Statement of David G. Strunce
President and Chief Executive Officer
Scientific Protein Laboratories LLC

Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
United States House of Representatives

April 29, 2008

Chairman Stupak, Ranking Member Shimkus, and Members of the Subcommittee, I am David Strunce, President and Chief Executive Officer of Scientific Protein Laboratories LLC ("SPL"). I am accompanied by Dr. Yan Wang, Vice President of Business Development and Research for SPL, and General Manager of Changzhou SPL Company, Ltd. ("CZSPL"), a Chinese joint venture company in which SPL holds a majority interest. Dr. Wang is an American citizen who holds a Ph.D. in chemistry and has worked in the pharmaceutical and fine chemical industries since 1993.

We are here today to provide you with our perspective on the issues that have been raised regarding heparin products of Chinese origin. We also hope to contribute to your consideration of the broader issues surrounding the inspection by the Food and Drug Administration ("FDA") of foreign drug manufacturing facilities.

We would first like to provide some background about SPL and CZSPL. SPL is a supplier of active pharmaceutical ingredients ("API") used by other manufacturers to produce and market finished drug products. Our manufacturing facility in Waunakee, Wisconsin has more than 150

employees. We have been producing heparin sodium USP API at the Waunakee facility for more than thirty years, with an exemplary regulatory record. SPL also holds a majority interest in CZSPL, a joint venture company in Changzhou City, China. CZSPL, which has just over 30 employees, has been producing heparin API since 2004.

SPL and CZSPL are absolutely committed to producing drug ingredients of the highest quality. We are deeply distressed by what appears to have been the intentional introduction of a synthetic contaminant into the crude heparin supply in China. As the Committee knows, the test methods used safely for many years in the heparin industry were incapable of detecting this substance in heparin API produced by SPL, CZSPL, or any other manufacturer of heparin API. As I believe you are also aware, both SPL and CZSPL have cooperated fully in the FDA's investigation of the root cause of the recent events. We are determined to do what we can to understand how this situation arose and to prevent similar events in the future. Of course, we have great sympathy and concern for any patient who has suffered adverse events potentially associated with heparin.

Background on Heparin Production

Heparin from porcine sources has been used in medical practice for decades, and it remains an important active ingredient in anticoagulant or blood thinning prescription drug products. Like certain other drug and biological products, the starting material for heparin is from a natural source. Specifically, the raw source material is derived from the small intestinal tissue of pigs. In the United States, SPL buys such raw source material from slaughterhouses and processing facilities located in the United States and Canada, and then processes those raw materials to make heparin API. The production process involves extracting heparin from the raw source

materials into an intermediate form from which the purified heparin API is produced. SPL also produces certain API products in the United States starting with Chinese crude heparin. This material arrives as a dried granular substance on which certain preliminary processing steps have already been performed. In China, CZSPL produces heparin API from Chinese crude heparin.

The supply chain in China begins with the slaughtering of pigs at government-regulated slaughterhouses, which provide the intestines to casing/crude heparin workshops. The workshops then separate the intestines into casings and mucosa, process the intestinal mucosa into crude heparin, and provide the crude heparin to consolidators. In the supply chain, SPL and CZSPL purchase crude heparin from approved consolidators who combine the crude heparin obtained in smaller quantities from workshops. CZSPL and SPL then test the crude heparin, process and purify it into heparin sodium USP, and perform final testing, all under current good manufacturing practices ("GMPs") applicable to heparin API products. The resulting product is bulk, packaged heparin sodium that meets United States Pharmacopeia and similar international pharmacopeial standards, as well as the specifications of our customers. Such products are sold to manufacturers of finished pharmaceuticals, who then further process, test, package and sterilize the finished heparin products for distribution to their customers pursuant to specific FDA drug approvals.

We have attached to this testimony photographs of facilities in the SPL and Changzhou SPL supply chains in China. As you can see from these photographs, our supply chain is quite different from the uncontrolled conditions depicted in the media.

Heparin raw materials are not sourced in China simply in order to access cheaper starting material. Indeed, at times, the price of Chinese crude heparin has exceeded the cost of North American raw material. However, the global medical demand for heparin products has increased dramatically over the last decade, and there is an insufficient supply of pigs in North America to satisfy that demand. China is the world's leading producer of pigs, slaughtering about five times as many pigs per year as the United States. The material from those pigs is necessary to meet the increasing medical need for heparin both in the United States and other countries around the world. More than one-half of finished heparin products in the United States and globally are made from Chinese source material.

Quality Controls and Regulatory Compliance by SPL and CZSPL

The SPL and CZSPL facilities are registered as drug manufacturers with the FDA, and the heparin sodium USP API products produced by SPL and CZSPL for commercial distribution in the United States are listed with the Agency. Both the SPL and CZSPL API products are the subject of drug master files ("DMFs") submitted to the Agency, which detail the manufacturing and quality control processes that SPL and CZSPL use in producing heparin sodium API from Chinese crude heparin. These DMFs are updated at least annually, and are referenced by our customers as part of their drug applications. SPL and CZSPL have been open and transparent with FDA regarding the specific controls in place for our various production chains, including the use of Chinese source materials.

Like SPL, the CZSPL facility in China was designed and engineered to manufacture heparin sodium USP under conditions meeting United States current GMP requirements (as well as

equivalent international standards) for API products. CZSPL produces the materials in modern facilities using modern equipment and methods, and employs qualified personnel who are trained and experienced in United States quality system principles.

At both facilities, efforts to ensure the quality of heparin API are extensive. Neither SPL nor CZSPL accepts crude heparin from Chinese suppliers on faith. Heparin quality controls begin with controls over sourcing and collection to assure that the porcine material is appropriately derived and processed. For more than a decade, SPL has conducted on-site audits of the crude heparin consolidators in China from whom we receive crude heparin. SPL obtains samples of crude heparin from each consolidator and manufactures test batches of heparin USP API using those sample materials to ensure the quality of the incoming materials. All of this work is done before approving a consolidator as a crude heparin supplier to SPL and CZSPL. SPL and CZSPL also maintain purchasing orders with each raw material supplier and our dealings with those parties are fully documented.

SPL and CZSPL have worked with the FDA in taking proactive measures to increase quality controls over Chinese crude heparin, even in the absence of any known problems with the quality of those materials. While it may seem ironic today, part of SPL's rationale for engaging in the CZSPL joint venture was to facilitate our ability to monitor Chinese crude heparin suppliers. Thus, for example, during 2006, well before there had been any news of blue ear virus in pigs or contaminated heparin, CZSPL established and implemented a process of auditing and individually approving the crude heparin workshops that supply material to the consolidators from whom CZSPL obtains crude heparin.

Recent Heparin Concerns

As you know, in January 2008, Baxter International initiated a recall of certain lots of finished heparin products manufactured using API produced by CZSPL. Subsequently, SPL announced our own recall of Chinese-sourced heparin API sold to other customers. It is important to note that, based upon extensive testing to date, only specific lots of heparin produced during 2006 and 2007 from Chinese crude heparin were subject to these recalls. SPL heparin API products produced solely from North American source materials have not been affected.

On March 19, 2008, FDA announced that it had identified a suspected contaminant known as oversulfated chondroitin sulfate in certain finished heparin products. SPL and CZSPL cooperated fully and proactively in FDA's scientific efforts to study the substance, including by identifying and making available leading academic experts. There remain many unanswered questions about the origin of this substance and how it was introduced into the crude heparin supply chain in China.

It has now been publicly reported that oversulfated chondroitin sulfate has been found in heparin products around the world, most of which are completely independent of our supply chain. This information, together with our internal testing, makes clear that the substance in question was present in the crude heparin material before it ever reached the SPL or CZSPL production processes. Rather, the evidence suggests that the contamination occurred at some point in the supply chain upstream from API manufacturers. Unfortunately, as the FDA has made clear, due to the nature of the suspected contaminant, current GMPs in the heparin industry and

pharmacopeial testing standards, including potency testing and purification processes, could not detect, identify or remove the substance.

FDA recently designated two sophisticated methods -- proton nuclear magnetic resonance ("NMR") and capillary electrophoresis ("CE") -- as useful in detecting the presence of oversulfated chondroitin sulfate. At the time of the release of the products that have now been recalled, however, these specific methods for detecting oversulfated chondroitin sulfate had not been required or even identified by FDA, the USP, or foreign pharmacopeial bodies. Nor were these tests used within the industry. Unlike ordinary chondroitin sulfate, which is a naturally occurring component of heparin, the oversulfated form is not found in nature. Only the sophisticated new tests, developed after weeks of inquiry by scientists at the FDA and academic laboratories, have been able to detect the specific "peaks" relating to the oversulfated contaminant.

Using these tests, we recently tested reserve samples of incoming crude heparin from Chinese sources. Those samples showed "peaks" indicating that oversulfated chondroitin sulfate was present in certain batches of crude heparin before they reached SPL and CZSPL. Again, these NMR and CE test results are consistent with the other evidence that shows that any contamination with oversulfated chondroitin sulfate occurred at a point in the supply chain upstream from SPL and CZSPL.

Going forward, SPL and CZSPL have committed to the FDA that we will not release heparin products without employing these two new tests. Should further information suggest the

advisability of other enhancements to practices, processes, or testing among heparin API producers, we will work with the FDA and other regulatory authorities to implement such changes.

Inspection of the CZSPL Facility

We understand that the Committee is concerned that the CZSPL facility was not inspected by the FDA prior to the 2004 approval of the Baxter supplemental NDA permitting sourcing of heparin API from CZSPL. CZSPL is not aware of FDA's internal handling of this issue. From our perspective, the CZSPL facility was fully available and prepared for an FDA inspection. SPL discussed the Changzhou joint venture with FDA field personnel as early as 1999, and formally notified FDA of the CZSPL joint venture in March of 2000. The DMF detailing the quality control and manufacturing processes for heparin API produced at the CZSPL facility was submitted to the Agency in 2002. Upon learning that FDA had approved Baxter's supplemental NDA authorizing it to manufacture and ship finished heparin products produced from CZSPL-supplied API, we assumed that FDA was aware of and was satisfied with the quality systems that had been put in place at CZSPL.

The CZSPL facility also has been subject to audits by various third parties to determine compliance with current GMPs and other manufacturer specifications. Such audits, like most thorough GMP audits, recommended certain improvements, which were implemented. However, these audits concluded that CZSPL's systems were GMP-compliant.

As you know, FDA inspected CZSPL in February 2008. After an extensive five-day inspection, FDA issued a list of observations, known as a Form FDA 483. On the day before Commissioner von Eschenbach's testimony before this Subcommittee a week ago, FDA issued a Warning Letter that repeated some of the observations from the 483. There is no relationship, however, between the FDA observations and the contamination of certain heparin sodium lots with oversulfated chondroitin sulfate. As the FDA and leading academic researchers have made clear, that substance simply was not detectable using then-existing testing methods for heparin. With all due respect to FDA, we believe that the CZSPL facility was and remains in compliance with United States and international current GMP and industry standards for a heparin API manufacturer, and that its products met and meet applicable pharmacopeial testing requirements, as well as additional customer specifications. On March 17, 2008, CZSPL submitted its response to FDA's 483, outlining in detail the steps it has taken and will take to address FDA's observations. A number of those activities are now completed. We are diligently pursuing completion of the remaining items, and we will be providing a comprehensive response to the Agency's Warning Letter.

SPL and CZSPL are fully supportive of FDA's mission. We support FDA's intention to place permanent inspectional staff in China, and applaud your efforts to provide the Agency with additional resources for foreign inspectional activities. Indeed, we believe such resources will ensure the maintenance of high standards across the industry and enhance the confidence of patients in an increasingly global drug supply environment.

Conclusion

In closing, we know that in spite of SPL's strong reputation for quality developed over decades, we – as well as others producing heparin products - must work to regain the confidence of the public. The quality and safety of our API products is our central concern, and we will take whatever steps are necessary to protect the public health. In particular, we will continue to work with regulatory authorities in the United States, China, and other jurisdictions to uncover the source of the contamination and implement new controls to guard against future events of this kind.

Mr. Chairman, Ranking Member Shimkus, and Members of the Subcommittee, thank you for the opportunity to participate in today's hearing. We understand your interest in these important issues, and we look forward to answering your questions.