companies can share their experience on a case by case basis. Their insights will also be more valuable because they are exposed to local political and cultural issues that are not apparent in the regulation.

***Political Feasibility**:* High

The political feasibility of the ethics code itself is high since it helps foreign companies in China comply with the HGR regulation. Creating a local network for BIO members in support of the ethics code should not be politically challenging as many similar trade organizations are operating in China. However, there might be caveats that render political opposition from Chinese officials since they are closely monitoring foreign interests in China as the tension between the two countries escalates. The ethics code and local network should follow the Chinese government's basic principles while not forgoing its primary goals in guiding local operations of BIO members.

Alternative IV: Establish a pool of potential Chinese partners for BIO members to connect

Even though both the interim and the new regulation requires foreign entities to establish an international collaboration before accessing HGR, no existing policy help pharmaceutical companies lower the barrier to entry. Furthermore, the new rule requires a significant level of cooperation. Given that Chinese companies have been accused of forcing technology transfer and intellectual property theft, companies and researchers face a high risk of keeping their HGR related results.

To address these two issues, BIO should consider helping its members to filter out risky partners and identify trustworthy institutions. Beyond that, BIO could establish a foundation for international collaboration, so when its member needs HGR access, BIO could reference suitable Chinese entities and offer a model for cooperation framework agreements. By doing so, BIO hedges the security of members' intellectual property. Lastly, the experience of building a

successful partnership with Chinese institutions is not only scalable in China but also in other countries. This alternative can help BIO members adjust to the recent regulation, and also expand BIO's global influence as the facilitator of biotechnology innovation.

***Membership Reach**:* Medium (~ 500 members)

Membership reach of this alternative is contingent upon BIO's advocacy effort. If BIO can effectively leverage its media and membership relations platform, then many members can be aware of this new initiative and find suitable partners for their future endeavors. On the other hand, if BIO's candidate pool was too small and restrictive for specific companies, then it might only be accessible for a few members.

Effectiveness: Medium (25 to 75 new application)

The effectiveness of Alternative IV is medium. Since at first BIO could only develop relations with a handful of Chinese partners, there will be limited opportunities for members to explore. However, this approach increases HGR access both among pharmaceutical companies with enough resources to establish partnerships and among start-ups with limited connection and experience in international collaborations. Having a pool of candidates that are screened and certified by BIO could allow its members to engage in data sharing and IP co-ownership confidently. Furthermore, for start-ups that find identifying a Chinese partner and constructing a framework agreement challenging, they could reach out to companies interested in their proposal through BIO. As the intermediary, BIO could effectively lower companies' barriers to enter the Chinese market and gain marketing rights for their drugs. China is a vast market for novel-therapies, and its patients have all types of medical needs. Once HGRs becomes more accessible for early to late-stage pharmaceutical companies, their marketing rights in China could fund future expansions and innovations.

***Cost-effectiveness**:* Low ($6571 to $2190 per additional application)

The cost of Alternative IV includes the time of 4 staffers working over five weeks to examine candidates for the pool of BIO certified Chinese partners, the cost of hiring legal consultants to develop the term of the cooperation framework agreement, travel expenses for staffers if necessary, and additional work time for BIO's membership relation management team. The sunk cost of Alternative IV is high because BIO's presence in mainland China is limited. Meeting representatives from Chinese entities requires in-person negotiations, and there is no available reference for terms of the agreement that BIO should propose. Ideally, once BIO has constructed a meaningful relationship with a handful of organizations, the experience will be scalable, because the marginal cost for legal consultation and time investment will decrease. Given its high sunk cost, this alternative is relatively less cost-effective.

***IP Security**:* High

Alternative IV has a high rating for IP security because it addresses companies' concern for IP security at its core: the trustworthiness of their partners. Identifying a credible Chinese partner is the foundational IP protection strategy recommended by multiple law firms (Hogan Lovells & Spruson & Ferguson, 2019). Informing BIO members of the best practices in setting up an IP

protection strategy is useful, but it does not guarantee successful implementation. Some companies do not have the necessary wherewithal to establish such a protocol. In contrast, BIO, with its industry knowledge, can filter out Chinese institutions that have a poor record of respecting traditional academic and market principles and identify those that offer valuable partnerships. Furthermore, since BIO is the intermediary, it could set guidelines and paradigms for the collaboration between its members and Chinese candidates. As a result, start-ups would face fewer challenges in designing the terms for initiating partnerships, IP co-ownership, and data-sharing mechanisms. Companies of all sizes can take advantage of this initiative.

***Political Feasibility**:* Medium

Although this alternative is primarily intended to facilitate partnerships between BIO members and Chinese hospitals, research institutes, and pharmaceutical companies, opposition from the Chinese government might be palpable. Chinese hospitals and biobanks, unlike those in the United States and Europe, are part of the public sector where bureaucratic regulation from the Communist Party is present. As mentioned in the background section, the purpose of the new rule was to prevent foreign companies from exploiting "HGR" as it becomes a national asset. If BIO is perceived as an organization that represents national interest rather than an independent supporter biotechnology innovation, Chinese entities that BIO has reached out to might be forced to withdraw from the agreement under political pressure.

Additionally, similar cooperation has long been criticized by American mainstream media. Recently, Professor Noah Smith (2019) from Stony Brook University pushed an article on Bloomberg encouraging President Trump to pressure China to drop its prevalent joint-venture rule. It is unclear whether Larry Kudlow's recent remark that urges U.S. companies to disband operations in China and phase-two of the trade negotiations will cause difficulty for BIO to find reliable Chinese partners. Besides, if BIO falsely identified certain Chinese entities as trustworthy and resulted in IP theft, then its mistake could also be called into question by officials outside of China.

Alternative V: Establish cooperative relations with China National Center for Biotechnology Development (CNCBD)

To assist members in taking joint ventures with Chinese entities, BIO could also establish a partnership with the China National Center for Biotechnology Development. The Center is under the MOST, responsible for making biotechnology-related policy and regulation, managing the storage and security of HGRs, and facilitate information transfer between China and other countries. Specifically, the International Cooperation Office is charged with promoting international collaboration on biotechnology and pharmaceutical development.

If BIO could develop relations with the International Cooperation Office, then its members from all areas of biotechnology innovation can participate in conferences and seminars held by the Center for Biotechnology Development. Having exposure to those events could help BIO members

get updates on regulatory policy over HGR, understand government priority in biotechnology development, and meet Chinese entities willing to provide access to HGR.

***Membership Reach**:* Low (~ 30)

Membership reach of this alternative is low because it is likely that only BIO members with an established presence in China can take advantage of this new relationship. Most of the roundtable discussions and seminars are hosted in China, so new networking opportunities are not accessible to most members.

Effectiveness: Low (1 to 3 new applications)

The center's current multi-lateral and international collaboration is primarily academic. For example, its collaborative effort with the International Center for Genetic Engineering and Biotechnology include lab experiments, doctoral and post-doctoral programs, and creating a bioinformatics database. However, BIO member's access to Chinese HGR is not primarily academic since most companies are using HGR to conducting clinical trials and R&D. These companies have vested commercial interests in the outcome of collaboration, which might be more challenging to deal with, given the type of cooperation that the center is used to.

***Cost-effectiveness**:* Medium ($8000 to $4000 per additional application)

The cost-effectiveness of this alternative is medium mainly because the effectiveness is projected to be low. The cost of partnering with CNCBD includes additional work time of BIO staffers, travel expenses, and funding for discussions and seminars. Since only a handful of companies under BIO would be exposed to new R&D opportunities, there will be few additional accesses to HGR as a result.

***IP Security**:* High

Universities, hospitals, and research institutions associated with the CNCBD have an excellent record of respecting the intellectual property of foreign entities, so BIO members anticipating working with these organizations should not be concerned. However, even so, companies should still take precautions and set up IP protection mechanisms.

***Political Feasibility**:* High

The political feasibility of this option is high because CNCBD is open to both bi-lateral and multi-lateral cooperation. The center has organized multiple discussions and conferences with organizations ranging from the World Health Organization to foreign universities. Therefore, BIO should face little challenges in reaching out to the center.

Outcome Matrix

Alternatives / Criteria	*Membership Reach*	*Effectiveness*	*Cost-Effectiveness*	*IP Security*	*Political Feasibility*
Alternative I: Status Quo	Low: Maintaining the status quo would prevent BIO from intervening companies' self-adjustment	Low: Companies might take a long time to adjust and lacks IP protection strategies	Medium: Status-quo will have no effect on broader HGR access but it also does not generate operational cost	Low: BIO members might be surprised by the level of cooperation and data sharing HGR access requires	High: BIO would not face any political challenge by maintaining the status quo
Alternative II: Conference Session	Medium: Breakaway Session during BIO conference could hold approximately 120 members	Low: Informing members of best practices might not lead to adoption; no new channels for HGR access	Medium: Hosting breakaway session has modest cost but effectiveness is low	Medium: IP protection strategies varies case by case, so an educational program can only be helpful for some members	High: Holding a conference session will face no political challenges
Alternative III: Ethics Code and Local Network	High: With proper broadcasting efforts, the ethics code would be accessible to all members with operations in China (300-400 members)	High: Ethics code offer permanent guidance and reference for best practices; network allows members to share partnerships and experience	Medium: Designing the ethics code and set up a network structure in China might involve considerable sunk cost but it is highly effective and scalable	Medium: Ethics code give members a good reference and local support, however some might still lack the ability to conduct due diligence and screen potential partners	High: Establishing a local network to generate buy-in might be closely monitored by the Chinese government thus it might face political challenges

Alternative IV: Establish a Partnership Pool	Medium: Membership reach is contingent on candidates in the partnership pool and broadcasting efforts (150-300 members)	Medium: Partnership pool allows BIO to filter out untrustworthy Chinese entities and promote access to HGR for start-ups	Low: Requires trial and error, considerable investment of staff time, and the risk of depreciating goodwill. However, it is effective and scalable	High: Filtering out untrustworthy Chinese partners directly address the IP security concerns. However, members still need IP protection strategy	Medium: Chinese entities might withdraw from partnership with BIO if BIO is no longer perceived to be an independent trade organization and represents national interests
Alternative V: Establish Partnership with CNCBND	Low: Additional seminars and networking opportunities would be mostly available for companies that have presence in China (30-50 members)	Low: Collaboration with CNCBND is primarily academic so it might not be effective in dealing with R&D that are commercial in nature	Medium: Partnering with CNCBND will involve limited human capital and funding but it has a low effectiveness rating	High: Partnership opportunities with CNCBND will include respected hospitals, research centers and biobanks	High: CNCBND has a record of establishing bilateral and multilateral partnerships with international organizations

Recommendation – Alternative III and IV

Given the outcome matrix, this analysis recommends a combination of Alternative III and IV, since they are highly complementary in nature. In terms of membership reach, both the ethics code and a pool of trustworthy candidates can be informative and useful for many BIO members if it successfully leverages broadcasting techniques on the website and newsletters.

Both alternatives are highly effective for different reasons. The ethics code serves as a permanent document where members can review the recommended best practices on ethics and IP protection. These standards would help members comply with the new HGR regulation and significantly reduce the risk of fines, confiscation, or rejection of their applications. Establishing a network of BIO members with business in China and only offer that membership to those who sign on to the ethics code can facilitate buy-in and concrete adoption of best practices. Furthermore, the representative could explore more collaborative opportunities during annual networking events. It is worth noting that the ethics code help members have easier access to HGR, but it does not lower the barrier to entry for emerging startups. They still lack the wherewithal to establish international joint-action with a Chinese entity. To overcome this challenge, BIO should construct a pool of potential candidates for BIO members to collaborate with. As the intermediary, BIO can prepare a model that includes the necessary legal and business framework for the collaboration. Starts-ups could thus reach out to BIO and capitalize on these existing partnerships to forward their R&D initiatives. Ideally, BIO would also incorporate these certified Chinese institutions to its local network so its members could have better industry insights and communication with Chinese representatives.

These two strategies are also highly complementary in protecting the IP of BIO members. The ethics code offers guidance on structuring an IP protection strategy and understanding China's IP landscape. In addition, the partnership pool helps companies that cannot conduct due diligence to find trustworthy partners, addressing IP concerns at its root.

Lastly, a combination of Alternative III and IV is the most politically feasible. If BIO creates a network that is only open for BIO members, its intent might be suspicious for Chinese officials. By identifying a pool of credible Chinese institutions, BIO could integrate them into the local network. Ideally, this dynamic could promote both foreign access to Chinese biospecimens and collaborations initiated by the Chinese party.

Implementation

As BIO moves forward with the recommendation, it should start forming two task forces, each with four staffers working full-time for five weeks. One team would be responsible for conducting research and drafting the ethics code. The other team would screen for credible Chinese hospitals, universities, and biobanks that might agree to establish collaborative relations with BIO members. It is important to note that BIO's initiative has multiple stakeholders:

The Ministry of Science and Technology of PRC:

BIO needs to respect the new rule's underlying principle, which is preventing foreign entities from exploiting China's HGR and privacy. Therefore, in creating the ethics code, BIO should focus on compliance rather than strategies that may be perceived as taking advantage of the regulatory loopholes. It should endorse companies to share HGR informed data and results with the Chinese party, within the framework of IP agreements. Furthermore, as an international trade organization, BIO must represent no particular national interest. The United States is wary of Chinese investment in its biotechnology sector since it is one of America's leading industries. As U.S.- China trade tension escalates, MOST will likely become suspicious of BIO's local presence and advocacy efforts if it loses its independent status. By establishing the record-filing process, China is opening up its HGR market to foreign enterprise, as it sees more international collaboration as a "win-win" opportunity. Therefore, BIO's implementation of both alternatives should be inclusive to Chinese companies, capitalizing on their industry insights by incorporating them into the local BIO ecosystem.

The provider of HGR:

Any clinical trials using HGR requires approvals from the ethics committee because of its sensitive nature. Genetic resources can reveal much personal information and do not quickly deteriorate. Therefore, any finding from utilizing the HGR should protect the anonymity of its provider. Researchers should return it to the storage facility upon the project's termination. Moreover, companies should consult legal personnel before commercializing the product derived from HGR, since in some cases, the provider may have ownership rights.

Patients in China:

Patients in China and all over the world are potential stakeholders of BIO members innovation with HGR, as more and more companies move into precision medicine research and immune-therapies. These highly customized medicines will offer novel solutions to patients who have been suffering from current treatments that have lackluster effectiveness. Therefore, when implementing Alternative IV, BIO could prioritize establishing relationships with Chinese partners that could bring more collaborative opportunities for a specific line of pharmaceutical research. For example, given the recent COVID-19 outbreak, blood samples of received patients in China are valuable HGRs for developing antigens and future vaccines. Fudan University Hospital has successfully used plasma therapy to treat patients. Thus, collaborating with similar institutions could be crucial for BIO member Inovio Pharmaceuticals, who has been developing vaccines for

the COVID-19. Strategically identifying potential partners could allow BIO to make the most impact on patients' health around the world.

BIO members:

By incorporating both alternatives, BIO is helping members that are self-sustainable in China and those that have limited resource and access to the Chinese market. The former would benefit from adopting the ethics code. At the same time, the latter relies on BIO to minimize the barrier to entry. Thus, the implementation of Alternatives III and IV should be cognizant of the need for both types of members. Because the purpose of accessing the HGR and IP protection mechanism differs considerably across pharmaceutical companies, BIO should focus on fostering a local network where each company's unique issue could be heard and supported by a community.

The Biotechnology Innovation Organization:

BIO is also a crucial stakeholder because, as the facilitator of biotechnology innovation, its effort could also backfire. BIO's goodwill might be at risk if it endorses members that abide by the ethics code, and they intentionally or unintentionally violated the regulation. Admittedly, it is the company that will be penalized by a MOST with greater authority. However, such an event could also jeopardize the legality of BIO's local network and its standing in China. Therefore, BIO must make its statement for compliance and cooperation clear so potential events like these will have limited effect.

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Appendix

Cost-effectiveness Analysis

The cost-effectiveness analysis makes the following assumption:

Annual interest rate = 1%
Hourly wage of policy coordinator at BIO = $ 25
Hourly wage of external legal consultant = $ 225
Traveling expenses to China = $ 2000
Broadcasting effort by BIO (through newsletter webpage) = $200

- **Alternative I: Status Quo**

Under the status quo, BIO would maintain its current policies and allow members to self-adjust to the new regulation. Therefore, the annual cost of this alternative is 0 over the next five years.

Year	Cost($)
1	0
2	0
3	0
4	0
5	0

- **Alternative II: Breakaway session at BIO conference**

Adding a breakaway session about IP protections in China and accessing HGR would incur the following costs: attendance fees of the speaker ($4000), three staffers time for 1 hour ($25/hour*3*1 hour=$75), the rental fee for the conference room ($300). These annual costs amount to $4375.

Year	Cost ($)
1	4375
2	4375
3	4375
4	4375
5	4375

The net present value (NPV) of Alternative I would then be $21233.76. Assuming that each breakaway session can host 120 representatives and over the next five years, a total of 300 different representatives would attend the conference. If 5% to 10% of the representative would launch new

international collaborations with a Chinese institution, then the cost-effectiveness of Alternative II could range from (21233.76/300*0.05) $1415 to (21233.76/300*0.10) $707.

- **Alternative III: Ethics code and establishing local BIO network**

Cost for Alternative III includes five staffers' time over for weeks to conduct research (5*8 hours/day*5 days/week*2 weeks* $25/hour =$10000), a broadcasting effort through BIO newsletter/website ($200), the additional workload for membership coordinator (600 hours*$25/hour = $15000), and funding for the annual network-wide event ($5000). These costs amount to $30200. Notice that the research cost is non-recurring, so cost after year 1 equals to $20200.

Year	Cost ($)
1	30200
2	20200
3	20200
4	20200
5	20200

The NPV of Alternative III is $107940.3 over the next five years. With a successful broadcasting effort, the new initiative could reach 1200 members. If 5% to 10% of these members adopt the best practices that the ethics code recommends and launch new projects involving HGR, the cost-effectiveness of Alternative III ranges from (107940/1200*0.05) $1799 to (107940/1200*0.05) $899.

- **Alternative IV: Establish partnership pool**

Cost for Alternative IV includes five staffers' time over for weeks to conduct research (5*8 hours/day*5 days/week*2 weeks* $25/hour =$10000), broadcasting effort through BIO newsletter/website ($200), legal consulting fees for establishing partnerships with the first 5 Chinese institutions (5 hours*$225/hour*5=$5625), travel expenses for four client coordinators to meet with representatives in China (4*$2000 = $8000), and additional workload for client management team (600 hours* $25/hour = $15000). These costs amount to $38825. After establishing partnerships with the first five institutions, BIO could scale up its initiative with lower marginal costs of research and legal consultation. Thus, we assume an adjustment rate of 0.6 for research and legal consultation cost after year 1, rendering the cost after year 1 to be $32575.

Year	Cost ($)
1	38825
2	32575
3	32575
4	32575
5	32575

The NPV of Alternative IV is 164298. If, on average, each of the 25 Chinese partners could participate in 1 to 3 new HGR projects, then the cost-effectiveness ranges from $6571 to $2190.

- **Alternative V: Establishing partnership with CNCBND**

The cost of establishing a partnership with CNCBND is low because it only requires one staffer's time over four weeks ($25*8 hours/day*5days*4 weeks) = $4000 and travel expenses for three staffers ($2000*3), amounting to $12000. This cost is non-recurring since, after establishing the relationship, BIO members would afford the cost of attending seminars.

Year	Cost ($)
1	12000
2	0
3	0
4	0
5	0

The NPV of Alternative V is $12000. Since seminars could only reach out to approximately 30 BIO members in China, if 5% to 10% initiated new HGR projects, the cost-effectiveness of Alternative V ranges from $8000 to $4000.