Overview of Human Drug Regulation in China and the United States

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State of Health Law, Policy, and Research in China
Temple University, July 20-21, 2005
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.phrma.org/whoweare/members/](http://www.phrma.org/whoweare/members/)
China SFDA

- China State Food and Drug Administration (2003-present)
  - 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
Primary regulations

- Implementation Rules of the Drug Administration Law of the People’s Republic of China
  - Originally promulgated and effective February 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
Post Market

- Advertising
  - Pre-approval of advertising materials by provincial FDA
  - No direct to consumer advertising of prescription drugs
- Adverse event reporting
Post Market

- 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
Sufficient data exist in published literature

Usually filed by owner of an NDA for a new indication or dosage
Post Market

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

- 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
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
QUESTIONS?
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