Legal Commentary

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Top 10 Traps to Avoid: Navigating China's HGR Applications[1]

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In recent years, the regulatory framework for human genetic resources ("**HGR**") in China has become increasingly mature. Regulatory authorities have issued and updated a series of laws and regulations, including the *Regulations on the Administration of Human Genetic Resources* (the "***HGR Regulations***"), the *Implementation Rules on the Administrative Regulations on Human Genetic Resources* (the "***Implementation Rules***"), the corresponding administrative guidelines, as well as the *Answers for Frequently Asked Questions on Human Genetic Resource Administration.* The regulatory system for HGR in China has been thereby established and refined (For our insights on the regulations of HGR in China, please refer to: *Highlights on HGR Regulation Implementation Rules*; *Key Takeaways of the New HGR Guidelines*; *Key Takeaways on the New HGR FAQs issued by the MOST of China*).

Meanwhile, significant progresses have been made for the review and approval process of HGR applications. According to the approval results for HGR projects publicly disclosed on the HGR Management System, 105 collection projects and 704 international scientific research collaboration projects have obtained approval to date this year. The rate of approval is high, and the average time for approval ranges between 16 to 20 working days[3].

Since May 1, 2024, the regulatory authority of HGR in China has been transferred from the Ministry of Science and Technology (the "**MOST**") to the National Health Commission (the "**NHC**"). (For our insights on the changes of HGR regulatory authority, please refer to: *汉坤 • 快评 | 《人类遗传资源管理条例》再次修订*). On April 25, 2024, the MOST issued an announcement that the application process and management system for HGR projects will remain unchanged. Furthermore, there are reports indicating that the NHC has thereafter commenced the revision of the *Implementation Rules*, where the NHC may consider further widening the scope of the "Chinese entities" and streamlining the application process for HGR projects to reduce the burden on industry in the future[4]. Such relaxation of the future standards and

[1] For the Chinese version, please click *十大雷区：中国人类遗传资源项目申报避坑指南*.

[2] Shuwen Sun have contributions to this article.

[3] HGR Management System: https://apply.hgrg.net/.

[4] Moting Jiang, Xiaotian Cui (2024, May 13), 独家 | "人类遗传资源管理条例实施细则"修订提上日程, *Caixin*, https://m.caixin.com/red/2024-05-13/102195539.html?s=6d1d82d074b45ff0376cf93f789cba1b813014478d3b719ab1fc919d78206db00c0be4674434d5b0.

requirements for the applications of HGR projects may facilitate the ongoing and future research projects. However, we have also observed that due to a lack of understanding of compliance requirements, a number of common traps in HGR applications have emerged across various projects in recent years, resulting in failure to obtain the approval. Regardless of any future revision, foreseeably China's current regulatory system for HGR will not undergo any fundamental changes unless any amendments to the *Biosecurity Law of the PRC*. Therefore, failure to avoid these traps may still pose significant obstacles to the process of HGR projects, whether there will be any relaxation to the specific requirements. In light of this, in accordance with the latest regulations, policies and regulatory practices, this article specifies ten common traps in the application of HGR projects in China. We also hope that this article could help the industry better understand regulatory requirements, mitigate risks, improve efficiency in obtaining approvals and facilitate smooth process of HGR projects.

Trap one: inappropriate pathway for the application

Choosing an appropriate application pathway is the initial step for a compliant and smooth HGR application. Current HGR pathways include procedures of the collection approval, the biobanking approval, the material exportation approval and the international scientific research collaboration approval of HGR, as well as the international clinical trial collaboration filing and data sharing reporting of HGRs. Based on the specific characteristics of the projects, applicants shall select the right pathway and complete the application process in accordance with the laws and regulations. Failure to choose the right pathway may lead to the failure to obtain approvals for the projects or result in potential legal risks for the projects.

For instance, if a foreign entity plans to utilize Chinese HGR information for scientific research, the procedures of the international scientific research collaboration approval, the international clinical trial collaboration filing, or the data sharing reporting may be applied based on the project's collaboration arrangements and specific circumstances. If the foreign entity merely intends to provide investigational drugs or funding for such HGR-related scientific research without any substantial involvement in the research, no application procedures are required. However, if the foreign entity intends to substantially participate in the project, obtain the HGR and the related research data, share the project's intellectual property rights ("**IPR**"), or share or jointly publish research findings, it is necessary to complete the applicable application procedures.

Trap two: safety risks and inadequate risk mitigation methods in the projects

The safety risks associated with the projects have always been a significant concern in the regulation of HGR in China. The legislative intent of the *HGR Regulations* is the effective protection and reasonable utilization of the HGR, as well as to safeguard public health, national security and public interests[5].

Therefore, whether a project poses potential safety risks, including risks to public health, national security, or public interests, is a key focus of the regulatory authority in the review. To manage such safety risks, applicants shall make proper arrangements for the biobanking, use, and mitigation measures of the involved HGR in the project and provide specific explanations of such arrangements in the application

[5] Article 1 of the *HGR Regulations*.

materials. For instance, it shall be provided that no personally identifiable information of subjects/patients shall be uploaded to public platforms. Key data generated in the project, such as raw data from whole-exome sequencing or whole-genome sequencing, shall be stored on domestic platforms. If no reasonable and effective risk mitigation measures is implemented in the project, it is highly likely that the application will not be approved.

Trap three: insufficient research capabilities of the collaborating parties

Another key focus during the review and approval of HGR projects is the foundation and capability of the collaborating parties to conduct relevant research. If the necessity and reasons for the collaboration are not sufficient, or if the collaborating parties do not have sufficient personnel, technologies, equipment, or HGR materials and information related to the proposed research project, it may be difficult for the corresponding project to obtain an approval.

For example, if a Chinese research institution wants to collaborate with a foreign pharmaceutical company specializing in cardiovascular drugs to conduct a study on mental illness, but the Chinese institution fails to provide sufficient explanation of the foreign partner's research capabilities in the field of mental illness, the regulatory authority is likely to consider whether the collaboration is unreasonable. Therefore, the research capabilities of the collaborating parties and the provision of relevant basic information are crucial for the project to be approved. The collaborating parties shall be able to demonstrate their research strength and resources in the relevant field to increase the chances of the project being approved smoothly.

Trap four: questionable source of the HGR

The legitimacy of the source of the HGR is also an important consideration in the review of HGR projects. If the source of the HGR to be used in the project is not legal, it is likely that the project will fail the review.

The applicant shall provide an explanation of the source of the HGR involved and the administrative procedures already completed (if applicable). If the applicant cannot prove the legitimacy of the source of the HGR, the project is likely to be denied by the regulatory authority.

Trap five: unreasonable HGR utilization plan, or the mismatch between the proposed utilization plan and the types and quantities of the HGR applied

During the review process of HGR projects, the regulatory authority will review the proposed utilization plans of the HGR involved, such as the international collaboration research plans, HGR collection plans, and HGR material export plans, to ensure that the utilization of the HGR is both reasonable and legitimate. The applicants must ensure the legitimacy, reasonableness, and consistency of the proposed plans to smoothly pass the review. Meanwhile, the applicants shall also ensure that the types and quantities of the HGR applied are consistent with the proposed plans when submitting their applications.

Specifically, the following issues regarding the utilization plans of HGR are likely to result in the project application being denied:

- Unclear or unreasonable description in the HGR utilization plan, or the inconsistency between the

utilization plan and other project materials (such as the collaboration agreements).

- Unreasonable specifications, quantities, etc., of the HGR materials or information involved.
- Unclear, unreasonable, or even illegal research purposes reflected in the plan.
- Failure of the plan/solution to adhere to the established standards and guidelines set forth by the relevant professional field or industry.

In addition, the types and quantities of the HGR applied shall match the research plan. Otherwise, it may raise doubts from the regulatory authority regarding the scientificalness, reasonableness, and even the authenticity of the research plan. If the types of the HGR applied do not match the research plan, or if the quantities of the HGR applied are excessive or insufficient, it may lead to delays in the review process or even the rejection of the applications.

Trap six: unclear or unreasonable disposal arrangements for the remaining HGR

The regulatory authority pays special attention to the entire lifecycle of HGR utilization to maximize the safety of the HGR, ensuring the implementation of research ethics, subject rights, and social responsibility.

Therefore, the proper arrangement and disposal of the remaining HGR is crucial. If the disposal arrangements for the remaining HGR are not clearly and reasonably outlined in the plan, or if there are inconsistencies in the disposal arrangements for the remaining HGR in the application materials, the project may fail to get an approval. For the applicants, it is crucial to develop a clear and reasonable plan for the disposal of the remaining HGR in advance, and to clearly describe such plan in the application materials for the smooth approval of the project.

Trap seven: unclear or incomplete arrangements in the collaboration agreements

The application materials also include the agreements between the collaborating parties, which may include international collaboration agreements as well as agreements related to the collection, transportation, testing, and disposal of the HGR. In the collaboration agreements, the clarity of the relationship between the collaborating parties and their division of work, and the completeness of the agreement are all key points of the review.

In practice, if there are disagreements between the collaborating parties regarding their division of work, the parties need to reach a consensus on the solution to such disagreements before the final submission of the application, and such consensus shall be clearly reflected in the submitted agreements. For example, a university biotechnology research institute plans to collaborate with a US pharmaceutical company on an international scientific research project involving Chinese HGR. During the drafting of the collaboration agreement, the two parties disagreed on the selection of the sample transportation provider and testing site. After negotiation, the two parties reached an agreement on the specific division of work for sample transportation and testing, and this agreement was clearly recorded in the collaboration agreement, providing a solid foundation for the smooth application and approval of the project.

Trap eight: failure to obtain compliant informed consent according to law

According to Chinese laws and regulations, a written informed consent of the individual shall be obtained for the collection, biobanking, utilization, and external provision of HGR of China to protect the individual's legal rights and interests[6]. Applicants shall ensure that the informed consent form, a common and important document in project ethics review and regulatory procedures, fully complies with the relevant regulations. If necessary, the informed consent forms may need to be modified and the informed consent of the individual shall be obtained again.

In practice, the utilization of an informed consent form (ICF) that does not fully comply with the relevant regulations poses significant risks to the overall application process. In certain projects, for example, the individuals are simply informed that their genetic resources will be used for clinical diagnosis, yet not informed that the same may be used for research activities other than clinical diagnosis. Similarly, some informed consent forms fail to disclose that the genetic materials or data may be sent abroad for testing or research, resulting in failure for the project to pass ethics review and regulatory procedures.

Trap nine: lack of legal and valid ethics review approval, or inconsistency between application materials and ethics review approval

The collection, biobanking, utilization, and external provision of HGR shall comply with ethical principles and undergo ethics review[7]. Ethics review is usually conducted by the ethics (review) committee of the medical institution involved in the project. Obtaining an ethics review approval is a prerequisite "checkpoint" for HGR projects and is also an important document to be reviewed by regulatory authority.

In practice, there are situations where the project may be rejected in obtaining ethics review approvals, causing delays in the progress of HGR project. For example, the ethics review approval may be expired or invalid at the time of application; the composition and number of the ethics committee may fail to meet the required standards; the information in the ethics review approval may be inconsistent with that of other project materials such as protocols or informed consent forms; the version of the ethics review approval submitted is not be the final version.

Trap ten: incompliance with legal requirements regarding IP ownership

In terms of HGR international scientific research collaboration projects, the ownership of IPR have always drawn close attention from and have been scrutinized by the regulatory authority. The laws and regulations clearly stipulate that, the corresponding patent rights shall be jointly owned by the collaborating parties if any Chinese HGR is used in the international scientific research collaboration; and the right to use, transfer rights, and arrangements for sharing the benefits of other scientific and technological outcomes shall be agreed upon by the collaborating parties through a collaboration agreement[8]. Furthermore, provincial regulatory authorities are specifically required to supervise and inspect the

[6] Article 9 of the *HGR Regulations*, Article 9 of the *Implementation Rules*.

[7] Article 9 of the *HGR Regulations*.

[8] Article 24 of the *HGR Regulations*.

arrangements of IPR and benefit-sharing of these projects[9].

Therefore, it is necessary to stipulate that any patent right generated from HGR international scientific research collaboration projects shall be jointly owned by the collaborating parties; otherwise, the projects may not be approved. However, in practice, there are different approaches regarding the specific distribution of benefits of patent rights and other project outcomes. Based on our experience, many projects that consider multiple factors and make separate arrangements for economic benefits have also been approved by the regulatory authorities. During the application process, it is important to pay special attention to the rationality of the allocation plan of IPR and ensure consistency between the provisions in the collaboration agreement and the application materials regarding IPR ownership and distribution.

Conclusion

In terms of HGR regulation, the companies always find it of challenges as well as opportunities, and it is crucial to understand and address various issues concerning the review procedures. This article aims to summarize common issues the companies may encounter in the regulatory authorities' review procedures of HGR projects, facilitating practitioners better comply with regulatory requirements. In addition, with shift in HGR regulatory authorities and the buildup of regulatory experience, regulatory requirements may also be adapted through amending HGR rules such as the *Implementation Rules*. We will closely monitor the latest regulatory trends and share our latest insights with the industry to facilitate the review progress of HGR projects in China and promote the development of life sciences.

[9] Article 56 of the *Implementation Rules*.

Important Announcement

This Legal Commentary has been prepared for clients and professional associates of Han Kun Law Offices. Whilst every effort has been made to ensure accuracy, no responsibility can be accepted for errors and omissions, however caused. The information contained in this publication should not be relied on as legal advice and should not be regarded as a substitute for detailed advice in individual cases.

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