

Overview of Human Drug Regulation in China and the United States

Andrew Chen

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Davis Wright Tremain LLP



ANDREW CHEN

- **Beijing University graduate**
- **Probably the only bi-lingual attorney focusing on U.S. food and drug law: approval and marketing of drugs, biologics, and medical devices**
- **Was FDA's own attorney (2000-2004)**
- **Now at a 400-lawyer firm in Seattle**
- **Davis Wright Tremaine in Shanghai**
- **Gary Locke recently joined as a partner**



Three Sections

- **U.S. and China: different environments**
- **Regulation of human drugs in China**
- **Regulation of human drugs in the U.S.**

Different Environments

■ China

- Population 1.3 billion
- Currently has 1.4% of the world's drug market, ranks #7
- Expected to become the fifth-largest drug market by 2010 *

* various sources

Different Environments

■ U.S.

- Population 0.3 billion
- Currently has 45% of the world drug market, ranks #1
- Will remain #1 for many years to come*

* various sources

Different Environments

China in 2004*

- 17,000 drug applications reviewed
- 5,000 GMP certified drug manufacturers
- 7,500 GSP certified whole-sellers
- 58,000 GSP certified retailers

* Shifei Chen, Deputy Director, Zhenjiang Province Food and Drug Administration, June 18, 2005

Different Environments

U.S. in 2004

- 167 original applications filed*
- 33 PhRMA members (large innovative drug manufacturers)**

*<http://www.fda.gov/ope/mdufma/report2004/default.htm>

**<http://www.phrma.org/whoweare/members/>

- **China State Food and Drug Administration (2003-present)**
 - **State Drug Administration (1998-2003)**
 - **State Pharmaceutical Administration Committee (pre-1998)**

China Drug Laws

- **The statute: Drug Administration Law of the People's Republic of China**
 - **Enacted in 1984, effective July 1, 1985**
 - **Amended in 2001, effective December 1, 2001**

China Drug Laws

- **Primary regulations**
 - **Implementation Rules of the Drug Administration Law of the People's Republic of China**
 - **Originally promulgated and effective Feb 27, 1989**
 - **New rules promulgated in 2002 and effective September 15, 2002**

China Drug Laws

- **Secondary regulations: more than 200**
 - **Drug application rules, effective May 1, 2005**
 - **Drug importation rules, effective Jan 1, 2004**
- **Provincial government regulations**
- **National law preemption**

Pre-market approval

■ New drugs

- **Definition: has not been marketed in China**
 - **1985 drug law: was not produced in China**
 - **Result: treating as a new drug if a Chinese mfr makes the generic of a foreign drug already marketed in China**
 - **2001 drug law: such a generic is not a new drug**
- **Clinical study data required**
- **6-year data exclusivity for new chemical entity**

Pre-market approval

- **Drugs with national standards**
 - **Quality standards listed in China Pharmacopoeia**
 - **Clinical data may be needed**
- **Imported drugs**
 - **Clinical data may be needed If not approved in the home country**

Pre-market approval

- **Types of permits and certificates**
 - **Drug approval number**
 - **Drug registration certificate**
 - **Drug manufacturing permit**
 - **Drug distribution permit**
- **5-year renewal**

Post Market

- **Manufacturing permit: provincial FDA**
- **GMP certification: provincial FDA**
 - **Injections, radioactive medicine, certain listed biologics need SFDA inspection**
- **Wholesale permit: provincial FDA**
- **Retail permit: county FDA**
- **GSP certification: provincial FDA**

■ Advertising

- Pre-approval of advertising materials by provincial FDA
- No direct to consumer advertising of prescription drugs

■ Adverse event reporting

- **Gov-controlled price**
 - Listed on the basic medicine state insurance formulary
 - Not on the formulary, but could be monopolized
 - Factors: average cost, supply/demand, affordability
- **Market price**

Enforcement

- **Unapproved/unregistered drugs**
- **Counterfeit drugs**
- **Inferior quality drugs**
- **Warning**
- **Seizure**
- **Monetary penalties**
- **Factory shutdown**
- **Withdrawal of approvals**

Challenges

- **Fragmented**
 - **5000 manufacturers**
 - **Many regulating entities**
- **Insufficient funding for gov or industry**
- **Immature R&D system**
- **Weak IP protection**
- **Poor production quality**

U.S. Drug Laws

- **U.S. Food and Drug Administration**
- **Federal Food, Drug, and Cosmetic Act, 21 U.S.C 301- 397**
- **Regulations, 21 C.F.R. 1- 1299**
- **Federal preemption: U.S. Constitution supremacy clause**

Applications

- **Definition of new drug: not generally recognized as safe and effective**
- **Investigational New Drug Application (IND)**
- **New Drug Application (NDA)**
- **Supplemental NDA (SNDA)**
- **Abbreviated NDA (ANDA)**
- **Paper NDA**

No pre-approval required

■ Non-drug claims

- Health, cosmetic claims
- Dietary Supplement Health Education Act
Structure/Function Claims

■ Monographs

- GRAS/E: generally recognized as safe and effective
- OTC product monographs: ingredient, dosage, indication, warnings

New Drug Application (NDA)

- **Approval requirements**
 - **Safety: risk and benefit balancing**
 - **Efficacy: two adequate and well-controlled clinical studies**
- **Additional OTC approval requirements**
 - **Labeling allows safe self-medication**
 - **Low potential for misuse and abuse**

New Drug Application (NDA)

- **NDA contents**
 - **Summary of information**
 - **Chemistry, manufacturing, and controls**
 - **Non-clinical pharmacology, toxicology**
 - **Clinical pharmacokinetic, bioavailability**
 - **Clinical safety data**
 - **Statistical analysis of effectiveness**
 - **Packaging, labeling**

New Drug Application (NDA)

■ Non-patent exclusivity

- 5 year new chemical entity exclusivity
- 3 year essential clinical data exclusivity
- 7 year orphan drug exclusivity
- 6 month generics exclusivity
- 6 month pediatric exclusivity

■ Patent Exclusivity



Abbreviated NDA (ANDA)

- For a generic drug based on a listed drug that has no patent/exclusivity
- Same active ingredient, strength, route, and dosage
- Full clinical data not required; only need to prove bioequivalence

Paper NDA

- **Sufficient data exist in published literature**
- **Usually filed by owner of an NDA for a new indication or dosage**

- **Bi-annual inspection**
- **GMP compliance**
- **Import sampling**
- **Export control**
- **Adverse event reporting**
- **Post market follow-up studies**

- **Advertising and promotion**
 - **No off-label claims**
 - **Fair balance (brief summary of risks or full package insert)**
 - **Substantial scientific basis for superiority claims**
- **Scientific/Educational Activities**
 - **Off-label references possible**
 - **Scientific, educational**
 - **Commercial free speech**

Enforcement

- **26 prohibited acts, 21 USC 331 (a)-(z)**
 - **Misbranded:** labeling is “false or misleading in any particular,”
 - **Adulterated:** “consists ... of any filthy, putrid, or decomposed substance.”

Enforcement

- **Inspection Observations**
- **Untitled letter; warning letter**
- **Disqualification; debarment**
- **Withdrawal of Approvals**
- **Recalls**
- **Civil Money Penalties**
- **Judicial**
 - **Injunctive relief to prevent violation**
 - **Seizure of violative products**
 - **Criminal fine and jail time**

The End

QUESTIONS?

Andrew Chen

**Direct: (206) 628-
7763**

**andrewchen@dwt.
com**

