*The information, in this section is derived from various private and/or government publications. Such information has not been prepared or independently verified by the Directors, the Company, the Vendors, the Sponsor, the Underwriters or their respective advisers.*

## BIOTECHNOLOGY AND PHARMACEUTICAL SCIENCE

Biotechnology is the technique that uses biological processes and other technology to extract or reconstruct living organism (including animals, plant and micro-organism) or its components, cells and tissues for specific uses. Biotechnology comprises genetic engineering (including protein engineering), fermentation engineering and enzyme engineering. Biotechnology has wide medical and industrial applications which help human beings to ease problems such as disease, food production and environmental pollution. Through the production of biological molecules, biotechnology can ease the reliance on substances of blood origin, thus alleviating shortage problems of such substances.

### The development and application of biotechnology in pharmaceutical science

The application of biotechnology in pharmaceutical science has brought a series of breakthroughs in the development of new drugs. The Directors believe that the development and application of biotechnology have contributed and will continue to contribute to the discovery and development of new pharmaceutical products. The advantages of applying biotechnology in the research and development of pharmaceutical products are as follows:

- biotechnology can create substances that cannot be found in nature and can avoid the use of blood born products; and

- biotechnology may be able to increase the quantity of some biological products at substantially lower production costs.

In 1982, human insulin, the world's first genetic engineering pharmaceutical product, was released to the market.

The recent availability of information from the Human Genome Program also helped in speeding up the progress of development in the biotechnology industry.

## PHARMACEUTICAL INDUSTRY IN THE PRC

The total production value of the PRC pharmaceutical industry increased to RMB233.2 billion in 2000. The total production value of the PRC pharmaceutical industry grew by approximately 20% compared with that of first half-year in 1999.

The PRC has the largest population in the world. Further, according to a survey conducted by the SDA South Medicinal Economic Institution (國家藥品監督管理局南方醫藥經濟研究所), 80% of the population is living in villages, where the population only enjoy 20% of the total medical resources provided in PRC. It is therefore expected that the demand for pharmaceutical products will increase in the forthcoming years.

**The supervisory authority**

In the PRC, the SDA is the authority which monitors and supervises the administration of pharmaceutical industry including pharmaceutical products and medical appliances and equipment. The SDA was established on 19th August, 1998 as an organisation under the State Council of the PRC to assume the responsibilities of the Ministry of Public Health of the PRC(中華人民共和國衛生部)("MPH"), the State Pharmaceutical Administration Bureau of the PRC(中華人民共和國藥品管理局)and the State of Administration of Traditional Chinese Medicine of the PRC(中華人民共和國中醫藥管理局).

The primary responsibilities of the SDA are:

(a) monitoring and supervising the pharmaceutical products and medical appliances and equipment;

(b) formulating administrative rules and policies concentrating the supervision and administration of the pharmaceutical industry;

(c) evaluating, registering and approving of new medicine, generic drugs, imported drugs and Chinese medicines; and

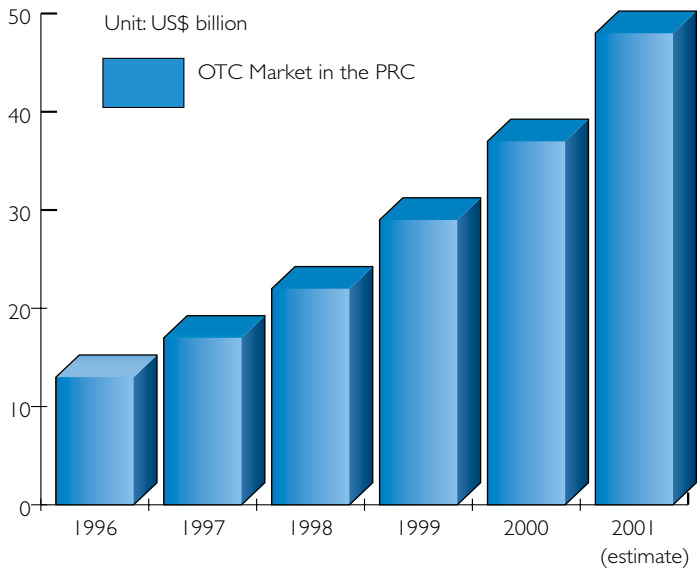
(d) approving and permitting the manufacture and export of pharmaceutical products and medical appliances and equipment and the establishment of enterprises engaging in the manufacture and distribution of pharmaceutical products.

**The laws and regulations**

The Law of the PRC on the Administration of Pharmaceuticals(中華人民共和國藥品管理法) was promulgated on 20th September, 1984 and amended on 28th February, 2001 by the Peoples' National Congress of the PRC. The amendments have come into effect on 31st December, 2001 and the Implementing Regulations of the Law of the PRC on the Administration of Pharmaceuticals(中華人民共和國藥品管理法實施辦法) was promulgated on 27th February, 1989 by the MPH, both setting out the legal framework with respect to the manufacture, sale, purchase and distribution of pharmaceutical products in the PRC.

**Over-the-counter pharmaceuticals**

In 1999, the sales of over-the-counter pharmaceuticals in the PRC market amounted to approximately US$29 billion. In 2000, the sales of over-the-counter pharmaceuticals in the PRC market amounted to approximately US$37 billion. In 2001, the sales of over-the-counter pharmaceuticals in the PRC market amounted to approximately US$48 billion, representing an increase of approximately 66% from the year of 1999 and 30% increase from the year of 2000.




*Source:* SDA South Medicinal Economic Institution (國家藥品監督管理局南方醫藥經濟研究所), 26th September, 2001

**Manufacturer of Pharmaceutical Products**

A pharmaceutical manufacturing enterprise in the PRC must obtain the following certificates, permits and licences from the relevant pharmaceutical supervisory bodies before it can manufacture pharmaceutical products:

***Production licences:***

- On or before June 1999, Pharmaceutical Manufacturing Enterprise Qualification Certificate (藥品生產企業合格證) and Pharmaceutical Manufacturing Enterprise Permit (藥品生產企業許可證) issued by the relevant pharmaceutical administrative authorities and the relevant public health department respectively at the provincial level where the enterprise is located were required for pharmaceutical manufacturing enterprises;

- During the period from around July 1999 to June 2000, pharmaceutical manufacturing enterprises were required to obtain a renewed Pharmaceutical Manufacturing Enterprise Permit (藥品生產企業許可證), which replaced the previous qualification certificate and permit; and

- From July 2000 onwards, the new Pharmaceutical Manufacturing Enterprise Permit (藥品生產企業許可證) issued by the relevant pharmaceutical administrative authorities and the relevant public health department at the provincial level where the enterprise is located is required for pharmaceutical manufacturing enterprises.

***Business licences:***

A business licence will be issued by the relevant administrative bureau of industry and commerce to a pharmaceutical manufacturing enterprise on application soon after it has obtained the requisite certificates and permits referred above from the relevant authorities.

Each qualification certificate and permit issued to any pharmaceutical manufacturing enterprise is effective for a period of five years. Any pharmaceutical manufacturing enterprise is required to apply for renewal of such certificate or permit within six months prior to its expiry and will be subject to re-assessment by the issuing authorities in accordance with the then prevailing legal and regulatory requirements for the purposes of such renewal. In addition, any pharmaceutical manufacturing enterprise which have obtained a qualification certificate or permit are subject to review by the relevant regulatory authorities on an annual basis.

The Group has obtained all certificates, permits and licences from the relevant pharmaceutical regulatory authorities in the PRC with respect to the manufacture of all its products.

**Registration of pharmaceutical products**

All pharmaceutical products which are produced in the PRC must bear a registered number approved by the appropriate drug administration authorities in the PRC, with the exception of Chinese herbs and Chinese medicines in soluble tablet form.

**GMP**

The World Health Organisation encourages the adoption of GMP standards in pharmaceutical production in order to minimise the risks involved in any pharmaceutical production that cannot be eliminated through testing the final products.

In 1988, the Ministry of Health, the PRC (中國國家衛生部) started to issue the GMP standards for the pharmaceutical manufacturing enterprises in the PRC. However, during the implementation of the Standards, it was discovered that some of the standards had to be revised to suit the situation in the PRC.

In 1999, the SDA passed the Guidelines on Good Manufacturing Practices (1998 revised) (藥品生產質量管理規範(1998年修訂)) which sets the basic guidelines on the manufacture of pharmaceuticals. Such guidelines cover issues such as the production facilities, the qualification of staff of management level, production plant and facilities, documentation, material packaging and labeling, inspection, production management, sales and return of products and complaints from customers, etc. The Guidelines came into effect on 1st August, 1999. Deadlines were laid down for the satisfaction of the standards. The SDA further issued the Notice on the Overall Acceleration of the Implementation and Supervision of Good Manufacturing Practice for Pharmaceuticals (關於全面加快監督實施藥品GMP工作進程的通知), which requires all the pharmaceutical manufacturing enterprises to comply with the GMP standards by the end 30th June, 2004. If the pharmaceutical

manufacturers fail to obtain a GMP compliance certificate within the specified deadline, their Pharmaceutical Manufacturing Enterprise Permits (藥品生產企業許可證) will not be renewed.

**New Medicines**

New medicines are generally referred to those medicines which have not been produced in the PRC, and include modifying the dosage form, change of delivery system, new indication or new formulation of existing drugs. The development of new medicines is governed by the Regulations on the Examination and Approval of New Medicines (新藥審批辦法) promulgated by the SDA in 1999.

Prior to 1999, under the "Procedure For the Approval of New Biological Product" effective from 1st July, 1985, new biological drugs were classified into 4 classes according to the criteria listed below and protected by the listed administration protection period respectively.

| Class name | Classification Criteria | Protection Period |
|---|---|---|
| Class 1 | attenuated live bacterial cultures, attenuated live vaccines | 8 years including trial production period of 2 years |
| Class 2 | dead bacterial cultures, dead vaccines, toxoids, anti-toxins, anti-sera, specific immunoglobulins, bacteriophages | 6 years including trial production period of 2 years |
| Class 3 | blood born products and immunology products processed from human or animal blood or tissues | 4 years |
| Class 4 | diagnostic materials for in vitro serology or immunology testing | 3 years |

Under the new regulation in 1999, before a new medicine can be manufactured on a commercial basis, a manufacturer is required to obtain approval from the SDA.

Application for a new medicine principally involves several approval procedures at various levels of the SDA. Based on the knowledge and experience of the Directors, the time required for the whole application process of a new medicine varies depending upon the category of the new drug under application and the Directors estimate that the process usually takes approximately 1 to 5 years.

Application for a new medicine should be submitted to the provincial pharmaceutical supervisory authority. Further, information on and samples of the new medicine for clinical testing and commercial production should also be submitted together with a completed application form to the provincial and state levels of the SDA. Clinical testing of the new medicine, as part of the application process, is required to be carried out at designated hospitals. Normally, a certificate of new medicine and a new approval number for the new medicine will be issued by the state level of the SDA upon completion of the third stage of clinical testing. Upon obtaining the certificate of new medicine from the SDA, a pharmaceutical manufacturer, having obtained a valid Pharmaceutical Manufacturing Enterprise Permit (藥品生產企業許可證), can, in compliance with the GMP standards, apply to the relevant authorities for an approval document regarding the production of the new medicine. After obtaining the approval document, the pharmaceutical manufacturer can commence production of the new medicine on a commercial basis.

The new medicine will be protected if it is a registered patent. According to the Law of the PRC on Patent (中華人民共和國專利法), only original manufacturer of an invention is eligible to apply for patent rights. Such invention must be completely new and must not be known to the public before and at the date of relevant patent application.

New medicines are divided into three main categories, namely, Chinese medicines, chemical medicines and biopharmaceutical products. The approval of new biopharmaceutical products is governed by the Measures on the Examination and Approval of New Biopharmaceutical Products (新生物制品審批辦法) promulgated by the SDA which came into effect on 1st May, 1999. Under these measures, new biopharmaceutical products are divided into five categories:

| | |
|---|---|
| Class 1: | biopharmaceutical products which have not been previously approved for sale in the PRC and overseas |
| Class 2: | biopharmaceutical products which have been approved for sale overseas but have not been included in the PRC pharmacopoeia and not yet imported into the PRC |
| Class 3: | new prescription medicine with biopharmaceutical products as its main component |
| | biopharmaceutical products which the technical processes have been significantly transformed |
| Class 4: | biopharmaceutical products which has been included in pharmacopoeia outside the PRC |
| | biopharmaceutical products which has been approved for import into the PRC |
| | biopharmaceutical products with new prescription and new method of application |
| Class 5: | biopharmaceutical products with added applications |

Under the Regulations on the Protection of New Pharmaceutical Products and Technology Transfer (新藥保護和技術轉讓的規定) promulgated by the SDA which came into effect on 1st May, 1999, the PRC government has introduced a classified product protection system for new medicines. The protection period (starting from the date of issue of the SDA new medicine certificate and where trial production period applies to a new drug, including the trial production period) varies with new medicines of different categories:

| **Class** | **Protection period** *(years)* |
|---|---|
| 1 | 12 |
| 2 | 8 |
| 3 | 8 |
| 4 | 6 |
| 5 | 6 |

During the protection period, an entity which is not the holder of the original certificate of new medicine granted by the SDA may not engage in the manufacture or simulation of such a product without entering into

any technology transfer agreement with such holder. A transferee must have first obtained the pharmaceutical manufacturing enterprise permit and the pharmaceutical GMP certificate. In the event that no production is undertaken for or no transfer is effected within two years from the date of the grant of the new medicine certificate without special reasons, the protection offered to that new product is liable to be revoked.

Before a new biopharmaceutical product can be manufactured on a commercial basis in the PRC, it has to obtain an approval number from the SDA. After completion of the clinical research and pre-clinical trials, an application, accompanied by the reports of such clinical research and preclinical trials, has to be made to the SDA at the provincial level for approval for clinical trial. The provincial SDA will, after evaluation, submit the application to the SDA at the state level for approval.

Save and except for the diagnostic reagent in vitro, a new biological medicine may undergo clinical tests only after the SDA approval has been obtained. After the third stage of the clinical tests has been completed, an application for approval of the new biological medicine can be submitted to the SDA. A new medicine certificate will be issued upon obtaining the SDA approval. If the products passed three consecutive trial productions during the sampling inspection by the PRC biopharmaceutical testing clinics, an application for an approved number can be submitted to the SDA. With the exception of category I new biological medicine which will be issued with an approved number bearing the words "國藥試字" (Guoyaoshizi), the other categories of new biological medicine will generally be issued with an approved number bearing the words "國藥准字" (Guoyaozhunzi).

New biological medicines with respect to which a "國藥試字" (Guoyaoshizi) approval number is issued is required to undergo a trial production period of two years. An application for commercial production of the new biological medicine may be submitted to the SDA within three months prior to the expiry of the trial production period. Upon obtaining the SDA approval, an approval number bearing the words "國藥准字" (Guoyaozhunzi) will be issued and the product can be manufactured on a commercial basis. If no application for commercial production is made within the prescribed time limit, the approval number will be revoked.

**Import and export**

The PRC has a registration system for importing medicines into the PRC. The SDA is responsible for the control of imported medicine in their respective administrative areas. A Certificate of Registration of Imported Medicine (進口藥物註冊證) must be obtained before any foreign pharmaceutical manufacturers or agents can import medicines into the PRC.

With respect to export, according to the Law of the PRC on the Administration of Pharmaceuticals (中華人民共和國藥品管理法), certain restrictions are imposed on pharmaceutical products. For example, medicines in scarcity are prohibited from being exported. Generally there is no restriction on the export of Chinese medicine by the state and export licences relating to Chinese medicine do not have any conditions attached to them. Export of Chinese medicine is also subject to the laws of the country or region to which the Chinese medicine is to be exported.

**Distribution of pharmaceutical products**

According to the Law of the PRC on the Administration of Pharmaceuticals (中華人民共和國藥品管理法) and the Implementing Regulations of the Law of the PRC on the Administration of Pharmaceuticals (關於貫切(中華人民共和國藥品管理法)的有關暫行規定) and Regulation on the Administration of Distribution

of Pharmaceutical Products（藥品流通監督管理辦法）, a manufacturer of pharmaceutical products in the PRC can only engage in the trading of the pharmaceutical products produced by it. Furthermore, such manufacturer of pharmaceutical products can only sell its products to the following:

1. wholesalers and distributors holding Pharmaceutical Trading Enterprise Permit（藥品經營企業許可證）;

2. other manufacturers of pharmaceutical products holding Pharmaceutical Manufacturing Enterprise Permit（藥品生產企業許可證）; and

3. medical practitioners holding Medical Practice Permit（醫療機構執業許可證）.

A pharmaceutical manufacturer in the PRC is prohibited from selling its products to end-users and other persons or institutions which have not obtained the Pharmaceutical Trading Enterprise Permit（藥品經營企業許可證）, the Pharmaceutical Manufacturing Enterprise Qualification Certificate（藥品生產企業合格證）; or the Medical Practice Permit（醫療機構執業許可證）.

**Price Control**

Pharmaceutical products which are included in the price control list published by the state and provincial price administration authorities from time to time will be subject to price control with respect to their (a) ex-factory price; (b) wholesale price; and (c) retail price.

Pursuant to the existing law, the ex-factory price will be determined by adding a maximum gross profit margin to the production costs of the relevant pharmaceutical products. The rate of the gross profit margin to be added will depend upon (i) the category of the pharmaceutical products; (ii) whether the products are newly developed products; and (iii) the manufacturer's GMP system implementation status.

The wholesale price of a pharmaceutical product is determined by adding a further profit margin into the ex-factory price ceiling. The retail price is then determined by adding a further profit margin to the wholesale price. Sales of pharmaceutical products to overseas markets are not subject to any price control imposed by the PRC government. The price of Opin is subject to the price control policy of the PRC government pursuant to an approval issued by the Hubei Price Bureau in August 2000 and a notice issued by the State Planning Commission in July 1999.

## ENVIRONMENTAL CONTROL REGULATIONS

Manufacturing enterprises in the PRC are under the administration of the environmental protection department at the provincial level where the enterprise is located. Different manufacturing enterprises are required to obtain different certificates required under the environmental regulation in the PRC.

Under the environmental regulations in the PRC, manufacturing enterprises are required to apply for the relevant certificates from the local environmental protection authority. The Group has obtained all relevant certificates required under the environmental regulations in the PRC for its productions.