Biomedical Research and Ethical Regulations in China: Some Observations about Gene Therapy, Human Research, and Struggles of Interest

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Abstract

The intricacies of China's biopolitics and bioethics are frequently assessed through the lens of "cultural peculiarity" of China's moral common sense. Thereby it is overlooked that major factors of influence on contemporary legislation are at best indirectly construed in cultural terms, if not in conflict with traditional moral views. This paper introduces some recent trends in the ethical regulation of the biomedical sector in China and explains how they are inspired and particularly moulded by state political and stakeholders' interests. The licensing and industrial production of the world's first commercial gene therapy drug, "Gendicine", in China, will be discussed as a case example for the remarkable role researchers play in promoting the development of bioethics.

Contents

1. INTRODUCTION

China's biopolitics and bioethics are frequently assessed through the lens of an assumed "cultural peculiarity" of China's moral common sense. This

approach seems to respond to an attitude of respect for the differences and the underlying substantial identities of cultures. We hesitate to submit countries or societies, such as China, with an apparently alien cultural, historical or political background under norms and practices that have been crafted, for instance, in Europe or Northern America. This, among others, owes to considerations of Europe's imperialistic performance in history and the, more recently, resulting attempt to "learn from the past".

However, closer scrutiny indicates some relevant intricacies. For example, without proper reflection and information, one might overlook major relevant factors that influence contemporary legislation, which can rather be construed indirectly in cultural terms. Sometimes these factors may even stand in conflict with traditional moral views of a given society's culture.

Moreover, the meaning of culture and what it means to pay attention to or to respect cultural factors cannot be taken for granted, neither as a pure motive nor as a material key for the examination of the impact of a given culture.

Not at least, there is a danger that a cultural bias, of any brand, can be abused in merely instrumental discourse so that it supports the agenda of inexplicit interests. I shall attempt to show in the following how they can be misleading and stand in the way of understanding, for example, when they are built upon invented traditions or ungrounded generalizations.

The chosen strategy of this paper, that is, viewed from a critical cultural perspective [22], is to begin with an analysis of policy making in the areas of the life sciences and bioethics, as related to the establishing of universal (global) standards, and, in light of the reconstructed empirical situation, to undertake a preliminary cultural assessment of the context and content of particular areas of bioethics in China.

2. A CASE OF GENE THERAPY – FACTS, FIGURES AND THE EMERGENCE OF POLICY

2.1. Background state of the art

The modern Chinese biotechnology industry started two decades ago, in March 1986, with the government's 863 program. It was further developed with a focus on application of basic sciences in the National Basic Research Program (dubbed "973 Program"; of.: *http://www.973.gov.cn/English/Index.aspx*). It has now reached the turning point for a qualitative change: From "follow and copy" the Western countries to begin to innovate. China's accession into WTO has contributed to this change. Resolute adoption of international technical and procedural standards, in many areas, is helping China to pass the long way through the bottleneck of structural underdevelopment

[1]. Landmark projects in Genomics, such as China's contribution to the Human Genome Project, the sequencing of model or strategic key genomes (notably rice), have confirmed this development. In the biopharmaceutical sector, alongside with the recombinant protein drugs now the world's first gene therapy drug is produced in China [23,24]. In the molecular diagnostics sector, various biochip products for clinical use have been brought to market by Chinese biotech companies [2].

2.2. On the market

In October 2003, according to Chinese and international response, Shenzhen SiBiono GeneTech made history. It became the first company approved to market a gene therapy medication. China's State Food and Drug Administration (SFDA) licensed Gendicine for treatment of head and neck squamous cell carcinoma (HNSCC).

In China, there are about 2.5 million new cancer patients every year. An estimated 7 million receive medical treatment. Company representatives project that 3% of the 7 million cancer patients would try Gendicine, as there is no other competitive drug available in the Chinese market at present (i.e., 210,000 potential customers).

Gendicine is sold at around 3,000 yuan (US$362) per injection. An average cancer patient needs to use six to eight injections, as SiBiono GeneTech's chief, Peng Zhaohui, explained. The annual market value for this particular drug amounts to US$532,140,000.

Meanwhile, the privileged status of Gendicine as the only gene therapy treatment available in China may not last long. H101 Adenovirus Injection, another biodrug against cancer developed by Shanghai Sunway Biotech Co. Ltd is in its third phase of clinical trials. Sunway's representatives expect that H101 will get SFDA drug authorization shortly.

The annual gene therapy market worldwide is expected to reach US$9.9 billion by 2007. In China, the annual market for the therapy was at least 4 billion yuan (US$483 million) at the beginning, Peng estimated. The biopharma's sales revenue was 6% of the total Chinese pharmaceutical industry revenue in 2000, and was over 24 billion RMB Yuan (*ca.* 2.4 billion Euro) in 2001.

The market is expanding and structuring itself, following the distribution of available wealth and technology, emerging brands, health insurance systems and new marketing strategies.

According to a report from the Chinese National Center for Biotechnology Development (Wang, 2003), 21 recombinant pharmaceuticals such as recombinant interferon, insulin and GCSF have been commercialized since China's first genetically engineered drug (recombinant human Interferon a1b) was brought to market in 1993 (Table 1).

As of 2002, in clinical trial stage, were more than 150 biopharmaceuticals (30 of which had type A New Drug status), 7 proprietary gene therapy drugs

Table 1. Biotech firms with gene therapy products for cancer in phase 2 or later of clinical development

Company or research institute	Indication	Delivered gene	Vector	Phase of clinical development
Shenzhen SiBiono Gene Technologies (Shenzhen, china)	HNSCC	Tumor protein p53	Adenovirus	Approved
Shanghai Sunway Biotech (Shanghai, China)	HNSCC	HAdv5 oncolytic virus	Adenovirus	Phase 3
AnGes MG (Osaka, Japan)	Arteriosclerosis obliterans	Hepatocyte growth factor	Plasmid	Phase 2
GenVec, Inc. (Gaithersburg, MD, USA)	Pancreatic, esophageal and rectal cancers	Human tumor necrosis factor	Adenovirus	Phase 2
Introgen (Austin, TX, USA)	Head and neck, lung, breast, esophageal, ovarian, bladder, brain, prostate and bronchoalveolar cancers	Tumor protein p53	Adenovirus	Phases 1–3
Transgene (Strasbourg, France)	Cervical cancer	Human papilloma virus type 16 E6 and E7 antigens and interleukin 2	Vaccinia virus	Phase 2
Transgene (Strasbourg, France)	Breast, lung, prostate and renal cancers	Human mucin 1antigen and interleukin 2	Vaccinia virus	Phase 2

including those for malignant tumor and hemophilia B, and 6 tissue engineering products (bone, cartilage, skin, tendon, etc).[1]

Sunshine Pharmaceutical Co., Ltd. (Chinese name: Shengyang Sanshen pharmaceutical Co. Ltd.) (*www.3sbio.com*) was founded in 1993. In its pipeline are products including therapeutic monoclonal antibody, recombinant peptides, DNA vaccine and molecular diagnostic products, according to the company.

Other gene therapy medicines in clinical trial in China include Thymidine Kinase Cyto by Shanghai Institute of Cancer, Recombinant adeno-associated Virus-2 Human Factor by Beijing-based AGTC Gene Technology Co. and Recombinant Interleukin-2 Adenovirus Antitumor Injection by Chengdu Centre of Gene Technologies.

For the time being, Peng Zhaohui argues that the upcoming competition is not a major threat to Gendicine. Technically, these medicines still need more time to get SFDA approval. SiBiono could utilize this period of time to develop more uses for Genedicine and new products related to the gene therapy medicine. In 2004 there were more than 700 gene therapy medicines in clinical trial.

2.3. Clinical trials

Advantages in conducting clinical trials in China include access to a very large number of patients or subjects, in addition to low cost. For example, in Southern China, nasopharyngeal cancer has an annual incidence of 10–150 (with an average of 80) per 100,000 population, compared to 5–9 (7) in Northern China, 15–20 (18) in Alaska and Greenland, and 1 in North America, Western Europe and Japan [3]. (Other sources refer to total rates of 2550 per 100,000 in China [4] From another perspective, of the 57,500 new cases that occurred globally in 1990 almost 45% was from China [5]. Whereas consumption behaviours and environmental factors have a causal impact on the distribution of this malignant tumour [3,63], genetic patterns have been described as significant [4,5].

Ideally, China's huge patient pool makes organization of trials faster and consequently shortens time in which the statistically meaningful data can be collected – hence shortening time to market. This was cited by SiBiono as one of the reasons for its being the first with a gene therapy drug on the market [7]. Surprisingly, however, observers noted that only 120 human subjects were enrolled in the final trial stage by Peng's team.

As far as Peng is concerned, the success story of his gene therapy enterprise has but begun (cf. "The Genesis of Gendicine: The Story Behind the

[1]These numbers looked slightly different according to the "Chinese Biotechnology Industry Development Report 2002". According to this report, about 30 biopharmaceutical drugs were in clinical trial phase up till 2002 and about 100 biopharmaceutical drugs and health care products were in R&D stage.

First Gene Therapy. BioPharm International exclusive interview," *http://www.biopharm-mag.com/biopharm/article/articleDetail.jsp? id=95485&pageID=1&sk=&date=*, site visited June 8, 2005).

He claims that, in May 2003, after 14 years, the results from phase 2 and 3 trials showed complete regression of tumours in 64% of the 135 patients with late-stage HNSCC who took part from November 2000 after eight weekly intratumoral injections of Gendicine in combination with radiation therapy 29% of the patients experienced partial regression. Among all the patients, about 75% suffered from advanced nasopharyngeal carcinoma, which is a sub-indication of head-and-neck cancer.

Accordingly, another 240-plus patients with late-stage HNSCC or terminal-stage non-HNSCC tumours were treated with Gendicine during the period from June 2003 to the present, continuing the phase 2 and 3 clinical trials. A patient receives one injection per week for four to eight weeks consecutively as a treatment cycle. A standard dose is 1×10^{12} viral particles (VP). Like the previous data, these trials also are said to show the safety and efficacy of Gendicine. Peng concludes that, in combination with chemo- and radiotherapy, that is proven effective to some degree especially in nasopharyngeal cancer treatment [8,9], Gendicine can improve treatment efficacy in symptomatic terms by a quantitative factor of 3.4. Furthermore, this combination appears to alleviate the toxic side effects normally associated with chemotherapy and radiation therapy.

Notably, all data narrated here from Pengs research still await scientific evaluation and further corroboration. As of today, no scientific publication of the experiments has appeared in a relevant international journal. Peng maintains that seven scientific papers reporting on the safety and efficacy of the clinical trials have been published in the National Medicine Journal of China (10 December 2003). This journal is not rated among international scientific standard literature. He also pledges international publication forthcoming any time soon.

Although Gendicine has been formally approved by SFDA only for indications of HNSCC, terminal patients with no other avenue of treatment have been allowed, on a case-by-case basis, to receive Gendicine (with permission from the SFDA). Required were a request from the patient, the patient's family, and the agreement of the patient's doctor. The ethics protocol includes involvement of the patient, family, and the doctor-in-charge in giving informed consent. The relevant ethics protocols have been drafted by Pengs group and accepted by the authorities, although they appear to contradict the principles of recent Chinese bioethical regulations, which generally accept the international standard model of individual's informed consent, rejecting the formal participation of relatives (see Chapter 3). Peng Zhaohui is optimistic that Gendicine will be approved for a wider range of cancer indications: Clinical trials seem to corroborate that Gendicine can be used to treat cancers of the digestive tract (esophageal, gastric, intestine,

liver, pancreas, gallbladder, rectum), lung cancer, sarcoma, thyroid-gland cancer, breast cancer, cervical cancer, and ovarian cancer. The resulting market potential would be significant.

Peng's talk of success also builds upon the low incidence of relapse. According to his unpublished results, during more than three years of follow-up for the 12 patients with mid-to-late-stage laryngeal cancer who received Gendicine therapy in phase 1 clinical trials, no patient has relapsed. By contrast, among all patients who received only surgery, the three-year relapse rate is given by Peng as approximately 30% (with no more detailed data).

Although, statistically, 80% of the worldwide cases of nasopharyngeal carcinoma (a sub-indication of head-and-neck cancer), are in China, Peng claims that requests for Gendicine are also coming from the US, Germany, Denmark, Thailand, the Philippines, Greece, Canada, the UK, Singapore, Russia, Rumania, and Turkey. These patients are most likely of Chinese or Alaskan origin. Patients must come to China to be treated because the license is only valid in China (as to the profile of these patients, no data are available). In April 2004, about 400 patients had received the new treatment.

The development has been hailed in China as another sign of how the country is forging ahead in scientific research. However, the approval of Gendicine also provoked criticism because it is rather early to bring gene therapy to patients, especially the surprisingly small number of trial participants has raised concern about the scientific basis of the outcomes, although it should be noted that a small sample size does not necessarily indicate a flaw in the method. Still, a commentary noted that, "With 300,000 new cases of head and neck squamous cancers each year, China clearly thinks the benefits outweigh the risks" [10]. If Gendicine proves successful, SiBiono plans to launch the therapy in south-east Asia before seeking approval elsewhere.

2.4. Regulations and success

So why did the first commercial gene therapy treatment get produced and approved in China? "In China, where hundreds of thousands die of diseases such as cancer without access to the clinical options available to patients in the US and Europe, the potential for a one-time treatment that is relatively simple to administer is very appealing," explains Mark Kay, a director of the human gene therapy program at Stanford University (USA).

Public awareness of potential problems in gene therapy is just emerging. To my knowledge, there is no relevant scientific literature about the risk perception of Chinese people in the area of gene therapy. China has not been confronted with fatal failures, such as happened in the United States with the death of Jesse Gelsinger, who died from side effects of a gene therapy trial and more recently in Europe with the X-linked, severe combined immunodeficiency syndrome trials. Hence, it is assumed that the Chinese regulatory authorities may be more receptive to the potential benefits of the

technology and less alert towards the risks, until positive evidence suggests revision of policy.

Foreign competitors and commentaries have suggested that the regulatory process is less strict in China than elsewhere. "The recently approved gene therapy in China had only 120 people in clinical trials, whereas the same therapy in the US has hundreds of people and yet it has not been approved," says Hitoshi Kotani, senior vice president of gene therapy firm AnGes MG (Osaka, Japan). In a recent article dedicated to China as a test site and future market for new drugs, *Nature* magazine even speaks of an "ethical mire", regarding patients and trial subjects' rights, and refers to "the wilds of Chinese clinical research" [11]. Chinese bioethicists have rejected this statement as biased and poorly informed.

Researcher and entrepreneur Peng refutes that Gendicine was approved because of the allegedly looser regulation of the Chinese authorities. This sentiment is echoed, e.g., by Peng Shang, vice director of the Cell Engineering Research Center at the Fourth Military Medical University (Xi'an, China). "In fact, the SFDA had a routine practice not to approve any new kind of medicine if the kind of drug was not authorized by the US FDA," Shang says. Peng has been lobbying SFDA for years and the agency gradually changed its attitude, as shown by the approval of the new gene therapy and, for example, by giving a green light to clinical trails for a new SARS vaccine developed by Sinovac (Beijing) [12].

In general, expectations of combined economic and health-related benefits, with a special notion of international competition, and the obvious need for greater flexibility and efficiency as acknowledged through the SARS crisis, might have helped policy makers to adopt a less conservative attitude. Pressures on the administration, not to stand in the way of urgently needed good news in medicine and the health sector, provides keen researchers with new opportunities.

3. ON CULTURAL EXPECTATIONS

Interpreting legislation in the area of gene therapy can benefit from related research in China's bioethics. Let us now consider the debate about bio-policy making and its "cultural" dimension, in the area of human embryo stem cell research.

3.1. Culture misconceived

The assumed connection between cultural and research factors has been stated in a straightforward manner. For example, an alleged cultural peculiarity is propagated as a competitive advantage, in a special issue of *Nature*.

"Therapeutic cloning, stem-cell studies and other research areas that use animal or human embryos are controversial and raise religious and ethical questions (...).

These issues have led to unsupportive policies for cloning-related research, and the high costs of clinical trials for any proteins developed using this technology have forced many scientists and commercial companies to abandon promising research and to lose out on potentially profitable products.

China has a cultural environment with fewer moral objections to the use of embryonic stem cells than many Western countries, and (...) it could take a leading role in this field (...).

China has probably the most liberal environment for embryo research in the world (...).

In addition, the relatively easy access to human material, including embryonic and fetal tissues, in China is a huge advantage for researchers."

Together with China's cultural characteristics, "these technologies offer unprecedented research and commercialization opportunities for China" (Yang, 2004).

It is obvious that reference to culture can be more or less accurate. In these cases it plainly disguises vital stakes, such as in the competition between researchers for fame and funding. More often than not, culture is used as a magic stick to shun rational analysis and reason-guided discourse, which would uncover prevailing profane interest. Here, "culture" becomes an ideological pattern in the fabric of the frame to protect the purported humanitarian mission of biomedical and biotech research.

This observation indicates that "cultural arguments" require an educated assessment. It alerts us about the issue of sincerity among the proponents of "cultural diversity" and the "purity" of science.

3.2. China's approximation of ethical demarcations

However, proper research on this area reveals that, in sum, Chinese authorities establish a regulatory and ethical framework in relation to human embryonic and fetal stem cells that reflects emerging international standards. In the bioethical field, China is working towards a recognizable liberal European framework of regulation, in several cases based on the British House of Lords Select Committee recommendations. The main concern is, that it remains unclear, how fully such standards are accepted and reflected in practice outside the centres of international excellence.

According to findings from my own research, China's biopolitics can be characterized by two general moral demarcations, with notable Chinese peculiarities beyond pragmatic considerations of global harmonization of standards.

(1) *A Chinese Rubicon* defines the beginning of human worthiness of protection or dignity. The local transfer of an embryo, from the petri dish

into the uterus, demarcates the line between research and medical or invasive treatment. Manipulation *in vitro* might be permitted, but implantation into the female system is a taboo. (2) *A Chinese Limes* in bioethics is defined in terms of the social–moral dimensions that constitute the human being. As soon as a human is born alive, into the social environment, the full power of legal protection begins to apply.

3.2.1. A Chinese Rubicon

The Chinese Rubicon is based on a strong notion of natural purity and dignity, which can be traced back in the history of Chinese philosophy to Neo-Confucianism. Reference to other philosophical sources of naturalism are made, e.g., to the Han-dynastic amalgamation of cosmological, social–moral and political concepts, especially a sexualised interpretation of Yin and Yang [13,14].

According to an elaborated contribution on a New-Confucian background, biotechnology is, in principle a legitimate human endeavor. According to Taiwanese philosopher, Lee Shui-chuen, "assisting nature", e.g., biomedically, includes "purification" of humanity *and* the world. Moral quality and natural constitution are interconnected [25,26]. The natural constitution of an embryo may be altered if certain conditions apply, but, according to the Beijing school around bioethicist Qiu Renzong, an altered embryo may not become part of the causal chain, or, the human social–biological system. Products of hybridization and other forms of manipulation must remain inside the dish.

This *Imperative of Purity* already gained regulatory force in reproductive medicine (prohibition of nuclear transfer or ooplasma transplantation). The use of cloning technology for human reproduction is unlikely to be endorsed in China.

3.2.2. A Chinese limes

The second line of moral demarcation has a legal form. It can be adjusted through political or social process. This Limes in bioethics is defined in terms of the social–moral dimensions that constitute the human being. When a human is born alive legal protection begins to apply. It is the onset of a gradual development of the social career, in the course of which nobody may be manipulated or killed (exceptions apply).

Without the psycho-emotional and physical relationship with a mother, early in development, preceding immediate social relations, an embryo, accordingly, is "only a human life but not a full social entity". It may be taken as a commodity for "high ranking medical purposes".

Generally, any action in medical context is regarded as a challenge, because it interferes with the course of nature and humanity. Thus, it

assumes a practice that can, according to Confucianism, only be legitimate when interfering takes place in terms of "assisting Heaven and Earth", that is, not altering nature's course.

From a cultural perspective, both demarcations cannot be played against each other, nor can one be neglected. They constitute major elements in the fabric of cultural context.

Thus, the issues of moral status of human beings are not solved. In effect, the "embryo matter" is brought to the level of individual social relation clusters and taken out of the charge of the public and experts. It leaves room for a plurality of moral practices, without inviting ethical relativism.

The moral culture in China, as much as it can be described and as far as it is relevant for these issues, is far from being fundamentally at odds with moral views in European and North American countries. The moral landscape between the Chinese Limes and Rubicon is diverse.

Considering the adaptability of international bioethical regulations in China, consequentially, no major obstacles are expected from China's politics and administration, as far as technical issues and standards are concerned. The relevant Chinese policies respond to the pragmatic demand for harmonization of international standards. Practical implementation and monitoring of biopolicy, however, raises concern. Full assurance of respect of the powerful towards each individual's basic rights, born or unborn, is still a dream of the future.

Having said this, a word of caution should be in place. Even when described in fair and accurate manner, "culture" does not always help us to understand the factors involved and the major guiding motives in the expression of ethical norms. Nor is it always appropriate to discuss developments within the specific focus of an explicit cultural frame. Especially in areas of global competition and fast growth of vital stakes, as it happens in the case of biomedicine in China, the most articulate normative contributions are programmed to manifest pragmatic policy making in the light of the harmonization of international standards.

The theme of culture, though, is always present. But the proper level of attention to and emphasis on "culture" needs to be established.

4. THE ROLE OF RESEARCHERS IN ETHICS REGULATIONS AND THE INTERNATIONAL STATE OF THE ART: CHINA'S POSITION

It is part of the strategies of biotechnology-related policies to ally with internationally acclaimed researchers. James Watson, Francis Collins and other celebrities, for instance, have expressed admiration and support in particular for the genomics' activities organized by the Huada Genome Center at Beijing, under the directorate of Yang Huanming, with branches in Hangzhou and Xi'an. This ensured political backing in times of domestic competition

and political uncertainty (e.g., in 1998, the government was undecided, as to whether to adopt the HGO "public ownership" policy or Craig Venter's commercial approach to the sequencing of the Human Genome. These camps in China were represented by Yang Huanming and Chen Zhu, respectively).

Notably, Yang Huanming served as China's delegate to the UNESCO's IBC that drafted the relevant document for universal ethical standards in bioethics, such as the "Universal Declaration on the Human Genome and Human Rights", that is, the only international instrument in the field of bioethics, which was endorsed by the United Nations General Assembly (in 1998). Yang has been perhaps the most explicit and influential Chinese life scientist in the area of bioethics. In particular his engagement in the domestic movement of critics against the infamous "Mothers and Infants Health Care Law" (Eugenics Law, of 1995) (*Yousheng*) [15,16] has earned him international and domestic acclaim, supporting his humanistic call for responsible science.

In the case of Gendicine, gene therapy icon French Anderson, agreed to function as an unpaid adviser to SiBiono. His credentials confirmed the company's and researches' international standing. Anderson is quoted with a statement that is both, scientifically supportive and an exercise in a foreigner's politeness and a grain of symbolism that certainly was appreciated by his partners. Noting that the company's adenovirus is relatively simple compared with the gene-delivery systems being developed in the west. He offered, "but sometimes simple is better" [10].

In the absence of an explicit legal framework for his trials, Peng resorted to a method that had proven successful in other areas of the life sciences in China. He initiated the making of the relevant regulations, which would then be approved of and used as standards by the authorities in charge.

Here is an excerpt from the regulatory standards as they were accepted for the purpose of licensing for marketization of Gendicine (Taken from: http://www.biopharm-mag.com/biopharm/article/articleDetail.jsp? id=95486&pageID=1&sk=&date=; (visited June 8, 2005).

"Points to Consider for Human Gene Therapy and Product Quality Control State Food and Drug Administration of China. This document is authored by Shenzhen SiBiono GeneTech Co., Ltd. and the National Institute for the Control of Pharmaceutical and Biological Products, China. It is now SFDA's official guidance regarding gene therapy development. It was translated from the Chinese by Shenzhen SiBiono GeneTech Co., Ltd. May 1, 2004 by: Zhaohui Peng, State Food and Drug Administration of China, BioPharm International"... 8. Ethics study.

Special attention should be paid to medical ethics during clinical trials of gene therapy products. Details can be found in SFDA's GCP (Good Clinical Practice) regulations.[2] The study plan and potential risks associated with the

[2] SFDA guidelines for good clinical practice. Beijing, 1999, Sep 1.

clinical study should be clearly communicated to the patient and family members. Patients have the right to choose medical treatment options and terminate participation in the gene therapy clinical trial. The patient's medical history should be kept private. The patient cannot be enrolled in the study until the patient or family member signs the study consent form.

(These formulations are obviously sloppy and fall short of the standards set by other Chinese regulations, especially the "informed consent" regime that has been reformed according to international standards, namely stipulating that individual consent must be taken on the basis of strict non-coercion or compensation, full information of the patient/trial participant, anonymity of personal data and privacy protection.)

In the area of human embryo research and the related clinical activities, two outstanding females have contributed significantly to the enhancement of legislation. Lu Guangxiu and Sheng Huizhen serve as examples for individual leading scientists taking the initiative in making guidelines in the form of proposals, which would eventually be accepted as binding on the level of policy making.

Lu Guangxiu is a fertility doctor and medical researcher with a long career in both medicine and the political establishment of the central Chinese province of Hunan. It is generally known that she has taken the leading role in advising the process of legislation related to fertility, clinical research, IVF, embryo storage, and egg donation and sperm banking. Her internal rules stood model for the current state of national legislation. For example, the so-called "Human-Yale Pattern" [17] describes a practice of patient–physician co-operation that is designed to account for the peculiarities of Chinese families and culturally based attitudes towards reproduction and family matters. The current regulations of reproductive medicine and sperm banks largely result from Dr. Lu's experience as a second-generation reproductive doctor and her interests as well as concerns as a physician, researcher and policy maker [18].

When embryologist Sheng Huizhen returned to Shanghai from her research in the USA she brought alongside with her scientific excellence profound insight into the vital role of internationally accepted basic ethical regimes. In Shanghai, she found a situation that was characterized by an absence and an opportunity at the same time. The National Genome Center at Shanghai had established an ELSI group that was administratively connected with her Xinhua clinic (belonging to Shanghai Second Medical University). At that time, in 2001, there were no regulations on embryo research in place, except for a general and vague announcement by the Ministry of Health, rejecting human cloning, cross-species hybridization and "research contradicting common morality".

Sheng's personal intervention and research agenda eventually inspired the ELSI group to propose a set of guidelines, which were the first politically endorsed detailed standards for research on human embryos in China [19].

5. WHAT IT MEANS FOR US?

This overview has hopefully illustrated that a general reference to "culture" is misleading and not informative for the purpose of understanding bioethics in China properly. More empirical evidence must be provided, relevant levels of legislation and discourse must be distinguished and their content be protected from premature or out of context references to "culture".

Focused scrutiny on this area of society that is involved with policy making and the formulation of positive standards provides a realistic and detailed view of important patterns in the fabric of the country's normative culture, but it is still not adequately representing China's culture in her depth and wealth. It should be emphasized here, that in China, in particular, bioethics is not organized as a democratic or otherwise transparent and representative process, not to mention a discourse. This structural characteristic indicates the most imminent problem for bioethicists to face in China, from the perspective of ethics and in view of social sustainability of the life sciences [20]. Lack of transparency is detrimental to the overall political and ethical goal of trust, because it contradicts efforts to enhance individual and institutional accountability and responsibility. Evidently, this lack of transparency can be found in three interrelated areas. The scientific and medical facts are not clear and hence impossible to assess properly; the knowledge, understanding, communication and practice of ethical standards in this important area of the life sciences is inadequate (it is difficult to tell to what an extent this is owing to lack of compliance or insufficient knowledge); the practice of approval in this particular case indicates that authorities are challenged by opportunism and probably not fully trained and thus fail to implement state-of-the-art legislation. Altogether, the relevant process seems to take place inside a "black box" of decision-making, which creates grey areas of practice, inviting speculations and creating a discomforting public a scientific image.

European life scientists and ethicists have hardly begun to pay attention to China in this regard. In order to establish a culturally informed and sensitive bioethics research, more co-operative studies with Chinese colleagues are needed. They should obviously adhere to the fundamental scientific virtues of descriptive accuracy and methodological soundness. They should account for the real complexities of a heterogeneous society in transformation, that is, they should expect prescriptive uncertainty and be prepared to support ethics and legislation, even in places where they are not fully adhered to. This requires resolve in the ethics of science, especially self-discipline when facing the allure of non-scientific interests and to avoiding theoretical bias, such as in terms of culturalism.

Culturalistic flaws can be avoided if we methodically highlight the significant role of individual actors and institutions within the process of legislation. We can also benefit from systematic practical interaction, in the spirit

of critical partnership, with Chinese colleagues; given the intricacies of European bioethics this is certainly not a one-way street.

It has been the purpose of this paper to show an approach that can help to avoid cultural biases and presuppositions in a spirit of cultivated and interdisciplinary science, namely by distinguishing interpretative contexts, actors, and account for their respective relevance within a system that is as much in flux as it deserves serious attention.

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