Proceedings of U.S.-China Forum On Biotechnology and Biomedicine

Fogarty International Center
National Institutes of Health
Bethesda, MD USA

December 4-5, 2000

第二届中美科学政策研讨会论文集

生物技术和生物医学

美国国家卫生研究院佛哥特国际中心
美国马里兰州贝塞斯达
2000年12月4-5日

阿方斯•布克西罗［美］，乔友林 主编
Edited by Alphonse Buccino, You-Lin Qiao

PROCEEDINGS
OF
U.S.-CHINA FORUM ON
BIOTECHNOLOGY
AND
BIOMEDICINE

Fogarty International Center
National Institutes of Health
Bethesda, MD USA

December 4-5, 2000

Sponsors

National Science Foundation, USA
National Institutes of Health, USA
National Natural Science Foundation of China

Convener

J. Thomas Ratchford, Ph.D., George Mason University

Forum Co-Chairs

Gerald Keusch, M.D., National Institutes of Health, NIH
Ji-Sheng Han, M.D., Neuroscience Res. Institute, Peking University

Proceedings Editors

Alphonse Buccino, Ph.D., Emeritus Professor, University of Georgia
You-Lin Qiao, M.D., Ph.D., Professor, Chinese Academy of Medical Sciences and Peking Union Medical College.

Notes of Preparation

This proceedings document was compiled from written and audio-taped notes of the conference sessions and from printed texts submitted by session presenters and coordinators of discussion sessions. Wherever possible, for accuracy, the available printed texts were given precedence over written or audio-taped notes. In both cases, the presentations appearing in this document have been edited for clarity.

ISBN 0-9718564-0-0
Published by the George Mason University
National Center for Technology and Law

CONTENTS

Note: Chinese translation begins on page 121

Session IV: Clinical Research Systems Compared

Session V: Differences in Chinese and U.S. IPR and Bioethics Systems

PREFACE

U.S. - CHINA COOPERATION PROGRAM IN SCIENCE POLICY, RESEARCH, AND EDUCATION

The U.S. - China Cooperation Program in Science Policy, Research, and Education is a decade-long initiative built on the experience gained from more than twenty years of cooperation in science and engineering between the United States and the People's Republic of China. The productive, long-standing relationship between the National Science Foundation (NSF) in the U.S. and the National Natural Science Foundation of China (NSFC) is a cornerstone of this cooperation. Additional information and links regarding this program can be found at:
<http://techcenter.gmu.edu/programs/science_trade_policy/us_china.html>

This forum is the second in a projected decade-long series of dialogues between representatives from the principal sectors of the science and technology (S&T) enterprise in each of the two countries. The first was held October 24-27, 1999 in Beijing, People's Republic of China. That meeting, addressing issues with significant implications for the vitality of science and engineering in the increasingly borderless, knowledge-based global economy, was an auspicious beginning. The summary of the proceedings of the first event can be found at: <http://www.twics.com/~nsftokyo/rm00-01.html>.

This second event, addressing Biotechnology and Biomedicine, was held December 4-5, 2000 at the National Institutes of Health, near Washington, DC in the United States. The Executive Summary and Report of Forum Sessions below provide a snapshot of the forum as well as a summary record of the presentations and discussions.

I. EXECUTIVE SUMMARY

Biotechnology and biomedicine were chosen as topics for the second activity in the decade-long U.S.-China science policy dialogues, especially because of the rapid advances taking place in research and applications. The goals in convening this forum were to insure that the voices and opinions of the best scientists of the two countries would become part of the public record with regard to key policy issues raised by these advances and to seek opportunities for expansion of cooperation in biomedical research and biotechnology between the two countries.

The forum was divided into two parts, the first dealing with research opportunities, and the second with challenges posed to scientific cooperation. These come about because of differences in our systems for assuring ethical research and the protection of intellectual property. Topics of discussion in Part 1 included:

1. Areas That Offer Mutual Advantages for Collaboration
2. New Technologies Providing Opportunities for Cooperation
3. Biotechnology and Ecology of Infectious Diseases
4. Clinical Research systems Compared
5. Differences in IPR and Bioethics Systems of China and of the United States

PART ONE: OPPORTUNITIES FOR RESEARCH COLLABORATION

The sessions of Part 1 began with descriptions of each country's organization, structure, and funding of biotechnology and biomedical research. The corresponding national organizations are the National Natural Sciences Foundation of China (NSFC) and the National Science Foundation (NSF) and National Institutes of Health (NIH) of the United States.

1. Areas that Offer Mutual Advantages for Collaboration. Drug Research Strategic Priorities. After a review of recent drug research in China, research in the future is to be directed toward the following strategic priorities. First, are the needs of social development. While the disease spectrum has changed in China, as it has in developed countries, the vastness of China and its population along with the differences among China's different regions mean that different kinds of diseases will co-exist for a time.

Second, China aims to contribute to the advancement of learning, especially in molecular biology and neurobiology. The timely exploration of drug genomics will be pursued into the post-genomic era, based on structural genomics and the developments from functional genomics to disease genomics.

Third, China aims to utilize fully the achievements of new high technology (e.g. computer-assisted drug design, combinatorial chemistry, new group screening). As part of this effort, China has established implementation programs including those addressed to improving research on traditional Chinese medicine in order gradually to modernize Chinese drugs. This program involves introduction of international standards into

substantive work to ensure high quality green medicinal material. It also involves implementation by the U.S. of administrative and regulatory standards such as the development of modern dosage forms and application of the General System of Preferences (GSP) applying to taxes and tariffs. The first targets will be development of complex prescriptions of Chinese drugs for diseases intractable to Western medicine. This will be oriented toward harmonization of the traditional Chinese holistic approach of using complex prescriptions for multiple targets in contrast with the tendency of Western drugs to focus selectively on a single target.

2. Technologies and Research Tools. Three new technologies or research tools were discussed with reference to facilitation of research: information technologies (IT), human genomics, and plant genomics. The Chinese presenter used telemedicine as an example of IT and illustrated by real-time and non-real-time diagnosis and consultation, on-line publication, and e-learning (or distance education). The U.S. presenter discussed five new information technologies (enhanced data acquisition, communications and networking, advanced application, data archives, and tools for knowledge generation and dissemination) with specific reference to the understanding of bio-complexity in the environment.

Human Genomics as a technology or tool for research was discussed by presenters from both China and the U.S. through reviews of each country's programs. The U.S. presentation noted that at lease five percent of the funding for the Human Genome Project in the United States goes to studies and research of ethical aspects.

Plant genomics as a technology or tool for research was also discussed. The Chinese presenter reviewed present and prospective research in rice genomics. The U.S. presenter spoke about nutritional genomics – the use of plants to improve human health – via enhancement of nutrition. In her talk, she referred to Golden Rice, a transgenic phenomenon that enriches the beta-carotene in rice, featured as a cover story in Time Magazine (Vol. 156, No. 5, July 31, 2000) to illustrate the concept of nutritional genomics as well as the popular interest in it.

3. Biodiversity and Ecology of Infectious Diseases. Biodiversity is a global concern and is generating international conventions and bilateral and multilateral environmental treaties, including the Convention on Biological Diversity, Convention on International Trade in Endangered Species (CITES), and the Ramsa treaty.

The biodiversity presentations addressed the importance of non-human biodiversity to human health in the four areas of (1) drug discovety from natural products, (2) biology of disease vectors, (3) biological indicators of environmental quality, and (4) use of non-traditional organisms to model human systems. All appear to be subjects of increased academic or industrial sectors in the United States and in China. This perspective was elaborated by examples and case studies including a review of China's R&D for the conservation of several of the endangered species with habitats in China and work on gene transfer and biosafety as presented in a review of transgenic fish R&D and related to biosafety principles published by OECD in 1993. A U.S. presenter discussed the

chemistry of biotic interaction to illustrate scientific benefits of studying the chemistry associated with biodiversity.

The U.S. presenter described the initiation of an interdisciplinary program on the Ecology of Infectious Diseases engaging ecologists, epidemiologists, and biomedical scientists. This interdisciplinary program addresses the challenge to science to probe the likely ecological relationships between, on the one hand, the unprecedented global rates of change of ecosystems due to biodiversity loss, and on the other hand the emergence of infectious diseases. There have been parallel advances in ecological science and biomedical research, but the relationships among these advances offer opportunities for exploration leading to deeper understanding. A review of AIDS research in China also demonstrated the nature and effectiveness of this interdisciplinary program and its potential with respect to China-US scientific collaboration.

4. Comparison of Clinical Research Systems of China and the United States. An overview of some features of China's clinical research system was part of the discussion of the Telemedicine program. Added to that was a presentation on cancer research. An outline of present status and further research plans, including better integration between traditional Chinese medicine and Western medicines was included in the presentation. The American participants discussed issues of the Organization and Management of Clinical Research at NIH, including design, monitoring, reporting, and oversight. Data and Safety Monitoring Boards (DSMBs) – to monitor patient safety and required for clinical trials – were highlighted in this review. DSMBs are mandated for appropriate oversight and monitoring particularly for multi-site clinical trials, in addition to the Institutional Review Boards (IRBs) for each site. China is familiar with and extensively uses Institutional Review Boards (IRBs), but the DSMB is not a well-implemented function in some research institutes in the current Chinese system.

5. IPR and Bioethics. On Intellectual Property Rights (IPR), China is undertaking its international obligations regarding IPR – including copyright, trademarks, and patents -- as part of its ongoing reform policy. It recognizes that the level of IPR protection is lower in China than in developed countries, but progress is being made. Participants described the current Chinese IPR system that China has built up was described, identified the IPR problems in biomedicine and biotechnology were identified, and discussed newly emerging problems (e.g. WTO participation).

IPR in the U.S. was reviewed in terms of Technology Transfer at NIH describing the development and implementation of the system used in the U.S. The review began with technology transfer legislation (e.g. Stevenson-Wydler Act) and its implementation in the 1980s and moved to its refinement in the 1990s. Goals of Technology Transfer, licensing terms, patents, examples of executed licenses, and royalties were discussed and illustrated (e.g. via Cooperative Research and Development Agreements – CRADAS, and Materials Transfer Agreement – MTA).

On bioethics, Guidelines on Ethical Review of Medical Research were published in China in 1998. The Guidelines address such concerns as conflicts of interest, scientific

integrity, risk and benefits of randomized trials, genetic markers of cancer risk and notification, employment, and health insurance. Four principles of bioethics are involved – beneficence, non-malfeasance, justice, and respect for autonomy of persons. Qualitative methods of presentation are used rather than quantitative. Protecting privacy and equal treatment are requirements. Adequate health care and compensation for participants in research are also strongly recommended.

The US emphasis at the forum built on the current status of bioethics guidelines and implementation. The presentation emphasized the extensive funding allocated to studies and research related to bioethics and activity in a global arena. The work of the National Bioethics Advisory Commission (NBAC) was discussed particularly with respect to new concerns. Bioethics has always been understood to be involved in the protection of individuals in clinical trials. But now, there is growing concern about biological material — blood samples, biopsy materials, slides, and survey data. An important challenge to bioethics research is illuminating the issues involved when the individual source is not present and may be far away or from a different nation.

The NBAC also called a global summit of national bioethics commission to promote dialogue about ethical issues that arise in research. There are national commissions in 38 countries so far and two international meetings have taken place in London and Tokyo, respectively. All recognize that the aim is harmonization and collaboration – there is no single set of guidelines that can be agreed upon by every nation in the world. This situation is recognized not as a barrier to collaboration, but an opportunity to use collaborative activities themselves to identify areas where there are difficulties that need to be worked through.

The distinction between process and substance in bioethics was emphasized. Informed consent, for example, may be thought of as a process and involving distinctions like signed consent versus proxy consent. On the substantive side, there are all kinds of creative ways of implementing the process, but the overarching issue must focus on respect for the person to assure a genuine willingness and voluntariness for people to allow things to be done that they might not ordinarily allow.

PART 2: DISCUSSION OF ISSUES AND DIFERENCES

Frank discussion of such socially difficult subjects such as AIDS in both countries was matched by equally frank discussion of differences in clinical approaches to drug testing, human subjects protection and ownership of, and therefore profitability from, basic biological substances. There were two Small Group Discussions reporting in the Plenary Session. The report on the discussion of Biodiversity and Intellectual Property Rights presented the following issues identified in the group discussion as policy challenges to collaborative research:

1. Differences between U.S. and China policies on what constitutes a patentable invention.
2. Costs of patent prosecution and maintenance are prohibitively high.

3. Lack of legal clarity and/or consensus among scientists regarding shared rights in a collaborative research project.
4. Access to biological materials is complicated by unclear and developing regulations restricting their transfer and the absence of clear standards for informed consent and for compensation.
5. While the principle of special rights of indigenous peoples to biodiversity is widely recognized, in practice it is difficult to define the individuals, communities, organizations or tribes to whom these rights accrue.
6. The increasing probability of commercialized outcomes from a research project may already be inhibiting basic science in some cases. Proprietary interests in research products are in some cases slowing access to samples, sharing of data, and publication of results.

Some guidelines for cooperation that were suggested by the Chinese delegation and widely supported:
1) Equity and voluntarity in design of project
2) Mutual benefit
3) Mutual participation
4) Equitable sharing of benefits
5) Mutual ownership of patents

The second group report on bioethics agreed with the views of the first report that many of the issues being raised go far beyond the responsibilities of this particular forum. However, it is important to signal from the perspective of the scientific community our concerns and interests in the issue of intellectual property, from both the perspective of the protection of intellectual activity and stimulation of international research, and also our concerns and interests about the ultimate accessibility of the product of that research to the population in need of new medicine, new medical technology and all the fruits of biomedical research. It was agreed that the record of this meeting should reflect the concern and interest of the scientific community. The group did not recommend specific proposals for reform, but identified the following issues.

1. Recruitment of participants as a bioethical policy challenge, especially in three areas: HIV-AIDS, cancer, and drug abuse.
2. Disclosure of information in public health, distinguishing between those issues important for disclosing to individuals about their own risk-taking behaviors and the information that is needed in order to protect them from the reactions of the community. This issue has two components — medical records and privacy.
3. What to do when a study provides useful information and potentially even a useful product, including whether there is a responsibility to provide the "study benefit" to individuals, communities, or countries.
4. Whether, as a policy, the focus should be on the low-technology alternative as it may not be realistic to study and test a very expensive drug or intervention that has no chance of becoming available due to cost.
5. Establishing Data Safety and Monitoring Boards and insuring their expertise. It is doubtful that a local committee in a small community will have as much expertise as a

larger national committee that can review multi-center studies. The issue then, is how to address levels of expertise necessary in oversight of international or bi-national research including the ethics committees themselves, the investigators, and the research participants.

II. REPORT OF FORUM SESSIONS

The goals in convening this forum were to insure that the voices and opinions of the best scientists of the two countries would become part of the public record with regard to key policy issues raised by these advances and to seek opportunities for expansion of cooperation in biomedical research and biotechnology between the two countries.

These goals were addressed through a review of:

- **Research opportunities and cooperative research**: areas at the frontiers of biotechnology and biomedicine where collaborations offer promise to extend our capacity for discovery and examine factors that have historically have helped collaborations between China and the US be successful, and

- **Challenges:** common features and the differences of our systems for assurance of ethical research and the protection of intellectual property.

These issues were addressed in two parts of the Forum: Part One comprised five sessions of presentations by participants from both countries focused on the first bullet above. Part Two reports on the session that focused on the second bullet. The following is an account of the information delivered and exchanged, organized in the sequence in which the sessions occurred.

PART ONE: RESEARCH OPPORTUNITIES

Session I. Areas that Offer Mutual Advantages for Cooperation

Five papers were presented in this session:

- "An overview of funding for biomedical research in China in the Department of Life Sciences," NSFC by Xinsheng Ye
- "Present situation of new drug research in China," by Bo Yi Qin
- "Acupuncture: from pain relief to treatment of drug addiction," by Ji-Sheng Han
- "Establishing successful research collaborations," by Roger Detels
- "NCI intramural experience in collaborative cancer prevention research in China," by Philip Taylor.

The paper by Xinsheng YE provided an overview of the organization and structure for funding biomedical research in China. The National Natural Science Foundation of China (NSFC) is a government agency established in 1986. As with the National Science Foundation (NSF) in the U.S., NSFC does not perform research but directs, coordinates, and finances basic research and some aspects of applied research, identifies and trains research talent, and promotes the advancement of science and technology for economic and social development. NSFC is composed of seven academic departments plus bureaus and an administrative office. The Department of Life Sciences is the largest department

and is subdivided into three sections: biology, basic medicine, and basic agriculture. [See http://www.nsfc.gov.cn].

The NSFC budget has been increasing rapidly from 80 million yuan RMB in 1986 to 13 billion yuan RMB in 2000 (about the equivalent of 1.6 billion US dollars at the exchange rate of 0.121 USD per China Yuan RMB). Projects fall into three categories: general, key, and major. The general category includes investigator-initiated projects, projects for young scientists, and projects for developing regions. These projects each have an average funding level of about 180,000 yuan RMB (about $22,000 dollars US). The Department of Life Sciences funding pattern from 1996 to 1999 is shown in Table 1.

Table 1
Department of Life Sciences, NSFC
Funding Pattern, 1996-1999

Project Category	Number of Projects	Total Budget
General	16,027	10 billion yuan RMB
Key	153	127.8 million yuan RMB
Major	78	78 million yuan RMB

The research emphases among these projects included immunology, cancer (or oncology), neuroscience, traditional Chinese medicine, post-genomics, and research on infectious diseases.

With the completion of human genome sequencing, the biomedical sciences are at the threshold of extraordinary advancement. Genomic research will have great impact on research on diseases and human health. Accordingly, the NSFC's Department of Life Sciences will place an even higher value on biomedical research and provide encouragement to projects employing novel concepts, approaches, or methodology; projects making use of the advantages and resources of China, and projects integrating biomedical research with research in other disciplines such as mathematics, physics, and material sciences.

Bo Yi Qin's paper described the present situation of new drug research in China. New drug research in China has a long history and this is a favorable time for research in China. Ranks of professionals, integrated branches of learning, and supporting resources have been developed to a high level of excellence. In the last fifty years, many kinds of new and inventive drugs have been approved for marketing in China including recent success in treating leukemia with arsenides. Also, there has been repaid progress over the last fifteen years in the production of drugs by biological methods. These include success in the development of genetic recombinant human growth hormone and eleven kinds of drugs produced by genetic engineering that have been approved for marketing. Eight other such preparations have been included in the pharmacopoeia of the People's Republic of China and another fourteen are in the clinical trial stage.

Thus, China is in the position of applying achievements in biomedical research relatively quickly to medical care. For example, mortality data have shifted. Where infectious