New developments in China's pharmaceutical regulatory regime

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Abstract Since 1998, the People's Republic of China's (PRC) pharmaceutical regulatory regime has been undergoing a revolutionary change. A number of subsidiary regulations have been revised or issued. The new *Pharmaceutical Administration Law of the People's Republic of China* (Pharmaceutical Law) has been promulgated by the President of the PRC with Order No. 45 on 28th February, 2001, and came into effect on 1st December, 2001. This paper looks at the new developments and the challenges ahead. Traditional Chinese medicines are governed by various different regulations in the PRC. This paper will not go into such regulations.

Keywords: China, PRC, pharmaceuticals, drugs, law, policy

State Drug Administration

The People's Republic of China (PRC's) pharmaceutical regulator, the State Drug Administration (SDA), was established in August 1998, and it took up the responsibilities of the former Drug Administration Bureau in the Ministry of Health, the former State Pharmaceutical Administration Bureau and the former State Administration of Traditional Chinese Medicine. It is responsible for the administration of chemical pharmaceuticals, biological pharmaceuticals and traditional Chinese medicines. Currently, the SDA is directly under the State Council of the PRC.

Pharmaceutical manufacturing and business enterprises

Establishing pharmaceutical manufacturing and business enterprises used to require approval from both the local drug administrations and the local health administrations. Since 2000, only approval from the local drug administrations is required; this change is codified in the new *Pharmaceutical Administration Law of the People's Republic of China* (Pharmaceutical Law). The simplified examination and approval procedures are accompanied by a system of increased post-approval monitoring.

The new Pharmaceutical Law stipulates that pharmaceutical manufacturing and business enterprises must comply with good manufacturing practice (GMP) and good sales practice (GSP), respectively. Such compliance is rare at this time. It is expected that the requirement for compliance is to be phased in by stages. The establishment of pharmaceutical wholesalers must be approved by provincial level drug administrations, whereas pharmaceutical retailers are to be approved by drug administrations above the county level.

Toll manufacturing was made available

with the issuance of the Notice on Regulations Relevant to the Production of Pharmaceuticals in Places Other than Those of the Owners of the Pharmaceutical Approval Numbers, and Entrustment of Pharmaceutical Processing, effective 10th August, 1999. The availability of toll manufacturing is confirmed in the new Pharmaceutical Law.

Product registration

The new Pharmaceutical Law did away with local product registrations and local product quality standards of pharmaceuticals.

Drugs

New pharmaceuticals

'New pharmaceuticals' are defined as chemical pharmaceuticals and traditional Chinese medicines that have never been produced in the PRC, and pharmaceuticals and traditional Chinese medicines for which a new indication, a change in the route of administration, a change of dosage form or a new formulation is to be adopted. A discussion of the impact of the new legislation on traditional Chinese medicines is outside the scope of this paper. 'New biological pharmaceuticals' are defined as biological pharmaceuticals that have not been approved for the PRC market or that involve revolutionary changes to the processing technology, possibly affecting their safety and effectiveness. The regulatory regime for new pharmaceuticals was reformed with the issuance of the new *Measures for the Examination and Approval of New Pharmaceuticals*, the new *Measures for the Examination and Approval of New Biologicals* and the new *Regulations Concerning the Protection of and Transfer of Technology for New Pharmaceuticals*, all effective 1st May, 1999.

New chemical pharmaceuticals are separated into different categories:

- Pharmaceuticals that have not been approved in any country but for which studies have been reported fall within Category I of chemical new pharmaceuticals.
- Pharmaceuticals that have obtained market approval, are not yet in pharmacopoeias and have not been imported into the PRC fall within Category II.
- New formulations made from existing chemical pharmaceuticals fall within Category III.
- Formulations in non-PRC pharmacopoeia fall within Category IV.
- Existing pharmaceuticals that have new indications fall within Category V.

New biological pharmaceuticals are also separated into different categories:

- Biological pharmaceuticals that have not been approved in or outside the PRC fall within Category I.
- Biologicals that have already been approved outside the PRC, have not been included in a pharmacopoeia and have not been imported into the PRC fall within Category II.
- Biologicals that have been produced using new production technology fall within Category III.
- Biologicals that have been approved for importation into the PRC fall within Category IV.
- Biologicals with a new indication fall within Category V.

The protection for new pharmaceuticals is lengthened under the new regime: for Category I drugs protection is now 12 years, for Category II and III drugs it is 8 years, and for Category IV and V drugs it is 6 years. [During a protection period, no one except the holder of the relevant New Pharmaceutical certificate or its licensee may produce the same product.] Pharmaceuticals that are no longer able to obtain patent protection (for instance because of the lack of novelty) may still be eligible for new pharmaceutical protection.

Good laboratory practice (GLP) and good clinical practice (GCP) must be complied with in non-clinical and clinical researches respectively. Clinical researches must be

conducted at approved sites. Different categories of drugs have different clinical research requirements.

Imported drugs

All imported pharmaceuticals must be registered with the SDA, which issues *Import Drug Registration Certificates*. The pharmaceuticals must be imported through designated ports. Importers report the shipments to the local drug administrations at the ports of entry. Drugs to be sold in the PRC for the first time must be tested prior to importation or sales.

Under the *Regulations for the Recordal of Domestic Sales Agents for Imported Pharmaceuticals*, issued on 20th August, 1999, distributors of imported pharmaceuticals must record with SDA within two months of signing the relevant distributorship contracts.

Prescription drugs and over-the-counter (OTC) drugs

In the past, the PRC did not separate prescription drugs and OTCs, with the result that drugs that should be classified as prescription drugs may be obtained without a prescription. The separation of these two types of drugs was implemented with the effectiveness of the *Measures for the Classification and Administration of Prescription and Non-Prescription Drugs (for Trial Implementation)* on 1st January, 2000. Separate regulatory regimes govern these two types of drugs.

OTCs are further separated into Category A and Category B products, with tighter regulatory control being exercised over Category A OTCs. For instance, Category B OTC may be sold, but Category A OTCs may not be sold in shops that do not have licences for pharmaceutical business enterprise.

Marketing

Packaging

The *Measures for the Administration of Materials and Containers Used in Pharmaceutical Packaging (for Provisional Implementation)*, effective 10th January, 2000, classifies pharmaceutical packaging materials into different categories. Different approval requirements are stipulated for the production of the different packaging materials. Applications for the production of Category I packaging materials (which are in direct contact with the relevant pharmaceutical products and are used directly without further preparation) and applications for import licences are submitted to the SDA. Applications for the production of Categories II (which are in direct contact with the pharmaceutical products and may be easily cleaned) and III (packaging other than Categories I and II packaging which may directly affect the quality of the pharmaceutical product) packaging materials are submitted to the local drug administrations.

Labelling

Pharmaceutical labels and drug information inserts must be approved prior to use. Information must be provided in Chinese and written using standard Chinese characters. The SDA has prescribed standard forms for drug information inserts.

Drug information inserts with standardised contents have also been published for OTCs. The SDA has also prescribed a logo for OTCs (Figure 1). It must be used within 12 months of registration of the relevant OTC. The logo is to be used in red for Category A OTC and green for Category B OTC.

The SDA has given the industry until 30th June, 2002, for all products to comply with the new labelling requirements.

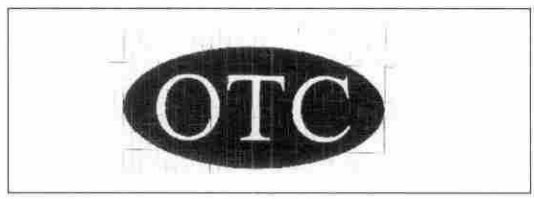

Fig. 1 OTC logo

Advertising

Pharmaceutical advertisements continue to require approval. Advertisements of prescription drugs in mass media have been banned. This is to be strictly enforced by 1st December, 2002. Prescription drugs may be advertised only in medical journals. Pharmaceutical manufacturers and distributors may not advertise and sell directly to patients.

Starting on 1st January, 2001, annual advertising fees of pharmaceuticals for tax deduction during the current year are limited to 8 per cent of sales income. However, excess amounts may be carried forward to subsequent tax years.

Medical insurance

Since the 1950s, state health benefits have been available to employees of government and state-owned enterprises. Based on reportedly successful results from various pilot projects undertaken since 1994, the PRC has commenced reform of its medical social security system with the issuance of the *Decision of the State Council Concerning the Establishment of a Basic Medical Insurance System for Urban Staff and Workers*, issued by the State Council on 14th December, 1998. A medical insurance system funded by employers and employees is to be developed. All employers and employees in urban districts are to enrol in the system.

The State Drug List for Basic Medical Insurance (Reimbursement List) identifies drugs selected at the national level that are subsidised under the medical insurance system. Provincial authorities develop their own lists for their jurisdictions. The Reimbursement List consists of Category A and Category B drugs. Category A pharmaceuticals are supposed to be pharmaceuticals for which there is a clinical need, and that are widely used, effective and cheaper than other pharmaceuticals within the same group. Category B pharmaceuticals are supposed to be pharmaceuticals that provide a choice in clinical use and are effective, but that are slightly more expensive than Category A pharmaceuticals. Category A remains unchanged for implementation at the local level, whereas local authorities may vary the items in Category B to a maximum of 15 per cent. If a drug is not on the local lists, patients may not obtain reimbursement for it and must pay for it themselves. Very few drugs that are imported or manufactured by foreign investment enterprises are on the lists.

Pharmacies and hospitals are selected to supply their products and services under the new medical insurance system. They are to enter into contracts with the local medical insurance authorities.

A separate account is set up for every employee for tracking the actual medical expenses of the employee. There is also a collective account for the benefit of all of the insured.

Pricing

Price controls are specifically addressed in the new Pharmaceutical Law, which specifies that pharmaceutical manufacturing and business enterprises and medical institutions must follow the government's set and guided prices. It also specifies that pharmaceutical manufacturers must provide the government with production and business costs. Pharmaceutical manufacturing and business enterprises and medical institutions must also provide the government with such information as the actual prices and quantities, etc., of their pharmaceuticals.

Off-the-books kickbacks are specifically prohibited in the new Pharmaceutical Law.

Sampling and testing

To prevent abuse and undue burdening of pharmaceutical enterprises, the new law specifically prohibits the collection of fees for sampling and testing of pharmaceutical products by the authorities in the course of routine monitoring of the industry.

Medical devices

Effective from 10th April, 2000, the new Measures for the Administration of the

Registration of Medical Devices superseded the old Measures for the Administration of the Registration of Medical Devices. The approval process for imported medical devices used to involve only a review of the registration documents from the government of the country of origin. Now, Category II and III medical devices must undergo local type tests.

Separate regulations have been issued with respect to advertising, manufacturing and business enterprises, new products and the categorisation of medical devices.

Joint venture

Investment can be made in Sino–foreign joint venture hospitals, under the Provisional Measures for the Administration of Sino–Foreign Equity Joint Venture and Cooperative Joint Venture Medical Institutions, effective from 1st July, 2000. The total investment value of a joint venture may not be lower than RMB20,000,000 (US$2.5m). The equity holding or rights of the Chinese party may not be lower than 30 per cent. The term of the joint venture may not exceed 20 years. Wholly foreign-owned hospitals are not yet possible.

Pilot projects of Sino–foreign joint venture pharmaceutical business enterprises require foreign participants to be financially strong, have advanced business experience and sales techniques and a wide international sales network, be reputable, have good business records and be able to promote exports. The average annual sales of the foreign party to a retail joint venture must be above US$2,000m in the three years prior to the application for approval of the joint venture. The capital of the foreign party in the year prior to the application should be more than US$200m. The annual wholesale value of the foreign party to a wholesale joint venture should be above US$2,500m for the three years prior to the application for approval of the joint venture. The capital of the foreign party should be above US$300m in the year prior to the application. As mentioned below, China is to permit foreign investment enterprises to engage in distribution services within three years of entry into the World Trade Organization (WTO).

R&D centres

R&D organisations for pharmaceutical research must be registered with the SDA through the relevant provincial level drug administrations, otherwise the SDA will not accept new pharmaceutical applications from such organisations. To obtain registration, the R&D organisation must meet qualification criteria with respect to its personnel and facilities.

Multinational companies have increasingly set up R&D centres in the PRC. The Notice of the Ministry of Foreign Trade and Economic Cooperation on Issues Relating to the Investment in and Establishment of Research and Development Centers by Foreign Investors, issued on 18th April, 2000, sets out the approval requirements for such centres.

The assignment or licensing of technology from a PRC entity, including an R&D organisation, to a foreign company, falls within the PRC's regulatory regime for technology export and must be approved or registered. The provision of technical services by a PRC entity, including an R&D organisation, to a foreign company, also falls within the same regime and also requires approval or registration.

Administrative protection for pharmaceuticals

Administrative protection for pharmaceuticals is available in respect of pharmaceutical product inventions:

- exclusive rights that were not available under the *Patent Law of the People's Republic of China* prior to 1st January, 1993;
- for which an exclusive right prohibiting the manufacture, use or sale by others in the country where the applicant is located was obtained between 1st January, 1986, and 1st January, 1993; and
- which have not been sold in the PRC prior

to the filing of an application for administrative protection.

Pharmaceuticals that are no longer eligible for patent protection may still obtain administrative protection for pharmaceuticals. The grant and enforcement of administrative protection are set out in the *Regulations on the Administrative Protection of Pharmaceutical Products* and the *Detailed Implementing Rules for the Regulations for the Administrative Protection of Pharmaceuticals*. The *Detailed Implementing Rules for the Regulations for the Administrative Protection of Pharmaceuticals* was revised on 24th October, 2000, codifying the existing practices for administrative protection applications and other procedures.

The *Measures for Review in Connection with the Administrative Protection of Pharmaceuticals* was revised on 7th July, 2000. Under the revised Measures, decisions of the Re-examination Commission for Administrative Protection of Pharmaceuticals may now be appealed to the court.

E-commerce

Online sales of pharmaceuticals are currently banned, although there are pilot projects for online sales of pharmaceuticals in Guangdong and Fujian Provinces, and Beijing and Shanghai Municipalities.

Online provision of information on pharmaceuticals and medical devices must be approved by the SDA or registered with provincial level drug administrations, depending on whether the set-up is for profit or non-profit. Entities providing online information on pharmaceuticals and medical devices must have two or more professionals (with technical and legal knowledge and having been approved by the relevant local drug administration), and have measures for ensuring that the sources of the information to be provided are legal, accurate and safe.

Online provision of information on medical and health issues is subject to approval by the Ministry of Health or provincial level health administrations. Online diagnosis or treatment is prohibited, excepting consultation between medical institutions in long-distance cases.

WTO

The PRC is to reduce its average tariff on pharmaceuticals by about 60 per cent. Reductions are to commence upon accession and will be completed by 1st January, 2003. The PRC will bind all its tariffs.

Currently, foreign products imported into the PRC generally must go through foreign trade companies. The PRC has agreed that any entity will be able to import pharmaceuticals into the PRC. This commitment is to be phased in over a three year period with all entities being permitted to import and export at the end of the period.

Currently, the PRC generally prohibits foreign investment enterprises from distributing imported products or providing related distribution services. The PRC has agreed to permit foreign investment enterprises to engage in the full range of distribution services. These rights will also be phased in over a three year period for pharmaceuticals.

Violations

China Daily has reported that in 2000, there were 50,000 cases of fake or inferior pharmaceutical products in the PRC and 1,345 factories were closed as a result. The new Pharmaceutical Law has stepped up enforcement against fake or inferior pharmaceutical products.

The new Pharmaceutical Law has introduced greater specificity with respect to its penalty provisions. Harsher punishments are set out and criminal liabilities are specifically stipulated. Liability for directly responsible personnel has been provided for. Violators may be prohibited from the pharmaceutical trade for long periods. Liabilities for those who provide such facilitating conditions as transportation or storage for what they know or ought to

know to be fake or substandard drugs have also been provided.

New subsidiary regulations, eg Regulation on Supervision and Management of Drug Distribution, Opinions on the Rectification and Regulation of the Pharmaceutical Market and Regulation on Procedure of Administrative Punishment on Drug Supervision, have been issued to provide further guidelines with respect to the administration of the pharmaceutical market.

Various blacklists of fake or substandard products were published, identifying the names of the manufacturers. Revocations of product registrations of fake or substandard products have been published. Certain imported pharmaceuticals that twice failed to pass tests also had their *Import Drug Registration Certificates* revoked or refused renewal.

The SDA and local drug administrations initiated campaigns against the manufacture and sale of fake and substandard products. In the campaign undertaken in 2000, there were reportedly 48,600 cases of fake and substandard pharmaceuticals, of value US$60m. Over US$10m of goods were confiscated, US$13m of fines imposed, operations of 1,345 enterprises suspended, cancellation made of 162 approval numbers and 38 licences, 147 cases transferred to the judicial authorities and seven individuals sentenced.

Patent law

The *Patent Law of the People's Republic of China* was amended and the amended Law came into effect on 1st July, 2001. The PRC has extended protection to pharmaceutical products and substances obtained by means of a chemical process since 1993. Preliminary injunctions may now be granted prior to commencement of patent infringement proceedings.

The amended Patent Law has enhanced protection for patents. The method of calculation of damages is codified. The Supreme People's Court judicial interpretation entitled *Several Regulations of the Supreme People's Court Regarding the Question of the Applicable Law for the Adjudication of Patent Disputes* ('Opinion'), effective on 1st July, 2001, has also introduced statutory damages up to RMB500,000 (US$60,000).

The 'offering for sale' of products that infringe a utility model patent or an invention patent constitutes infringement under the amended Patent Law. The use for production or business purposes or sale of patent infringement products without knowledge of the infringement also constitutes infringement.

The statute of limitations for patent infringement litigation is two years from when the patent owner or the interested party should have known about the infringement activities. The Opinion stipulates that if the patent owner commences proceedings after the two year time limit, but if the infringing activities persist at the time of commencement of the proceedings, the court should order injunction to be implemented during the period of validity of the patent and compensation for the two years prior to the commencement of the proceedings should be awarded.

Passing off another's pharmaceutical patent, such as the labelling of one's pharmaceutical products using someone else's patent number without authorisation, may be subject to criminal prosecution.

Product quality

The production or sales of fake or substandard pharmaceuticals may be subject to criminal prosecution. The PRC Supreme People's Court and the Supreme People's Procuratorate issued a formal interpretation entitled *Interpretations of the Supreme People's Court and the Supreme People's Procuratorate on Several Issues Concerning the Specific Application of Law to Criminal Cases of Producing and/or Selling Fake and/or Inferior Goods* ('Interpretation'), effective as of 10th April, 2001, with respect to Articles 140 to 149 of the *Criminal Code of the People's Republic of China*.

Article 141 provides for a fixed term

imprisonment of not more than three years against parties that produce or sell fake or substandard pharmaceuticals where their properties are such that they seriously harm human health. The Interpretation stipulates that this provision, *inter alia*, applies to a drug that contains toxic and/or hazardous substances in excess of the relevant limits, or that does not contain the active ingredients such that use of the drug could adversely affect treatment.

Article 145 of the Criminal Code provides for a fixed term imprisonment of not more than five years against parties that produce medical apparatus and instruments or medical hygiene materials that are substandard or sell such articles with knowledge of such offence thereby causing serious harm to human health. The Interpretation stipulates that this provision applies where minor injury or other serious consequences are caused by the substandard medical apparatus or medical health material.

Conclusion

With the PRC's entry into the WTO, it is expected that the pharmaceutical business in the PRC will experience even greater growth. In general, the recent new developments in the pharmaceutical regulatory regime provide clearer rules for the industry and enhanced protection for intellectual property protection for pharmaceuticals. However, it remains to be seen how these new laws and regulations are to be put into practice by the law enforcers.