US-China Joint Commission on Commerce and Trade
Medical Device and Pharmaceutical Subgroup
Pharmaceutical Task Force Meeting
August 30, 2005
Beijing, China

Overview

The Pharmaceutical Task Force under the U.S. – China Joint Commission on Commerce and Trade (JCCT) Medical Devices and Pharmaceuticals Subgroup met in Beijing, China on August 30, 2005. Please note that this meeting built on previous meetings, notably the April 2005 JCCT Medical Device and Pharmaceutical Subgroup meeting that took place in Washington D.C. To access the official minutes from that meeting, click on http://www.ita.doc.gov/td/health/jcctpharma2005.pdf

The U.S. Delegation was led by Jeffrey Gren, Director of the Office of Health and Consumer Goods (OHCG) at the U.S. Department of Commerce (DOC) and consisted of DOC officials and representatives from major U.S. pharmaceutical trade organizations. Those pharmaceutical trade organizations were Biotechnology Industry Association (BIO), Generics Pharmaceutical Association (GPhA), Pharmaceutical Research and Manufacturers of America (PhRMA), Plasma Protein Therapeutics Association (PPTA), and Research & Development based Pharmaceutical Association – China (RDPAC).

The Chinese Delegation consisted of SFDA officials that represented the full range of discussion topics on the agenda. They represented Department of Drug Safety, Office of Inspection, Office of Market Compliance and Office of International Cooperation.

Opening Remarks

Mr. Bruce Blakeman, Secretary's Special Representative to China, provided opening remarks.

He said it was heartening to see the Task Force used as it was intended – as a means for U.S. and Chinese stakeholders to actively engage in discussion on current, pressing pharmaceutical regulatory concerns. He conveyed the Secretary Gutierrez's wish for continued success and said the Secretary was interested in the discussion outcomes, especially those connected with IPR, such as data exclusivity and drug counterfeiting.

Pharmaceutical Task Force Meeting

The Pharmaceucal Task Force was Co-Chaired by Mr. Zhang Zhijun, Deputy Director General, Department of Drug Safety and Inspection, and Mr. Jeffrey Gren, Director of the Office of Health and Consumer Good at U.S. Department of Commerce. The Pharmaceutical Task Force focused on five issues:

1) Data Exclusivity/Patent Linkage
2) Anti-Counterfeiting Enforcement Strategies (including increased regulation of bulk APIs)
3) Clinical Trial Authorization/Acceptance of Foreign Clinical Data
4) Distribution and Import Rights
5) Duplicative Local Testing Requirements

Pharmaceutical Task Force Opening Comments
Mr. Gren began the Pharmaceutical Task Force meeting with opening comments. He spoke for the U.S. delegation in expressing thanks to SFDA for the preparation necessary in hosting this event. Mr. Gren thanked SFDA for its commitment to our long lasting partnership, making the JCCT Pharmaceutical Task Force an important forum through which stakeholders work towards mutually agreed upon working solutions to pressing issues.

Mr. Gren pointed out that 2006 will mark the 10th year of the JCCT Medical Device and Pharmaceutical Subgroup. Mr. Gren proposed the weeks of March 20th or 27th, 2006 as possible dates. He noted that the pursuit of the best healthcare for the citizens of both countries has remained the steadfast guiding principle of this JCCT Subgroup.

Mr. Zhang welcomed the U.S. delegation and noted that he was pleased that many of the agenda items had the Secretary's direct interest. He and the rest of the SFDA officials looked forward to a full day of discussion.

Issues of Interest

Data Exclusivity/Patent Linkage
Mr. Gren was pleased to introduce Mr. Mark Cohen, IPR attaché to Beijing from U.S. Patent and Trademark Office as the leader of this discussion. He expressed appreciation for SFDA's willingness to continue the dialog on these issues that were broached at the last Task Force meeting in April 2005.

Mr. Cohen framed the issues. Data exclusivity (DE) has a clear place in TRIPS Article 39.3. U.S. government has been appreciative of Chinese government's clear commitment to its WTO ascension terms. However, confusion remains regarding implementation of DE provisions. The three areas of confusion pertain to 1) the application procedure, 2) transparency mechanism, and 3) scope of protection.

Mr. Zhang spoke for the SFDA delegation. He acknowledged the confusion surrounding the issues. Even the definitions of fundamental terms have yet to be adopted. For example, what qualifies as a New Chemical Entity (NCE)? There has been the suggestion that any chemical entity within two years of marketing should be considered NCE. It has also been suggested that if a chemical entity has not been marketed in a country, it should be considered a NCE to that country. Then there is the opposite thought that DE should apply to product first marketed in any market in the world, rather than first marketed in China (in other words, the 6 year exclusivity period would run concurrently once the product obtained approval anywhere in the world). Mr. Zhang said SFDA would like to see a uniform WTO definition.

Another question Chinese authorities face is what should be considered new data? Should data disclosed over the internet qualify as new data? Finally, how does data protection relate to data reliance? Again using the internet to illustrate, suppose information is

available over the internet in the public domain, can it be cited? (Mr. Zhang noted that SFDA's practice is to NOT rely on the internet as basis for any application review.)

To resolve these issues, Mr. Zhang suggested that more information on data protection is needed. What is the current practice worldwide? Emphasis should be placed on obtaining data on other vibrant developing countries such as Brazil. A helpful tool would be a case study.

Mr. Zhang was asked to clarify protection provisions for Traditional Chinese Medicine (TCM). Mr. Zhang answered that legislation was issued on TCM in 1980s (State Council is in midst of updating). They are not patentable, because there's much variation in formulation. For TCMs their value and uniqueness lie in formulation and the manufacturing process. Since they are not patentable, TCMs are separate from current data exclusivity discussions.

The U.S. delegation further asked about special provisions for Orphan Drugs. SFDA acknowledged that there was a lack of protective regulations for Orphan Drugs. SFDA sees two possible strategies as solutions: 1) decrease clinical trial requirements, 2) fast track evaluation. However, State Council has to issue these legislations before SFDA can implement.

Mr. Zhang clarified that DE is aimed at fostering new technology, older products that already launched many years earlier in other markets should not be eligible for DE.

To Mr. Zhang's earlier point about learning from case studies Mr. Cohen offered the services of U.S. Patent and Trademark Office. SFDA is welcomed to bring cases for mutual study.

Patent Linkage

Again Mr. Cohen framed the issues. Articles 11 and 13 of the Chinese Drug Registration Regulation lay the foundation for Patent Linkage. But greater transparency is needed in implementation. The question was raised whether SFDA was working with SIPO to make system more robust?

Mr. Zhang responded with the following points:

1) SFDA lists all drug registration applications on its website (also lists CT application/approval, and registration approval).

2) Drug registration applications are listed by chemical name, and do not contain name of applicant for proprietary reasons as is practice in many countries.

3) It is up to companies to have a designated person who frequently checks SFDA website.

4) Once a patent holder discovers a drug application registration has been received which it believes infringes one of its patents, the holder should immediately notify SFDA in writing.

5) The SFDA process regarding patent issues has evolved to the following: First, in initially accepting an application, SFDA requires subsequent registrants to first check the patent status of the product and provide information/report that indeed its product would not infringe on a patent, and to acknowledge it would be liable for damages if indeed there is infringement. Second, if SFDA is contacted by a patent holder claiming infringement, then SFDA would contact the subsequent registration applicant in writing, sending a copy to the patent holder. This document would presumably be admissible in court. It would ask the applicant to review the situation again, and state whether it intends the SFDA to continue the registration process. If the answer is affirmative, the applicant must submit a second letter claiming non–infringement and again acknowledging liability for damages if there is infringement. Otherwise the applicant should withdraw its application.

6) The patent type greatly affects the process. Essentially, if the patent is on the compound/composition, it would be relatively easy to determine if there is an infringement. However, if the patent is for a "process," then SFDA feels it cannot and should not be put in the position of needing to make a determination, and will often approve the registration application if the generic (subsequent) applicant claims non-infringement and agrees to bear the legal liability of infringement.

7) The fact that the first registrant is now copied on the letter to the subsequent registration applicant should help in three ways:

a) It eliminates any confusion as to the identity of the subsequent applicant thereby assisting patent holder's (first registrant's) legal counsel (internal or external) in drafting appropriate warning letters;

b) In some instances, it may actually result in the patent holder learning earlier in the process about the identity of the subsequent applicant (although the patent holder often learns at an earlier stage through informal channels);

c) The procedure to formally identify the subsequent applicant would enable the patent holder to complete the materials needed to file an infringement case in court at an earlier stage.

Anti-Counterfeiting Enforcement Strategies/Bulk Chemical Regulation

Mr. Gren introduced the topic. Counterfeiting has escalated to become a serious global problem. Many of the current containment measures focus on finished products. Attention needs to be directed upstream, to increasing regulatory oversight of bulk active pharmaceutical ingredients (API). Emphasis needs to be placed on the tracking of the bulk chemicals' movement, perhaps using associated money trails. Other countries, including U.S., have internal counterfeit efforts but there is no concerted global effort. The U.S. has made a proposal to the EU for counterfeit drug bilateral cooperation, but has yet to receive a response. China would be an important partner since it is among the largest suppliers of

APIs. A joint US-China partnership may serve as a model for a concerted, globalized anti-counterfeit initiative.

Mr. Cohen suggested that DoC JCCT IPR Working Group can be a valuable partner and noted that TRIPS has clear provisions regarding trademark infringement. Namely, Article 46 stipulates that any country can seize infringed products.

Mr. Chris Costigan of Pfizer provided a statement on behalf of Pfizer Asia on regulation of bulk chemicals having medical use. Pfizer Asia advocates that SFDA be sanctioned a leadership role in the supervision of all APIs, whether they are manufactured for licensed pharmaceutical manufacturers or not.

In response to the U.S. delegation comments, Mr. Chen Xu of the Office of Market Compliance offered some remarks. The main difference between SFDA and U.S. FDA is that U.S FDA has powers of enforcement, while SFDA can only pursue administrative recourses. So SFDA must cooperate with Chinese Customs and Ministry of Public Security to strengthen its enforcement capabilities. An alliance between these agencies does exist and it is used to implement enforcement actions once a counterfeit is found in the drug supply. Once a counterfeit drug is detected, SFDA, in partnership with other agencies and the courts, aims to:

1) Trace the origin and extent of problem
2) Find responsible perpetrators (e.g. by using full capacity of the media to provide publicity, offering rewards of $50,000RMB, etc.)
3) Understand how the perpetrators took advantage of loopholes
4) Administer adequate punishment
5) Install preventive measures

In addition, numerous initiatives are underway to strengthen the sampling powers of pharmaceutical products in all provinces. Central government carries out training and equips provincial municipalities with anti-counterfeiting vehicle scanner that can detect counterfeited packaging. Mr. Xu encouraged the U.S. delegation to bring Chinese illegal websites to its attention.

In June 2004 all finished product manufacturers have to get GMP license and distributors GSP certificates.

Mr. Zhang added a few additional comments. Regarding increasing bulk chemicals regulation, SFDA welcomes more discussions, including in interministrial settings. It would be of great interest to have a step by step analysis of how bulk chemicals can be made into counterfeit products. As noted earlier however, SFDA currently cannot regulate bulk chemicals that are not used for pharmaceutical manufacturing. Mr. Gren responded that the JCCT IPR Subgroup and the Medical Device and Pharmaceutical Subgroup should join forces and enter the discussion with SFDA and other Chinese ministries.

Mr. Zhang also noted that the Chinese definition of "counterfeit drugs" might be broader than what is accepted in other countries, thus accounting for the higher incidence.

Distribution Rights

Mr. Peter Scheuer introduced the topic. SFDA issued a regulation on requirements to obtain distribution license one to two years earlier. Industry feels the regulation is appropriate. However, MOFCOM has still not issued its regulation as part of WTO process (MOFCOM is to issue a specific regulation for the pharma industry on import rights, and would most likely include some regulations on distribution as well). Therefore, as of now, finished import drugs still need to enter a separate distribution channel. A desirable outcome would be for Foreign Invested Enterprise (FIE) to be able to import finished drugs from mother group companies and put them in same channel of distribution together with the locally manufactured drugs of the Foreign Invested Enterprise. By raising this issue the U.S. delegation hopes that SFDA can give status of the situation and forward MOFCOM some input from this discussion.

Ms. Han Bing of Marketing Supervision Department responded that SFDA operates in a transparent manner. There is no difference between foreign and domestic companies – all are subjected to same requirements.

Mr. Bryan Qin Xue of the U.S. delegation made the further point that under WTO, a FIE manufacturer should get full trading and distribution rights. Currently a drug importer must have a drug distribution license as well as import rights in its business license. FIE manufacturers can distribute their own product without need of a drug distribution license because they have manufacturing license. But the powers are limited, and they can distribute only own products and cannot import drugs even from their own parent company. This is contrary to WTO provisions.

Clinical Trial Authorization (CTA)/Acceptance of Foreign Data

Mr. John Farah of the U.S. delegation made a presentation to frame the issues and stressed that U.S. companies wish to view China as a R&D partner and to include the Chinese population in multinational trials. Currently the long review period for clinical trial authorization and the heavy data requirements significantly impact those possibilities.

Mr. Zhang thanked Mr. Farah for the presentation. The domestic Chinese companies are equally upset he said. But by law, SFDA must approve (unlike U.S. FDA where IND are allowed to proceed) and must act on different criteria. What SFDA does review up front during CTA period is not reviewed again at full drug application stage – so no duplication. Mr. Zhang cautioned that China just entered market economy. So the Chinese investigators cannot be at the same level as the foreign investigators. Very strict standards still must apply and every clinical trial proposal scrutinized.

Other circumstances unique to China also must be considered during CTA period. For example, China's one child policy exerts a great influence on clinical trial review since every person is someone's only child.

Mr. John Stigi, of U.S. FDA asked whether the provincial offices have the right to review? The answer is no, and actually the foreign applications go directly to the headquarters while domestic companies have to first submit to the provincial level. The SFDA provincial offices conduct administrative review for completeness, take samples and test them. SFDA has no way to inspect foreign trial sites, so samples from foreign companies are accepted.

Duplicative Local Testing

The U.S. delegation expressed concern that testing requirements, e.g., NICBP testing, are proving to be a rate-limiting step in obtaining market approval.

Mr. Zhang clarified that the tests are necessary to ensure that SFDA have adequate standards against which quality can be assured once the drug reaches market. Three testing procedures are required:

1) NICBP testing to ensure authenticity
2) Registration testing to ensure consistency
3) Batch testing on imported shipments

The U.S. delegation reported that there have been six to eight month long delays at the NICBP step. SFDA responded that that length of delay was irregular, most likely due to inability to reproduce a particular standard.

Mr. John Stigi of U.S. FDA said that U.S. FDA used to test every batch of antibiotics due to quality concerns. But when the agency found incidence rate to be low, it stopped the practice. Mr. Zhang responded that SFDA can stop the practice only if a corresponding law were enacted by People's National Congress. In the meantime batch testing actually reduces sampling requirements during marketing.

Ms. Ling Ye of the U.S. delegation said that timing is important in streamlining the market approval process. There could be informal contact between testing lab and manufacturers prior to dossier submission to SFDA (although formal contact would start only upon SFDA acceptance of complete dossier).

Mr. John Farah asked whether there is a test model to streamline testing procedures. Mr. Zhang said there is a current effort and will be asking for open input, though he noted that it would be difficult to make quick changes.

Pharmaceutical Task Force Closing Comments

Mr. Gren said he was pleased with the day's proceedings. The discussions were very focused and benefited greatly by having the appropriate expertise present. The U.S. delegation continues to gain valuable insights through these Task Force meetings. He was especially pleased at the discussion on counterfeiting and bulk chemicals and looked forward to future collaborations with SFDA as well the JCCT IPR Working Group. He suggested adding language about anti - counterfeiting to the JCCT Medical Device and Pharmaceutical Subgroup WorkPlan.

Mr. Gren proposed weeks of March 20th and 27th for the Subgroup 10th anniversary meeting next year in Beijing. The plan is to make it a two-day event, with a Subgroup meeting and concurrent Medical Device and Pharmaceutical Task Force meetings.

Mr. Zhang echoed Mr. Gren's sentiment about the day's proceedings. This JCCT task force remains an important platform not only to meet foreign stakeholders but as a means to gain foreign input on regulatory issues. It is important to remember that though current implementation approaches might differ, both China and U.S. have same goals. He hoped that U.S. can take greater account of China's economics, culture and social environment. He looked forward to working together on the 10th Anniversary celebration.

Summary Bullets/Accomplishment:

- Ascertained the need and solicited support for further talks dedicated to appropriate regulation of bulk active pharmaceutical ingredients (APIs). This issue is to be viewed on a global scale, requiring input from Chinese, EU, developing world, and U.S. regulators, as well as multinational partners such as WTO.

- Clarified current patent linkage regulatory structure. Obtained from SFDA strategies that will enable patent holders to defend against possible infringement.