

The Regulation and Approval of New Drugs in China

Rongling Deng

*WHO Fellow, Tufts Center for the Study of Drug Development, Tufts University, Boston, Massachusetts

Kenneth I Kaitin, PhD

Director, Tufts Center for the Study of Drug Development, Tufts University, Boston, Massachusetts

Chinese drug legislation, enacted in 1985, requires that new drugs be approved by the national drug regulatory authority before they can be marketed in China. Since enactment of this legislation, China has significantly improved its regulatory review process for new drugs. During the same time period, the pharmaceutical industry in China has shown considerable expansion. With China's membership in the World Trade Organization, the Chinese pharmaceutical industry is experiencing change and will continue to do so. The new Drug Registration Regulation, which is compatible with the World

Trade Organization agreement, went into effect on December 1, 2002. This paper reviews China's new drug approval history, regulatory policy and administration, and related issues with respect to China's climate for pharmaceutical innovation and the Chinese pharmaceutical industry. We provide approval data for new chemical entities (NCEs) approved from 1985 through 2000, and draw a picture of China's NCE review policies and the NCE approval process. We also offer views on changes to China's environment for pharmaceutical innovation since joining the World Trade Organization.

Key Words

China;
World Trade Organization;
New chemical entity;
Drug development;
Pharmaceutical industry

Correspondence Address

Kenneth I Kaitin, PhD,
Director, Tufts Center for the Study of Drug Development,
192 South St., Suite 550,
Boston, MA 02111 (e-mail:
kenneth.kaitin@tufts.edu).

*Ms. Deng is Senior Officer at the Sichuan Drug Administration, Chengdu, China. She conducted this research while on a two-year World Health Organisation fellowship at the Tufts Center for the Study of Drug Development.

INTRODUCTION

China's pharmaceutical industry has made significant progress since the early 1990s. As the industry developed, intellectual property became more important and intellectual property protection has improved, especially after China gained membership in the World Trade Organization (WTO) on December 11, 2001. China's pharmaceutical market offers great potential to both national drug firms and foreign firms interested in doing pharmaceutical research and development in China.

In this paper, we review China's history of NCE regulatory policy and administration, and discuss related issues with respect to China's climate for pharmaceutical innovation and changes in the Chinese pharmaceutical industry. In our analyses, we use the Tufts Center for the Study of Drug Development's definition of an NCE; that is, any NCE not previously approved for human use, excluding diagnostic agents, vaccines, and other biologic compounds (1). In China, "new drug" includes more than NCEs, but we selected only class 1 NCEs (see below) for this analysis.

The new Drug Registration Regulation, which is compatible with the WTO agreement, went into effect on December 1, 2002. The most sig-

nificant changes in the new regulation are a revised definition of a new drug and a new policy of marketing exclusivity in China. We do not cover the details of the 2002 regulation in this paper. Rather, we focus on the development and approval of NCEs in China from 1985 through 2000. Our results provide a picture of the current climate for pharmaceutical innovation in China and offer a baseline for measuring the impact of initiatives to modify and improve the process for bringing new drugs to the Chinese market.

REGULATORY ISSUES

A BRIEF HISTORY OF NEW DRUG REGULATION IN CHINA

In 1963, the Chinese Ministry of Health planned drug regulation to manage new drugs. In 1979, the Ministry of Health and the State Pharmaceutical Administration of China jointly published the New Drug Management Regulation. Under this regulation, pharmaceutical manufacturers did not need to conduct systematic scientific experiments on new drugs. Local companies easily received approval from the provincial department of health to market a drug anywhere in China.

In the early 1980s, drug regulation became in-

creasingly important to the public health. China enacted its first comprehensive Drug Administrative Law in 1985 (2), which had the goals of protecting the public health and promoting economic development in the pharmaceutical sector by establishing a legislative process for the regulation of drug manufacturing, distribution, and purchasing. This marked the beginning of a new era of drug regulation in China. The Drug Administrative Law was revised on February 28, 2001.

The Drug Administrative Law stipulates the responsibilities and obligations of drug manufacturers, distributors, and institutions that provide services to the drug industry. It requires premarket testing and approval for new drug products, and prohibits drug adulteration.

In the same time period, two new regulations were added in an amendment: Provisions for New Drug Approval (3) and Provisions for New Biological Product Approval (4), which were revised in 1999. These regulations require sponsors of New Drug Applications to provide adequate preclinical data to verify the drug's safety and to justify the commencement of clinical trials. They also provide drug classifications and outline the procedures for submitting New Drug Applications.

Other major regulations relate to new drug review. China's first importation rule was enacted in 1988, requiring certain imported drugs to be registered. Provisions for Importation Registration were enacted in 1991 (5) and revised in 1999 (6). Provisions for Drug Administrative Protection (7) were enacted in January 1993, providing 7.5 years of administrative protection (marketing exclusivity) for drugs that were un-

der patent protection from 1986 to 1992 in the United States and other major Western countries. These regulations were enacted as a result of international pressure to provide intellectual property protection, in accordance with the United States-China Memorandum of Understanding of January 1992.

In 1999, a new bureau responsible for new drug review was established. The State Pharmaceutical Administration of China, the Division of Drug Administration in the Ministry of Health, and the Division of Traditional Chinese Medicine in the Traditional Chinese Medication Administration Bureau were merged into the State Drug Administration. The new organization revised major provisions of drug regulation that had lagged behind the times and added new provisions and guidances related to new drugs, new biological products, and imported drugs. These regulations covered the drug registration procedure, new drug protection and technology transfer, Good Clinical Practice (GCP), and Good Laboratory Practice.

NEW DRUG CLASSIFICATION

From a regulatory perspective, NCEs fit into three classes of new drug classification. The statute defines "new drug" as any drug that has not yet been manufactured in China. Marketed drugs with a new dosage form, route of administration, or indication, and marketed drugs that are new combinations, are also subject to new drug regulatory review. New drugs are divided into five classes. NCEs fit into three classes. Under this definition, an imported NCE that has been sold in the marketplace but not manufac-

TABLE 1

Rationale for Classification of New Chemical Entities in China			
	Marketing Abroad	Foreign Pharmacopeia	Importation
Class 1	No	No	No
Class 2	Yes	No	No
Class 4*	Yes	Yes	Yes

* If the drug is either in a foreign pharmacopeia or imported, the drug is class 4.

tured in China is generally considered a new drug by local manufacturers. In the five classes of new drug classification, class 1, class 2, and class 4 are related to NCE review (Table 1):

- Class 1 NCEs are true NCEs that have not been marketed in the world,
- Class 2 NCEs are new drugs that have been marketed abroad, but are not part of foreign pharmacopoeia and have not been imported into China,
- Class 3 compounds are new combinations of already approved drugs,
- Class 4 compounds include the following: 1. NCEs that have been listed in the foreign pharmacopoeia of developed countries/regions (ie, the United States, the European Union, and Japan), or have previously been imported into China, 2. New dosage forms of approved compounds, or 3. New routes of administration for approved compounds, and
- Class 5 compounds are new indications for approved NCEs.

NCE review in China is based on whether an NCE is marketed abroad, and if so, for how long. According to the NCE classification above, marketing is the primary threshold, since it shows that the NCE has been used in humans for a period of time. The other threshold of inclusion in a foreign pharmacopoeia or importation provides information on the extent to which the NCE has been accepted worldwide. Different classes require different application data. Drugs that reach the Chinese marketplace are generally from one of three sources:

1. They are developed by local pharmaceutical companies,
2. They are the result of joint ventures, or
3. They are the result of importation.

THE REVIEW PROCESS

The Drug Administrative Law authorizes the State Drug Administration to approve new drugs for marketing. The State Drug Administration makes new drug approval decisions based on proposals from its Center for Drug Evaluation, which is responsible for scientific review of new drugs. The Center for Drug Evaluation plays an essential role in new drug registration. In 2000,

the Center for Drug Evaluation extended its mandate to include the review of imported drugs, generic drugs, and over-the-counter medications.

Provincial agencies also conduct part of the new drug reviews. These agencies review raw data, investigate facilities, and conduct establishment inspections. They assist the State Drug Administration in the preliminary drug registration work. The National Institute for Control of Pharmaceutical and Biological Products and Provincial Institutes for the Control of Pharmaceutical Products repeat certain experiments, particularly with regard to specifications, submitted in each application and determine whether the applicant's quality standards are adequate.

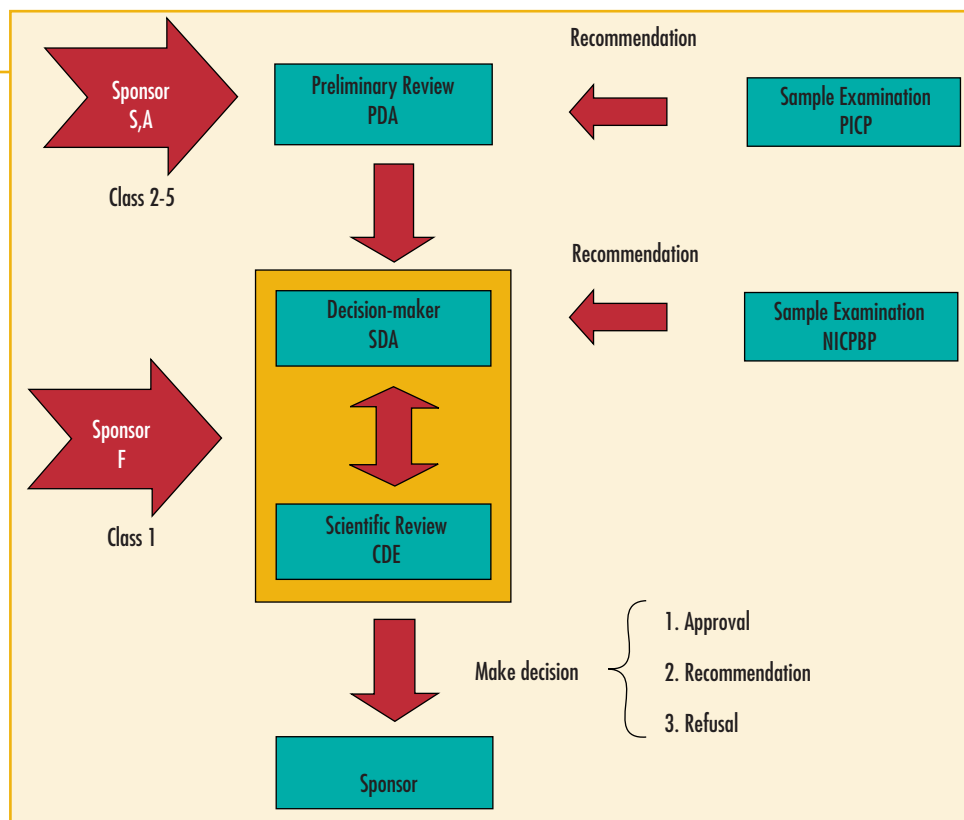
The new drug review process consists of the clinical study application and the new drug application. After receiving official approval, the applicant can conduct clinical trials. Prior to 1999, all NCE applications were first submitted to the Provincial Drug Administration. The NCE sample was sent to the Provincial Institutes for the Control of Pharmaceutical Products for examination, and the Provincial Institutes for the Control of Pharmaceutical Products offered suggestions to the Provincial Drug Administration, through which the application was transferred to the State Drug Administration or the Center for Drug Evaluation. After the State Drug Administration received the recommendation from the Center for Drug Evaluation, it made a decision as to whether the application should be approved, and this message was sent to the sponsor.

However, in the revised regulation of 1999 (see Figure 1), a class 1 NCE clinical and marketing application is submitted directly to the State Drug Administration for fast review. Via the State Drug Administration, the application is transferred to the Center for Drug Evaluation for a technical evaluation. The applied sample is sent to the National Institute for Control of Pharmaceutical and Biological Products for examination correspondingly. For class 2 and 4 NCEs, the process has not changed significantly.

FIGURE 1

The New Drug Application process in China.

Note: PDA=Provincial Drug Administration, SDA=State Drug Administration, CDE=Center for Drug Evaluation, PICP=Provincial Institute for the Control of Pharmaceuticals, NICBP=National Institute for the Control of Pharmaceutical and Biological Products, S=Standard Review, A=Accelerated Review, F=Fast Review



FAST REVIEW AND ACCELERATED REVIEW

The Provisions for New Drug Approval in 1999 include fast review and accelerated review (8). Fast review, intended to encourage drug innovation in China, is used for class 1 NCEs. Applications for fast review are submitted directly to the State Drug Administration. Accelerated review is intended to expedite the development of new therapies for life-threatening conditions and to limit the number of manufacturers producing the same new drug. Applications for accelerated review are submitted to the local drug administration. Accelerated review is used for new drugs in classes 2 to 5 that first submit clinical studies and for life-saving new drugs (eg, for cancer, HIV/AIDS, and orphan diseases).

NEW DRUG MARKETING EXCLUSIVITY

When the Drug Administrative Law was enacted in 1985, Chinese patent law considered drugs to be a special commodity used to treat diseases and save lives that, from a public health viewpoint, should not have patent protection. However, marketing exclusivity (ie, administrative

protection), which starts on the date of new drug approval, is an important incentive to sponsors. In China's regulations prior to 1999, class 1 new drugs have eight years of exclusivity, class 2 drugs have six years, class 3 drugs have four years, and class 4 drugs have three years. The exclusivity was extended in 1999; Class 1 NCEs have 12 years of exclusivity, class 2 and 3 NCEs have 8 years of exclusivity, and class 4 and 5 NCEs have 6 years of exclusivity (Table 2) (9).

Although marketing exclusivity is important in providing incentives for pharmaceutical research and development, it is a complex provision in China. Under this statute, several sponsors may develop the same compound and the same formulation simultaneously. This reduces the regulation's original incentive. Therefore, in revised provisions, the Chinese authority has the right to control the number of new drug manufacturers. In general, the authority prefers that no more than three companies produce the same new drug at the same time. This measure is to prevent too many companies from manufacturing the same product. This rule does not ap-

TABLE 2

New Drug Marketing Exclusivity			
	Class 1	Class 2 and 3	Class 4 and 5
Exclusivity	12 years	8 years	6 years

ply to new drugs that are currently under patent or have administrative protection.

NEW DRUG REVIEW TIME

Due to a scarcity of reviewing resources in China, many drug applications in the recent past were not reviewed in a timely manner. Every aspect of society criticized the slow review process. In an effort to improve the process, the Center for Drug Evaluation set limits on drug registration review time (Table 3). Total review time is not to exceed 3.5 months for fast review, 16.4 months for standard review, and 7.2 months for accelerated review. The clock stops when the Center for Drug Evaluation or a provincial agency issues an action paper (eg, approval, recommendation, or refusal). If the Center for Drug Evaluation requests more data to demonstrate the safety and efficacy of the new drug, it has 15 days to review supplemental data for fast and accelerated reviews and 4 months for standard reviews.

For standard reviews, the Center for Drug Evaluation usually holds consulting confer-

ences several times a year. The conference includes Center for Drug Evaluation staff, outside experts, and the sponsor. For fast reviews, consulting conferences can be held when the Center for Drug Evaluation finishes its review. Consulting conferences are similar to U.S. Food and Drug Administration advisory committee meetings, except that the meetings are closed to the public. Results of the conferences, however, are often accepted by the Center for Drug Evaluation.

PRECLINICAL AND CLINICAL REQUIREMENTS

Data and clinical study requirements differ by the class of drugs. The principle requirements are noted in Tables 4 and 5. Whereas applications for class 1 NCEs must include *in vitro*, preclinical, and clinical data, applications for class 2 and class 4 NCEs require fewer data. Class 2 NCEs can submit a pharmacology document. Class 4 NCEs do not require pharmacology research data and can substitute bioavailability studies for clinical trials (8).

TABLE 3

Timeframe for New Drug Review					
Time (days)	Provincial Drug Administration	State Drug Administration (file)	Center for Drug Evaluation*	State Drug Administration	Total
Fast Review	25 ¹	7 ²	30 (15)	29	106 days (3.5 months)
Accelerated Review	100	12	60 (15)	29	216 days (7.2 months)
Standard Review	100	12	180 (120)	80	492 days (16.4 months)
Imported Review	—	30	60 after meeting (60)	80	

Note: 1. The Provincial Drug Administration is responsible only for raw data review and facilities or establishment inspections.
 2. Before submitting an application to the State Drug Administration, the National Institute for the Control of Pharmaceutical and Biological Products should complete the technical test on the product in the application within 100 days, or for a vaccine, within 150 days.
 * Numbers in parentheses are supplemental review days.

TABLE 4

Data Requirements for NCEs			
	<i>In Vitro</i>	Preclinical	Clinical Study
Class 1	Yes	Yes	Yes
Class 2	Yes	+	Yes
Class 4	Yes	No	+

Note: += documented data or experimental data

IMPORTED DRUGS

Importing drugs is an effective way to provide patients with access to new therapies as soon as possible. It also promotes the progress of the Chinese pharmaceutical industry. The current regulations state that sponsors of imported drugs should conduct clinical trials (or bioequivalence studies) in accordance with Chinese procedures and requirements (5). If an imported drug has not previously been marketed in China, the sponsor must conduct clinical trials in compliance with the provisions for new drug approval and GCPs. Usually, imported products receive a five-year imported drug license. The sponsor must submit an application to renew the license six months before the expiration date.

CLASS 1 NCE REGISTRATION

CLASS 1 NCEs (FROM 1985 THROUGH 2000)

China approved 40 class 1 NCEs from 1985 through 2000 (10). Twenty-six of these NCEs were developed by Chinese pharmaceutical companies, 12 NCEs were developed by foreign-based, global pharmaceutical firms (in most cases, they submit applications in the name of their joint ventures in China), and 2 NCEs were developed by foreign start-up research companies that outsource manufacturing to local Chinese companies.

Of the 26 NCEs developed by Chinese companies, 17 were developed independently by domestic research institutes for the following categories: anti-malarial (6), anti-cancer (2), anti-platelet (1), anti-infective (1), anti-toxin (1), anti-AIDS (1), anti-allergin (1), anti-dizziness (1), abortifacients (2), and cardio-protective (1). The remaining nine NCEs used information provided in foreign publications at the outset of the research program, and were then developed by Chinese domestic institutions.

In 2000, China approved 17 NCEs: 6 of these were sponsored by Chinese pharmaceutical manufacturers, 10 were sponsored by foreign-based global pharmaceutical firms (or their

TABLE 5

Clinical Study Requirements for NCEs						
	Clinical Study	Number of Subjects		NCE Classification		
		Blinded	Open	Class 1	Class 2	Class 4
Clinical trials	Phase 1	No	20~30	Yes	+	No
	2	≥100	No	Yes	Yes	No
	3	≥300 (experiment)		Yes	No	No
	4	N	>2000	Yes	No	No
Bioequivalence	Bioavailability	18–24		No	No	Yes
(or Clinical equivalent)	Random comparative clinical trial	≥60	No	No	No	No or Yes

Note: += documented data or experimental data

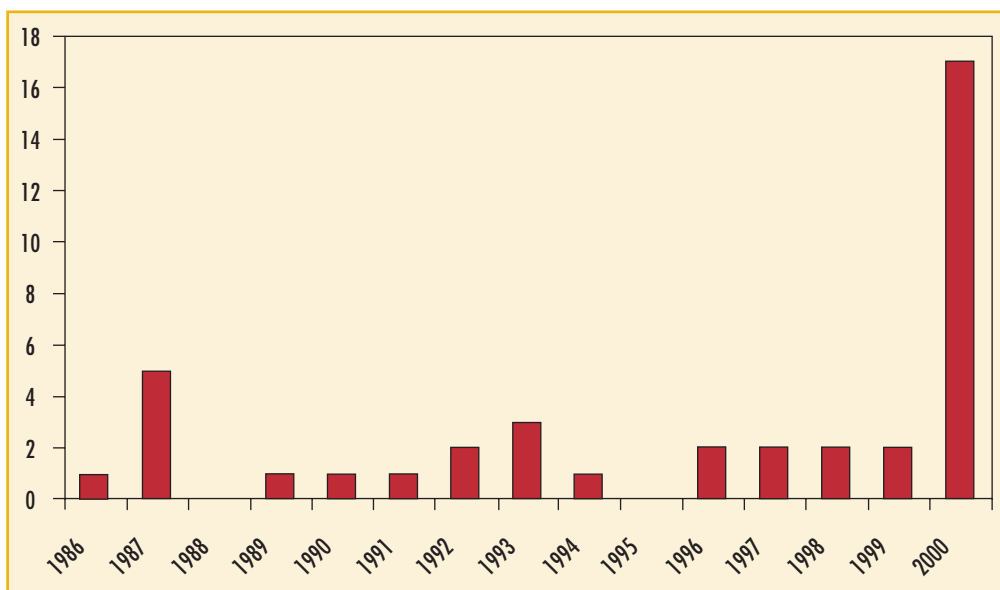


FIGURE 2

Annual new chemical entity approvals in China.

joint ventures in China), and 1 was sponsored by a foreign start-up research company which outsourced manufacturing to a local Chinese company.

ISSUES IN THE CHINESE PHARMACEUTICAL INDUSTRY

INTELLECTUAL PROPERTY PROTECTION

Before January 1, 1993, there was no patent protection for drugs. Local pharmaceutical companies could legally copy new drugs developed and patented in other countries. The Chinese authority now provides new drug marketing exclusivity to sponsors to provide incentives to, and stimulate the growth of, the pharmaceutical industry. In 1992, the United States and China negotiated a memorandum of understanding requiring China to protect intellectual property. As a result, on January 1, 1993, a new patent law took effect that includes drugs. Moreover, on the same day, the Chinese authority implemented the Drug Administrative Protection Law, which provides foreign companies with 7.5 years of administrative protection for drugs that had patent protection abroad from 1986 to 1992, but had not been previously marketed in China.

Since 1993, NCEs in China have had patent protection. This is a very important step toward improving intellectual property protection. En-

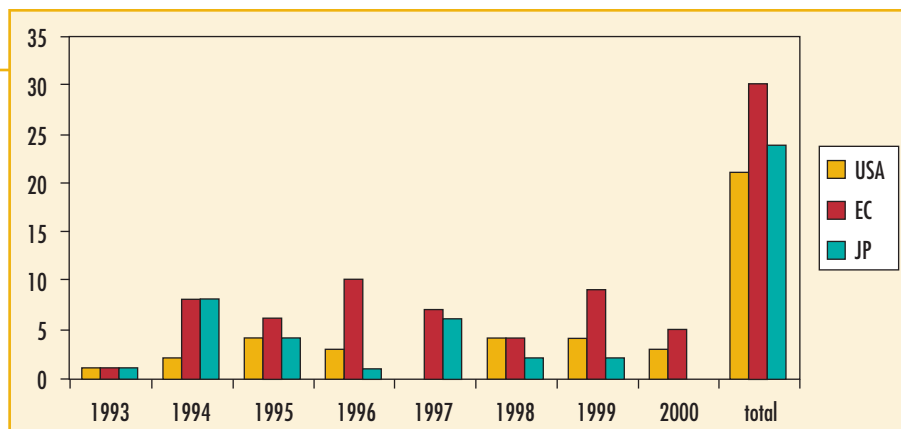
forcement, however, is not adequate. Foreign and domestic companies have complained that they could not gain effective intellectual property protection in the Chinese market. Protectionism and counterfeit drugs are the primary problems. The Chinese authority has acknowledged these problems and is revising pharmaceutical laws and regulations to eliminate provisions that violate the WTO agreement or Trade-Related Intellectual Property Rights, and China has agreed to protect undisclosed tests or data submitted in the marketing application process. In the meantime, China has taken measures to crack down on fraudulent pharmaceutical products.

ADMINISTRATIVE PROTECTION

From 1993 to 2000, China issued 75 administrative protection licenses to foreign pharmaceutical companies under the Administrative Protection Law (Figure 3). These were for drugs that had patent protection in their country of origin between 1986 and 1992, but had not been previously marketed in China (II). For drugs not previously marketed in China, companies submit an application via their agents or subsidiary companies in China. The license grants the sponsor monopoly status for 7.5 years, during which time local companies are

FIGURE 3

Administrative protection licenses in China.



prohibited from copying the drug. Sponsors of drugs with administrative protection licenses must apply to import the drug into China or manufacture it in China within one year of the date of the license.

THE CHINESE PHARMACEUTICAL INDUSTRY

From 1990 to 2000, the Chinese pharmaceutical market expanded rapidly. Pharmaceutical sales climbed from 32 billion Yuan (\$3.9 billion) in 1990 to 162.7 billion Yuan (\$19.7 billion) in 2000 (Figure 4). There are 6731 pharmaceutical manufacturers in China. Sixty companies produce 33% of the revenues and generate 70% of the profits of the entire pharmaceutical industry. One thousand and one manufacturers have 1256 Good Manufacturing Practice certificates.

Nearly all major international pharmaceutical companies have joint ventures in China (12).

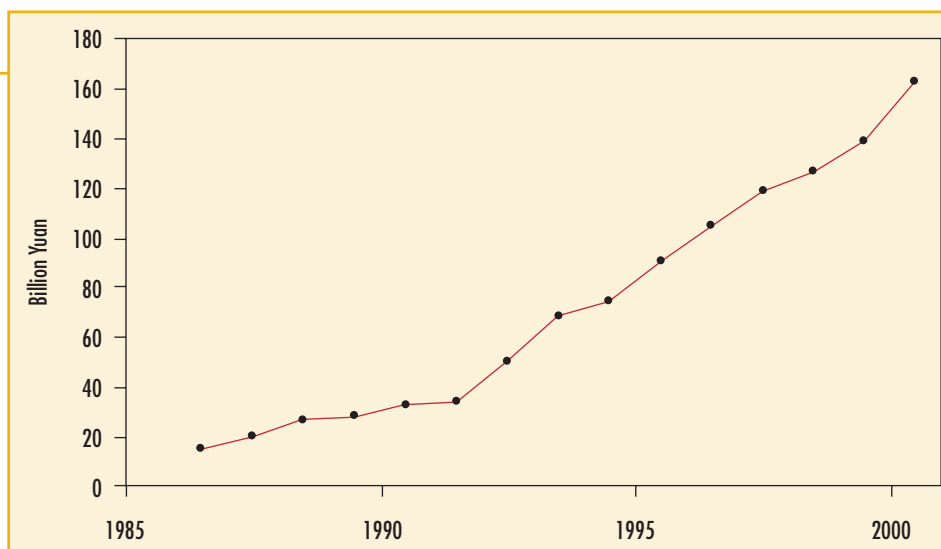
Many pharmaceutical companies are part of China's stock market, and many other types of companies invest in pharmaceutical research. These companies have the funds to recruit talented professionals and invest in new drug development. Many other small manufacturers, however, are disorganized and of poor quality. When these small companies close, start-up companies take over their businesses. These start-up companies have new technology and knowledge of the market. They take advantage of policies to obtain funding. Start-up companies are a promising part of China's future pharmaceutical industry.

The Chinese authorities have encouraged the development of NCEs by enacting more favor-

FIGURE 4

Annual pharmaceutical sales.

Source: Data from State Statistics Bureau in China.



able policies. In addition, some national programs focused on pharmaceutical innovation invest in the development of certain NCEs. Some NCEs developed under these programs have been approved for marketing, and some are currently in clinical trials. Local companies are trying to increase their utilization of foreign advanced technology, although lack of money is often a major obstacle. In the future, more New Drug Applications submitted in China will be the result of joint sponsorship by international and local pharmaceutical companies. China will remain an attractive location to foreign drug companies, because China offers many advantages in terms of the size of its marketplace, the relatively easy access to patients who are available for clinical trials, and inexpensive investigator costs for clinical trials.

CLINICAL TRIALS AND CONTRACT RESEARCH ORGANIZATIONS IN CHINA

As a site for clinical trials, China provides sponsors with potentially lower costs and a large patient base. An increasing number of foreign companies are conducting clinical trials in China. Some conduct clinical trials in China to market their products in the country and others seek additional research data to support product development and their applications in foreign markets.

In recent years, several foreign contract research organizations (CROs) have established a presence in China. However, due to the relatively high expense of working with these CROs, non-Chinese pharmaceutical companies are their primary clients; that is, CROs typically conduct clinical trials on behalf of foreign pharmaceutical companies. CROs have remained active in China since the country joined the WTO.

Many domestic drug companies hesitate to work with foreign CROs due to the price barrier, although this creates a competitive disadvantage for local firms. Domestic start-up CROs meet some needs of domestic drug companies; although these start-up CROs currently submit applications to the regulatory authority on behalf of their clients, many do not yet conduct clinical trials.

REGULATORY REVISIONS

The Chinese authority will be revising China's drug administrative regulations to comply with the WTO agreement. The definition of a new drug will be harmonized with worldwide standards. This will lead to other changes, such as the creation of new drug classifications, domestic administrative protection of new drugs, generic drug regulatory procedures, a registration process for imported drugs, simplification of registration procedures, clinical trial regulations, and other new regulatory practices.

The Chinese authority is likely to cancel all administrative protection procedures in the near future in favor of internationally recognized patent protection, but it is still possible for China to protect life-saving drugs, in a manner similar to the orphan drug program in the United States. Drug registration policy and registration procedures will be more transparent and easier for applicants, whether the sponsors are domestic or foreign companies. Provisions that limit the number of manufacturers of generic products will be eliminated.

The new drug policy will be quite different from current drug policy, and will greatly impact the development of China's pharmaceutical industry. Currently, China's pharmaceutical marketplace is complicated, with some products under patent protection and some under domestic administrative protection. The WTO agreement specifies the direction of new drug policy. This will simplify China's pharmaceutical regulation.

The new Drug Registration Regulation took effect on December 1, 2002. The new regulation changes the definition of China's "new drug," from previously "not marketed" to "not manufactured" in China. Under this definition and consistent with the WTO agreement, China's framework of drug regulatory review is fundamentally different from the past. For NCEs, marketing exclusivity will be protected by patent rather than administrative protection.

HEALTHCARE SYSTEM REFORM

Pharmaceuticals play an important role in China's healthcare system, especially because healthcare institutions rely greatly on drug sales

for their revenues. According to data from the Ministry of Health in 2001, 50% of hospital revenues are from pharmaceutical sales in urban areas. In rural regions, more than 80% of health center revenue is from pharmaceutical sales. Healthcare system reform will greatly change new drug development and delivery. Introduction of health insurance, hospital reforms, and changes in payment systems would transform the current model of pharmaceutical manufacturing and distribution.

Although healthcare reform is critical, it is not easy to achieve in China. While some metropolitan areas are well-developed, people in many rural regions still live in considerable poverty. Economic differences between rural and urban regions and the disparity between incomes in urban and rural areas make primary healthcare problematic. Limited resources add to the problem. The government is responsible for providing primary healthcare to all Chinese people. However, there are many competing goals in China. Decentralization makes local government at every level emphasize economic growth rather than investment in public health. In addition, healthcare costs are soaring.

Capping drug prices is a direct measure that governments take to control increasing expenses. Whereas containment of drug prices may be necessary in order to provide affordable drugs, price controls may hamper the development of the Chinese pharmaceutical industry. In-depth reform of healthcare financing and payment and organizations in the healthcare system is critical to ensure that primary healthcare services are available to all China's citizens.

PERSPECTIVES SINCE JOINING THE WTO

China's membership in the WTO promotes progress. China has agreed to establish a system to make laws and regulations more transparent and predictable and to treat domestic and foreign pharmaceutical companies in the same manner. Intellectual property rights are protected, and effective measures are being taken to ensure further the development of intellectual property protection. China's tariff for pharma-

ceuticals was reduced to 4.7% on January 1, 2003 (13). Registration for imported drugs is now similar to registration for domestic drugs.

Since China's accession into the WTO, Chinese companies have had the freedom to import and export products. As of December 11, 2002, joint ventures with foreign firms that have a minority ownership had importing and exporting rights. As of December 11, 2003, joint ventures with foreign firms that have a majority ownership will have importing and exporting rights. By December 11, 2004, all companies will have importing and exporting rights, and pharmaceutical wholesale and retail trade services will be open to foreign companies (14).

Over the next decade, the domestic pharmaceutical industry will lose its protection and face a high level of competition from foreign companies and joint ventures. Multinational research-based pharmaceutical firms will have advantages over Chinese firms in the NCE marketplace. Since most large pharmaceutical firms have been in China's marketplace through joint ventures, tariff reduction will not significantly lower the price of their drugs. Although the tariff is reduced, the drug prices of international pharmaceutical firms are still much higher than those of domestic companies that copy those drugs. Tariff reduction will not have a major impact on China's drug marketplace because of price controls, location of companies, and other factors.

The generic marketplace, however, will be a hot point for domestic and foreign companies. Most domestic companies implement their marketing strategies on generic products, and the WTO would offer opportunities for foreign generic companies.

The State Drug Administration has announced that all local drug manufacturing establishments should have approved Good Manufacturing Practice (GMP) certification by June 30, 2004. Establishments that do not have GMP certification will not be allowed to produce pharmaceuticals. Establishments that have GMP certification can do contract manufacturing, which would enable them to manufacture products for start-up

companies that have access to technology but no manufacturing facilities.

China's distribution system will also change. According to the State Drug Administration, 503 drug chain retailers in China own 18527 stores. The Chinese government plans to build large drug distribution centers to foster competition. Domestic distributors, however, do not have much experience in advanced management of distribution systems. A good distribution system is essential to the healthcare system and is very important in preventing the dispensing of counterfeit drugs. Foreign drug distribution companies will have a considerable advantage when they enter the Chinese marketplace, due to their experience and services.

Since China joined the WTO, the Chinese drug regulatory system has been in a constant state of change. This has created a degree of uncertainty and confusion for the domestic drug industry and for foreign firms operating in China. In the next few years, however, a new model for the Chinese pharmaceutical marketplace will be shaped, benefiting both the Chinese people and the Chinese pharmaceutical industry.

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REFERENCES

1. Kaitin KI, Healy EM. The new drug approvals of 1996, 1997, and 1998: drug development trends in the user fee era. *Drug Inf J*. 2000;34(1):1–14.
2. *Drug Administrative Law*. Beijing, China: National Law of the People's Republic of China; 1985.
3. Ministry of Health, China. *Provisions for New Drug Approval*. Beijing, China: Ministry of Health; 1985.
4. Ministry of Health, China. *Provisions for New Biological Product Approval*. Beijing, China: Ministry of Health; 1985.
5. Ministry of Health, China. *Provisions for Importation Registration*. Beijing, China: Ministry of Health; 1991.
6. State Drug Administration, China. *Provisions for Importation Registration*. Beijing, China: State Drug Administration; 1999.
7. State Pharmaceutical Administration of China. *Provisions for Drug Administration Protection*. Beijing, China: State Medical and Drug Administration Bureau; 1993.
8. State Drug Administration, China. *Provisions for New Drug Approval*. Beijing, China: State Drug Administration; 1999.
9. State Drug Administration, China. *Drug Registration Procedure*. Beijing, China: State Drug Administration; 2000.
10. Center for Drug Evaluation, China. National new drug registration database, 2001. www.cde.org.cn. Accessed May 2, 2002.
11. State Drug Administration. Administrative protection approvals: 1993–2000. www.sda.gov.cn. Accessed September 10, 2001.
12. Summary of the National Pharmaceutical Administration in 2001. Xinhua News Agency. big5.xinhuanet.com/gate/big5/news.xinhuanet.com/zhengfu/2002-02/07/content_272025.htm. Accessed May, 2, 2002.
13. US Department of Commerce, International Trade Administration. Pharmaceutical industry fact sheet: China. www.mac.doc.gov/China/Docs/industryfactsheets/pharmaceuticals.html. Accessed May 24, 2002.
14. Hamrock S, Whiting, C, Blaha C, Clark H, Lashley D. Market access and compliance: what it means for U.S. industry. www.mac.doc.gov/China/Docs/exportamerica/WTOChina.html. Accessed May 24, 2002.

