China’s pharmaceutical market has expanded dramatically in the past twenty years and is expected to become the largest in the world by the year 2050. However, entry to the market remains difficult for many international pharmaceutical manufacturers due to the country’s costly and complicated regulatory licensing requirements. This paper provides an overview of the regulatory licensing regime for pharmaceutical products in China. It evaluates three key features of the regulatory licensing regime through a law and economics approach. These features include the standards to be met by licence applicants, and the procedures to be followed by applicants before licences are granted.

The paper concretely describes the new and generic drug registration application through introducing the following details: qualification of the applicant, registration classification or type, the procedures for drug registration application review, the intellectual property rights concerning the pharmaceutical (drug substance and product), the process for submitting a drug registration application, and the materials required in application for registration. In conclusion, we have a thorough understanding of the organisational structure of China’s Food and Drug Administration, product registration application, and the regulatory requirements in China.

### Introduction
China’s pharmaceutical market has expanded dramatically in the past twenty years and is expected to become the largest in the world by the year 2050. The production value of China’s pharmaceutical industry has experienced an average annual growth of 20 per cent over the past decade.\(^1\)

There has been an increasing acceptance of western drugs in China, in spite of strong competition from the traditional Chinese medicine industry, e.g. prescription drug sales are set to reach RMB 442.5 billion by the end of 2014.\(^2\) Western medicines are generally regarded as more effective for infectious diseases, acute symptoms, illnesses, and many surgical procedures. However, market entry remains difficult for many international pharmaceutical manufacturers due to China’s complicated regulatory requirements.\(^2\)

China’s booming economy and high GDP growth make its pharmaceutical market the third largest, and one of the most attractive, in the world. With its volume 20 per cent growth projection, it is set to overtake Japan as the world’s second largest market by 2015.\(^1\)

China accounts for 20 per cent of the world’s population, but only 1.5 per cent of the global drug market. And because a large portion of the Chinese population is not covered by basic health insurance, low-cost generic drugs will account for the majority of the growth of China’s prescription drug market.

### Transformation of SFDA to CFDA
The China Food and Drug Administration (CFDA) was founded on the basis of the former State Food and Drug Administration (SFDA). In March 2013, the regulatory body was rebranded and restructured as the China Food and Drug Administration, elevating it to a ministerial-level agency. The CFDA replaced a large group of overlapping regulators with an entity similar to the Food and Drug Administration of the United States, streamlining regulation processes for food and drug safety. The China Food and Drug Administration is directly under the State Council of the People’s Republic of China, which is in charge of comprehensive supervision on the safety management of food, health food and cosmetics, and is the competent authority of drug regulation in mainland China.\(^4\)

### Objectives
1. To study the market value of the Chinese pharmaceutical industry.
2. To compile data required for the pharmaceutical regulatory requirements for product registration in China.

### China Pharmaceutical Product Registration
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.

### Concept of New Drugs in China
[Figure 1: Ranking of China in the pharmaceutical market according to IMS health]

[Figure 2: Market of various categories of drugs in China]

[Note: OTC includes both patented and generic over the counter pharmaceuticals. Source: CAMRDI, SFDA, BMA, China Customs]
1) New chemical entity never marketed in any country
   - Drug substance and its preparations made by synthesis or semi-synthesis
   - Chemical monomer (including drug substance and preparation) extracted from natural sources or by fermentation
   - Optical isomer (including drug substance and preparation) obtained by chiral separation or synthesis
   - Drug with fewer components derived from marketed multi-component drug
   - New combination products
   - A preparation already marketed in China but with a newly-added indication not yet approved in any country

2) Drug preparation with changed administration route and not marketed in any country

3) Drug marketed ex-China, including
   - Drug substance and its preparations, and/or with changed dose form, but no change of administration route
   - Combination preparations, and/or with changed dose form, but no change of administration route
   - Preparations with changed administration route and marketed ex-China
   - A preparation already marketed in China but with a newly-added indication approved ex-China

4) Drug substance and its preparation with changed acid or alkaline radicals (or metallic elements), but without any pharmacological change, and the original drug entity already approved in China

5) Drug preparation with changed dose form, but no change of administration route, and the original preparation already approved in China

6) Drug substance or preparation following national standard.

The Review Process

- The Drug Administrative Law authorises the China Drug Administration to approve new drugs for marketing. The China Drug Administration makes new drug approval decisions based on proposals from its Center for Drug Evaluation, which is responsible for the 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 China 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 China 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.
- In the revised regulation of 1999, a class 1 NCE clinical and marketing application is submitted directly to the State Drug Administration for fast review. Via the China 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.

1. Submitting an application - If the Application Dossier is appropriate, you shall obtain Clinical Trials Permission (CTP) within approximately 10-12 months after submission.
2. Conducting the clinical trials - If just carrying out bioequivalence trials, it might take 3 to 6 months, but other clinical trials might take more than 1-1.5 years to complete.
3. Submitting the Application Dossier - (including the reports of clinical trials). If the Application Dossier is appropriate, you shall obtain IDL within approximately 12-18 months after submission.

**Figure 3: Drug Approval Process**
<table>
<thead>
<tr>
<th>Items</th>
<th>Contents</th>
<th>Detail or Example</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA (Format &amp; Categories)</td>
<td>Acceptance of CTD format</td>
<td>CTD or ACTD or others?</td>
<td>CTD of CMC for chemical drug with registration category 3-6 can be acceptable.</td>
</tr>
<tr>
<td></td>
<td>Category</td>
<td>NCE, Generic</td>
<td>There are 6 categories as discussed in the text</td>
</tr>
<tr>
<td></td>
<td>Requirement of CPP</td>
<td>Timing of submission.</td>
<td>Import drug requires CPP at NDA. CPP granted either by manufacturing country or marketing country is acceptable.</td>
</tr>
<tr>
<td></td>
<td>Foreign clinical trial data</td>
<td>Bridging data and Global clinical trial data</td>
<td>Global/MRCT clinical data for chemical drugs are acceptable, but Chinese P3 and PK data is indispensable.</td>
</tr>
<tr>
<td></td>
<td>Application fees</td>
<td>Indispensable</td>
<td></td>
</tr>
<tr>
<td>NDA (application material)</td>
<td>CMC summary/body</td>
<td>Yes (Chinese)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-clinical summary</td>
<td>Yes (Chinese)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-clinical report</td>
<td>Requirements and language</td>
<td>Usually synopsis or abstract of each report in Chinese is required, attached with source report.</td>
</tr>
<tr>
<td></td>
<td>Clinical summary</td>
<td>Yes (Chinese)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clinical report</td>
<td>Yes (Chinese)</td>
<td>Usually synopsis or abstract of each report in Chinese is required, attached with source report.</td>
</tr>
<tr>
<td>Approval review</td>
<td>Review organisation</td>
<td>Review &amp; Decision</td>
<td>Review- CDE (Center for Drug Evaluation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decision- CFDA (China Food &amp; Drug Administration)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Review process</td>
<td>Flow of review</td>
<td>As discussed in the text</td>
</tr>
<tr>
<td></td>
<td>Review time</td>
<td></td>
<td>145 working days. However, actual timeline is much longer</td>
</tr>
<tr>
<td>Pre-approval inspection</td>
<td>GCP inspection</td>
<td>On-site inspection</td>
<td>For import drug is not mandatory yet.</td>
</tr>
<tr>
<td></td>
<td>GMP inspection</td>
<td>CPP/GMP certificate from source country accepted.</td>
<td>For import drug, CFDA started GMP on-site inspection at the end of 2011. GMP on-site inspection was done after IDL (Import Drug License) approval at this moment.</td>
</tr>
</tbody>
</table>
The current provisions for drug registration have added many new items, such as regulation on the qualification of drug registration applicants, the classification of drug into various categories, the regulatory requirements for NCE registration, etc. Consequently, the provisions are more reasonable and suitable for China’s entry into the WTO, and further guarantee that safe and effective drugs are available to the Chinese people.

References
3. China seen as No. 2 drugs market by 2015, 8 Nov 2010, Reuters.
7. CFDA China Food and Drug Administration http://eng.sfda.gov.cn/W503/CL0755/

Figure 4: Clinical Studies

Conclusion
The current provisions for drug registration have added many new items, such as regulation on the qualification of drug registration applicants, the classification of drug into various categories, the regulatory requirements for NCE registration, etc. Consequently, the provisions are more reasonable and suitable for China’s entry into the WTO, and further guarantee that safe and effective drugs are available to the Chinese people.

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