Regulatory Considerations and Oversight: A Chinese Perspective

12

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History and Current Status

Currently, the National Health Commission of the People's Republic of China regard organ xenotransplantation technology as medical technology of Class III—a high tier category that includes medical technologies with major ethical issues as well as safety and effectiveness concerns [1]. The 2008 and 2018 Changsha Communiqué stimulated the efforts in China in the following areas: (a) xenozoonosis; (b) regulatory; (c) biorepository; (d) transgenic pig facilities; (e) biomaterials and encapsulation; and (f) immunosuppression and tolerance induction [2, 3]. Also, the General Offices of the CPC Central Committee and the State Council released a set of guidelines to Strengthen the Governance over Ethics in Science and Technology on March 20, 2022 [4]. These guidelines clarified the principles and requirements of science and technology including xenotransplantation ethics principles and governance requirements, governance system and governance system guarantee. According to the guidelines, it is important that scientific activities serve humanity, respect people's rights to life, adhere to fairness and justice, control risks appropriately, and maintain openness and transparency. All the above efforts reflect the state of xenotransplant science and support in China.

There are three guidelines and expert consensuses related to xenotransplantation. Firstly, the Chinese Medical Association of Organ transplantation Xenotransplantation group released the Clinical Research Guidelines on xenotransplantation on Nov 15, 2018 (2018 Expert Recommendations, see Table 12.1) [5]. Secondly, the above association released the Clinical Trial Expert Consensus

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Table 12.1 Key points of the Clinical Research Guidance on xenotransplantation (2018 Expert Recommendations) [2]

No.	Contents
1.	Clinical research should be approved and controlled by the health commission of province or nation
2.	This guidance includes: general principles, project application and review, technical standards, ethical requirements, biosafety, project management, donor requirements, recipient selection, project implementation, follow-up, etc.
3.	Donors are limited to pigs without specific pathogens (SP), including wild-type and genetically modified pigs. Samples should be stored for more than 50 years
4.	The cell transplantation center require compliance with current good manufacturing practices (cGMP)
5.	Collected data of the project should be reported to the authorities regarding the information of implementation

Table 12.2 Key points of the expert consensus in clinical research on islet xenotransplantation (2019 Expert Recommendations) [3]

No.	Contents
1.	Clinical research should be approved and controlled by the National Health Commission (NHC)
2.	Islet cells from genetically modified pig (or devices containing islet cells) should be approved by the National Medical Products Administration
3.	This guideline include: general principles, application and approval of clinical research for islet xenotransplantation, donor requirements, ethical requirements, technical and related equipment standards for clinical research, biological safety standards, project implementation, project management, etc.
4.	The cell transplantation center require compliance with current good manufacturing practices (GMP)
5.	Collected data of islet xenotransplantation should be controlled by NHS and public open source permitted by law
6.	Donors should be specifically cultured without designated pathogen free (DPF). Samples should be stored for more than 30 years

on islet xenotransplantation on Nov 15, 2019 (2019 Expert Recommendations, see Table 12.2) [6]. The quality standards and ethical requirements of islet xenotransplantation are stipulated, which facilitate the development of clinical islet xenotransplantation technology. Thirdly, the China Organ Transplantation Development Foundation released the "Expert Consensus on Clinical Trials of Human Xenotransplantation in China" on April 6, 2022 [7]. The "Consensus" states that xenotransplantation is essential and that its academic findings can contribute in the advancement of the transplantation field. The "Consensus" stated that the technological preparations, ethics, and development of regulations are still lacking compared with globally advanced levels.

The above guidelines came as a result of advanced allotransplantation efforts in China. Especially, most of the experts who release the guidelines are from the allotransplantation field. The guidelines were prepared by a subcommittee of experts from regulatory, clinical, and scientific research specializations. The guidelines will guide the further development and standardization of clinical research on xenotransplantation.

References

1. National Health Commission of the People's Republic of China. The third category of medical technology catalog; 2013. http://www.nhc.gov.cn/wjw/ywfw/201306/4d1b9d11323342dcacedd31e893efac0.shtml. Accessed 28 Mar 2022.
2. First WHO global consultation on regulatory requirements for xenotransplantation clinical trials: Changsha, China, 19–21 November 2008. The Changsha Communiqué. Xenotransplantation. 2009;16(2):61–3.
3. Hawthorne WJ, Cowan PJ, Bühler LH, Yi S, Bottino R, Pierson RN 3rd, Ahn C, Azimzadeh A, Cozzi E, Gianello P, Lakey JRT, Luo M, Miyagawa S, Mohiuddin MM, Park CG, Schuurman HJ, Scobie L, Sykes M, Tector J, Tönjes RR, Wolf E, Nuñez JR, Wang W. Third WHO global consultation on regulatory requirements for xenotransplantation clinical trials, Changsha, Hunan, China December 12–14, 2018: "the 2018 Changsha Communiqué" the 10-year anniversary of the international consultation on xenotransplantation. Xenotransplantation. 2019;26(2):e12513. https://doi.org/10.1111/xen.12513.
4. China releases guidelines to strengthen governance over ethics in science, technology. http://english.www.gov.cn/policies/latestreleases/202203/21/content_WS6237b179c6d02e5335328099.html. Accessed 12 Jun 2022.
5. Chinese Medical Association of Organ transplantation, Xenotransplantion group. Guidance for clinical research on xenotransplantation (2018 recommended version). Organ Transplant. 2018;9(6):405–8.
6. Chinese Medical Association of Organ transplantation, Xenotransplantion group, Wei W, Kefeng D, et al. Experts consensus on islet xenotransplantation clinical trial (2019 Expert advice edition). Organ Transplant. 2019;10(6):672–7.
7. How far is the clinical success of xenotransplantation? http://www.news.cn/2022-04/07/c_1128537299.htm. Accessed 16 Jul 2022.