

ONE HUNDRED FIFTEENTH CONGRESS  
**Congress of the United States**  
**House of Representatives**

COMMITTEE ON ENERGY AND COMMERCE

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WASHINGTON, DC 20515-6115

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February 2, 2018

The Honorable Scott Gottlieb, M.D.  
Commissioner of Food and Drugs  
Food and Drug Administration  
Silver Spring, MD 20903

Dear Dr. Gottlieb:

As part of a long-standing investigation into the contamination of crude heparin manufactured in China that reached the U.S. heparin supply, and harmed U.S. patients a decade ago, the Committee has been monitoring the Chinese heparin market. We write today to forward information for FDA's further review and action, as appropriate, related to inconsistencies and red flags in Chinese heparin export and import data that could impact the U.S. heparin supply. The areas of concern relate to the following: (1) whether the Chinese heparin supply is in fact shrinking or increasing, which could affect the risks of a heparin shortage in the U.S. and could raise the risk of economically-motivated adulteration; (2) whether Chinese customs data accurately reflect Chinese heparin export and import activity; and (3) whether the recent emergence of significant U.S. heparin imports to China is further constraining the U.S. domestic supply of heparin.

The FDA has a substantial oversight interest in heparin, having taken numerous steps over the last decade to protect the safety of the U.S. heparin supply. Such steps have included: (1) identification of a previously unknown contaminant, overly sulfated chondroitin sulfate (OSCS), in heparin; (2) development and dissemination of a test to detect the contaminant in heparin supplies; (3) publication of FDA guidance on monitoring crude heparin for quality; (4) review of test data for each lot of heparin imported into the U.S.; and (5) increased surveillance inspections of heparin API (active pharmaceutical ingredient) and crude heparin manufacturing facilities.<sup>1</sup>

Background on Heparin Contamination and the Committee's Investigation

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<sup>1</sup> Letter from Dayle Cristinzio, Associate Commissioner for Legislation, FDA to The Honorable Fred Upton, et al, Chairman of the House Energy and Commerce Committee (December 1, 2016).

The Committee's investigation into the contamination of crude heparin manufactured in China began a decade ago, after contaminated heparin reached the U.S. heparin supply and harmed U.S. patients in late 2007 and early 2008. Although the perpetrators have not been identified, test results and other evidence point to the contamination occurring upstream in the Chinese heparin supply chain. Dr. Janet Woodcock, Director of FDA's Center for Drug Evaluation and Research (CDER) observed, "the heparin problem [was] a landmark type of event[.] . . . It demonstrated that an essential drug used every day all over the health care system c[ould] be contaminated. That is pretty bad."<sup>2</sup> Dr. Woodcock further stated in 2008 that "[i]n the 22 years that [she] ha[d] been at the Food and Drug Administration, the . . . worldwide situation related to the contamination of heparin [was] the most serious threat that [she] ha[d] faced regarding the integrity of [the U.S.] drug supply system."<sup>3</sup>

Heparin is the only drug used in the U.S. for open-heart surgeries and kidney dialysis<sup>4</sup>, which reflects the drug's effectiveness and relatively inexpensive cost. One pharmaceutical executive called heparin "an essential hospital product used in very sick people" that "is priced well below a box of Band-aids."<sup>5</sup> It is also the only intravenous anticoagulant with an antidote (protamine sulfate) for overdoses, and is a polytherapeutic with wide clinical applications. Heparin is on the World Health Organization's Model List of Essential Medicines.<sup>6</sup>

One of the lessons learned from the heparin crisis was that industry and the FDA should monitor significant changes in supply and demand in the Chinese heparin market that could raise the risk of economically-motivated adulteration. In addition, Chinese business acquisitions in 2013 of Smithfield Foods (a major crude heparin supplier for the U.S. market)<sup>7</sup> and Scientific Protein Laboratories (a U.S. heparin manufacturer) indicate increasing Chinese market dominance through horizontal and vertical integration of the heparin market. FDA's ongoing concerns over the Chinese heparin industry is indicated by FDA placing nearly 40 Chinese heparin manufacturers on import alert over the last decade and even sending a warning letter in

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<sup>2</sup> Stephen Barlas, *FDA's Janet Woodcock Riding High*, 33 PHARMACY & THERAPEUTICS J. 396 (2008), available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2740944>.

<sup>3</sup> Woodcock "Dear Colleague" Letter to Physicians 2008 (undated, but substance of letter suggests the timing would have been around May or June of 2008).

<sup>4</sup> Dialysis is a life sustaining treatment for nearly 400,000 Americans with kidney failure. American Association of Kidney Patients (AAKP), "AAKP & Fresenius Medical Care Team Up to Honor Dialysis Patients," November 11, 2010 (press release). [http://www.aakp.org/print-version/dsp\\_article.cfm?cat=7&subCat=20&topic=674&art=3268](http://www.aakp.org/print-version/dsp_article.cfm?cat=7&subCat=20&topic=674&art=3268). At the end of 2010, 594,374 dialysis and transplant patients were receiving treatment for end-stage renal dialysis (ESRD), a 3.8 percent increase from 2009. 2012 United States Renal Data System (USRDS) Annual Data Report, 166.

<sup>5</sup> Testimony of Clive Meanwell, Chairman and CEO of the Medicines Company, "The Heparin Disaster: Chinese Counterfeits and American Failures," Hearing before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, U.S. House of Representatives, Serial No. 110-109, 167 (April 29, 2008).

<sup>6</sup> WHO Model List of Essential Medicines, 19<sup>th</sup> List (April 2015).  
[http://www.who.int/medicines/publications/essentialmedicines/EML2015\\_8-May-15.pdf](http://www.who.int/medicines/publications/essentialmedicines/EML2015_8-May-15.pdf).

<sup>7</sup> Based on information provided by Smithfield Foods to the Committee in 2013, Committee staff estimated Smithfield's share of the domestic pig-intestines-for-heparin supply at about 27.5 percent based on certain industry-based assumptions. The estimate is consistent with a heparin manufacturer management presentation in July 2006 that included a slide, "Heparin/U.S. Heparin Supply Chain," showing Smithfield represented 26 percent of U.S. hogs processed. The estimates may understate Smithfield's share of the U.S. crude supply because some U.S. companies export porcine intestines to European markets.

June 2017 to a Chinese contract testing laboratory because it failed to ensure a suitable system for testing heparin samples for the presence of the OSCS contaminant.

Heparin is a drug derived from pig intestines. Although heparin can also be derived from other animal sources, for more than 20 years the U.S. and many other countries have adhered to a porcine origin requirement because of concerns over mad cow disease. Given the porcine requirement for heparin, the U.S. is largely dependent on China for its heparin because almost half of the global pig supply is in China.<sup>8</sup> About 60 percent of the crude heparin used to manufacture finished heparin in the U.S. is sourced from China.<sup>9</sup>

U.S. dependence on Chinese heparin and on one animal source raises risks of shortages.<sup>10</sup> The pig supply is vulnerable to reductions of availability because of disease outbreak. In 2006-2007, an outbreak of the Blue Ear Virus in China is believed to have been a contributing factor to the reduced heparin supply and the volatility of the heparin market immediately preceding the heparin contamination crisis in early 2008. The United States encountered a similar problem in 2014, when the porcine epidemic diarrhea virus (PEDv) spread to 30 states, wiping out 10 percent of the U.S. pig population. Outbreaks such as PEDv could adversely affect the availability of heparin and heparin-derived products because of the reduced number of hogs available.<sup>11</sup> Even before PEDv, the FDA at times over the last decade has assessed the U.S. heparin supply as “stressed” or even in shortage.<sup>12</sup>

FDA has recognized these concerns about U.S. over-reliance on the Chinese heparin supply and possible shortages, given the agency’s 2014 proposal to re-introduce bovine-sourced heparin in the U.S.<sup>13</sup> Because heparin is a widely used essential medicine with no medical alternatives in certain clinical situations, the U.S. health care system could be vulnerable to

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<sup>8</sup> Kevin Chen and Jimin Wang, Hog Farming in Transition: The Case of China, The Pig Site (February 28, 2013) (“China is the world’s largest hog producer and pork consumer, accounting for almost half of global pork consumption and production.”). <http://www.thepigsite.com/articles/4262/hog-farming-in-transition-the-case-of-china/>.

<sup>9</sup> *Id.* According to an April 10, 2010 industry slide provided to the FDA, China-sourced heparin supports at least half of the world demand and more than 80 percent of the U.S. unfractionated heparin market.

<sup>10</sup> Janet Woodcock, MD, Director, CDER, FDA, Introduction: Proposal for Reintroduction of Bovine Heparin to the US Market, Slide Presentation before Science Board to the FDA, June 4, 2014, Slide 9 (“Single animal sourcing/single country sourcing is risky due to animal-specific/country-specific risk (e.g., blue-ear disease.”)).

<sup>11</sup> GAO, Emerging Animal Diseases: Actions Needed to Better Position USDA to Address Future Risks, GAO-16-132, 24 (May 2016) (“Pigs produced in the United States have more uses than supplying pork, according to the U.S. Department of Agriculture. For example, several human medical treatments such as heparin are developed from pig by-products.”). See also Celsus Laboratories Press Release, April 28, 2014: “[PEDv] may adversely affect future availability of Heparin Sodium USP, and derivatives thereof, by reducing the number of hogs available for slaughter.”

<sup>12</sup> As of November 1, 2017, the American Society of Health-System Pharmacists listed several heparin injection products on its drug shortages list. <https://www.ashp.org/drug-shortages/current-shortages/Drug-Shortage-Detail.aspx?id=1289>.

<sup>13</sup> “This ‘heparin crisis’ demonstrated the vulnerability of drug supplies produced from increasingly global manufacturing chains and highlighted the risks inherent in reliance on one country and one animal species as the primary source for a crucial drug.” D. Keire, et al, Diversifying the Global Heparin Supply Chain: Reintroduction of Bovine Heparin in the United States?, *Pharmaceutical Technology*, 2 (November 2015).

fluctuations in the crude heparin supply.<sup>14</sup> Further, in 2016 the Committee presented analysis to the FDA indicating concerns that China may not have enough pigs to make all the heparin it produces.<sup>15</sup> However, FDA's recent briefing with Committee staff suggests that the reintroduction of bovine heparin in the U.S. that could reduce the vulnerability may still be a few years away. Thus, in the near future, the U.S. will still depend heavily on China for its supply of heparin.

#### Chinese Heparin Exports Increasing? Leading Manufacturer Does Not Accept Customs Data

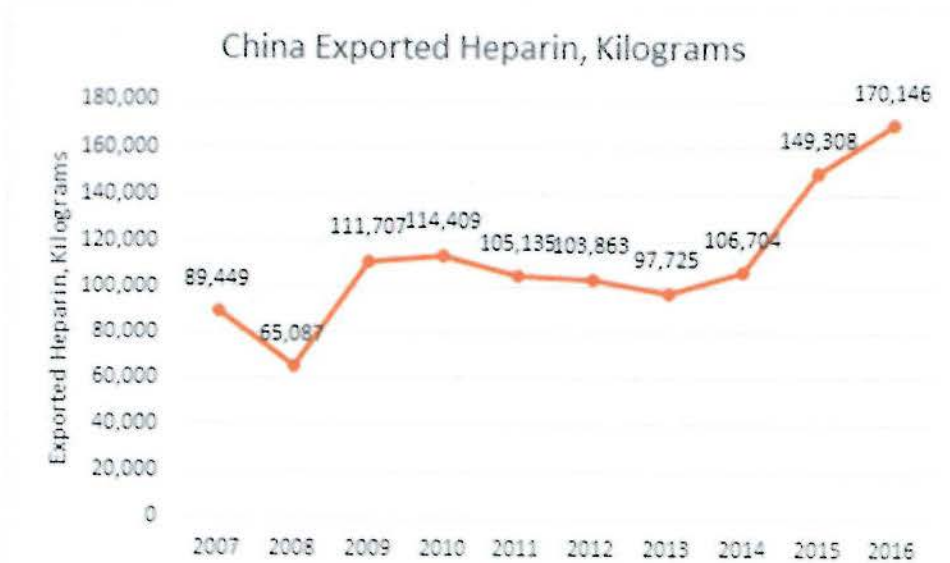
Given the United States' continued reliance on heparin sourced from China, recent trends and interpretation of Chinese customs data for Chinese heparin exports and imports raise troubling concerns. Committee staff reviewed Chinese customs data on heparin exports from three different sources: China Customs data obtained by an industry source; China Customs data downloaded by Global Trade Atlas and obtained by the Congressional Research Service; and China Customs data as presented for the 2016 Annual Report of Shenzhen Hepalink, one of China's leading heparin manufacturers and heparin importers to the U.S. The statistics from the three data sets are not identical, but correlate closely during the 2007-2014 timeframe, with some minor differences showing the same trend overall. During the heparin crisis, Chinese heparin exports declined about 27 percent from 2007 to 2008, with only about 65,000 kilograms in 2008. However, from 2009 to 2014, the level of heparin exports recovered to a level fluctuating around 100,000 kilograms exported annually, and about 10 percent higher than the export volume prior to the heparin crisis. See Exhibit 1.

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<sup>14</sup> Background Information for the FDA Science Board Meeting, June 4, 2014, Proposal to Encourage the Reintroduction of Bovine Heparin to the US Market.

<sup>15</sup> Letter from The Honorable Fred Upton, Chairman, House Energy and Commerce Committee, et al., to The Honorable Robert M. Califf, M.D., Commissioner, FDA (March 29, 2016) <https://archives-energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/documents/114/letters/20160329FDA.pdf>

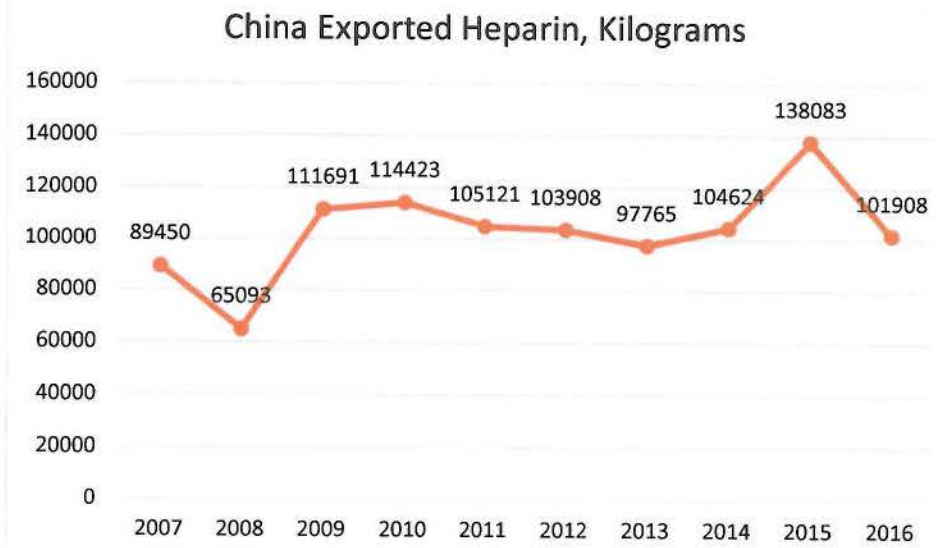
Exhibit 1



Source: China Customs data downloaded by Global Trade Atlas, as reported to staff by Congressional Research Service.

Starting in 2015, Chinese heparin exports surged about 32 to 40 percent above the volume of 2014 Chinese heparin exports. However, for 2016, the data sets conflict over whether Chinese heparin exports were surging or declining. The industry data set and the Global Trade Atlas (GTA) set show Chinese heparin exports increasing from about 150,000 kilograms in 2015 to about 170,000 kilograms in 2016, about a 13 percent increase, and an almost 60 percent increase in Chinese heparin exports between 2014 and 2016. In contrast, Shenzhen Heparlink's Annual Report for 2016 showed the volume of Chinese heparin exports declining from 138,083 kilograms in 2015 to 101,908 kilograms in 2016, a decline of more than 26 percent. See Exhibit 2. As detailed later in this letter, the 2016 Chinese export statistics presented by Heparlink were based on the company's interpretation of the Chinese customs data because of credibility concerns; the 2016 statistic was not what was reported by Chinese customs in the data set obtained by Heparlink.

Exhibit 2

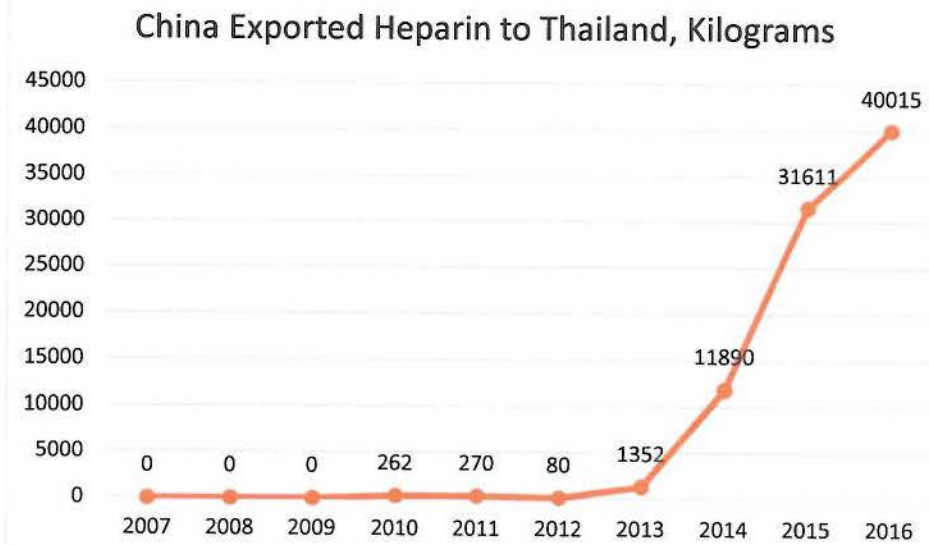


Source: Shenzhen Hepalink, Annual Report for 2016 (April 2017).

### Unexplained Surge in Chinese Heparin Exports to Thailand and Hong Kong

In addition, the industry and GTA data sets showed significant increases in Chinese heparin exports in recent years to Thailand and Hong Kong. From 2007 to 2009, there were zero exports of heparin from China to Thailand. From 2010 to 2012, Chinese heparin exports to Thailand ranged from 262 kilograms to 1 kilogram exported annually. Starting in 2013, Chinese heparin exports jumped from 1 kilogram to 1,352 kilograms. In 2014, exports increased nearly nine times to 11,890. In 2015, Thailand became China's largest heparin export destination, with 31,621 kilograms, and then increased again in 2016 to 40,015 kilograms, still the leading heparin export market. See Exhibit 3.

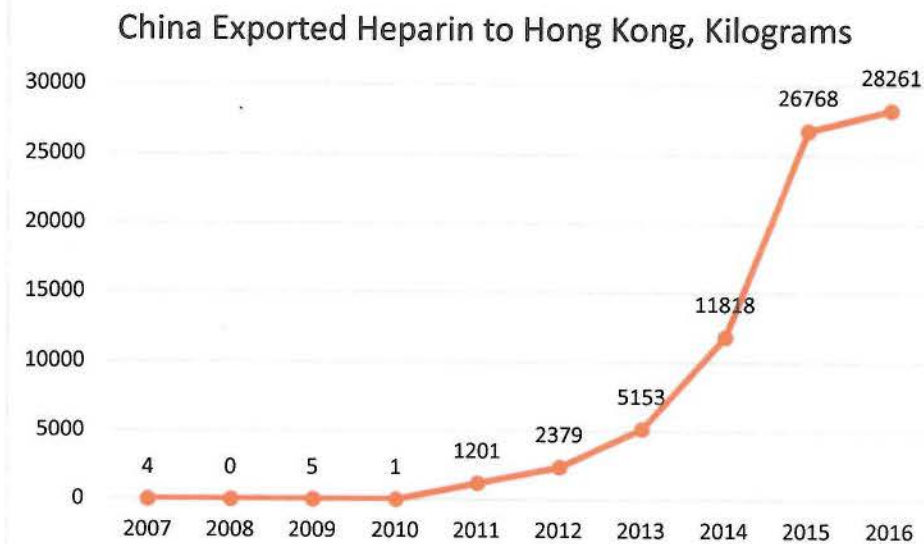
Exhibit 3



Source: China Customs data downloaded by Global Trade Atlas, as reported to staff by Congressional Research Service.

Similar trends were observed with heparin exports to Hong Kong. From 2007 to 2010, exports to Hong Kong were either zero or in single digits. In 2011, exports to Hong Kong jumped to 1,200, nearly doubling in 2012 to 2,104 kilograms, doubling that volume in 2013 to 5,153 kilograms, then doubling again in 2014 to 11,818 kilograms, and doubling yet again in 2015 to 26,768 kilograms. In 2016, Chinese exports to Hong Kong were 28,261 kilograms, ranking as the second-largest export market after Thailand. See Exhibit 4.

Exhibit 4



Source: China Customs data downloaded by Global Trade Atlas, as reported to staff by Congressional Research Service.

It is not apparent why Thailand and Hong Kong became leading export markets for China. Neither location has a large heparin manufacturing presence. Further, Chinese heparin exports were surging to Thailand, at a time that Thailand was experiencing declines in exports, generally.<sup>16</sup> For more than a year, Committee staff has contacted various industry sources, but no one has yet provided an actual explanation for this trend.

Committee staff contacted outside counsel for Shenzhen Hepalink to get an explanation for why the Annual Report's statistics showed a sharp decrease in Chinese heparin exports in 2016 while the other data sets of Chinese heparin exports showed an increase and at a volume more than 50 percent higher than two years earlier. Outside counsel provided the following information:

Hepalink has informed me as follows: they noticed that since 2016 the quantity of Heparin exported from China to Hong Kong and Thailand had increased significantly, and a lot of that heparin appeared to be coming from casing factories and trade companies. In July 2016, Hepalink purchased the custom data for Hong Kong and Thailand. It was found that Thailand imported 40,015Kg and exported 484Kg of heparin, and the difference between import and export of heparin for Hong Kong was also big (27,753Kg). There was no reasonable explanation for the imports based on consumption/population in those two jurisdictions, and there were no heparin manufacturers in those jurisdictions which were registered in Europe or the US, to Hepalink's knowledge. Hepalink viewed these numbers as 'abnormal' and did not include them in their annual report for Year 2016.<sup>17</sup>

Hepalink, through outside counsel, informed Committee staff that they did not realize the number was unusual until 2016.<sup>18</sup> Once they recognized the aberration relating to Thailand and Hong Kong, they excluded the data in their annual report for 2016.<sup>19</sup>

#### Heparin Imports to China – Including Significant Imports from U.S.

In addition to the questions over Chinese heparin exports, Chinese customs data also shows some significant growth in the volume of heparin imported to China. According to China Customs data downloaded by Global Trade Atlas, for the 2007 to 2010 timeframe, China only imported 1 to 1,195 kilograms of heparin annually. However, starting in 2011, China's heparin imports increased to 18,264 kilograms, then doubled to 38, 223 kilograms in 2012, nearly increased 85 percent to 70,597 kilograms in 2013, increased about 72 percent to 121,425 kilograms in 2014, decreased 82 percent in 2015 to 21, 673 kilograms, and then increased back to 104,092 kilograms. See Exhibit 5.

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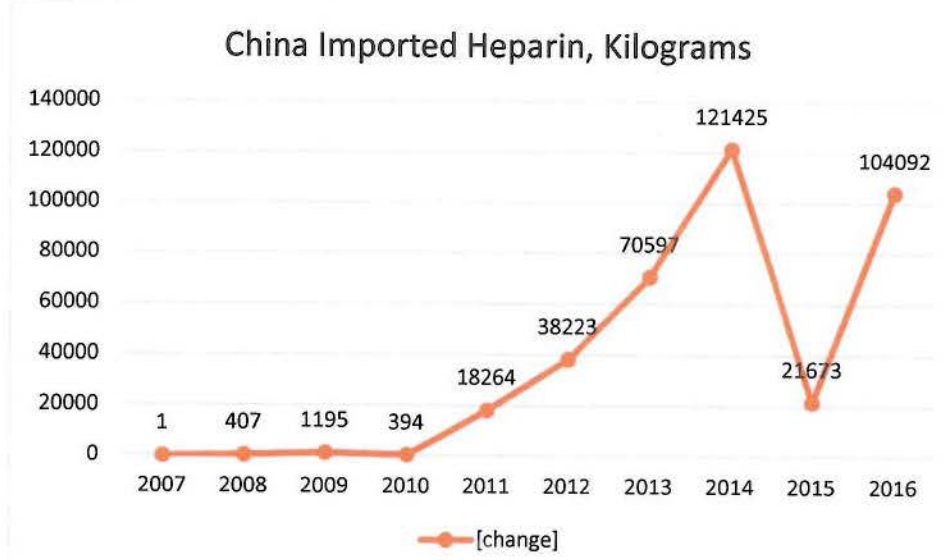
<sup>16</sup> Agence France-Presse, Thai Exports Suffer Worst Drop in Four Years (February 26, 2106), <http://www.industryweek.com/trade/thai-exports-suffer-worst-drop-four-years>

<sup>17</sup> Email from Hepalink outside counsel to Committee staff, July 11, 2017.

<sup>18</sup> Email from Hepalink outside counsel to Committee staff, July 14, 2017.

<sup>19</sup> *Id.*

Exhibit 5

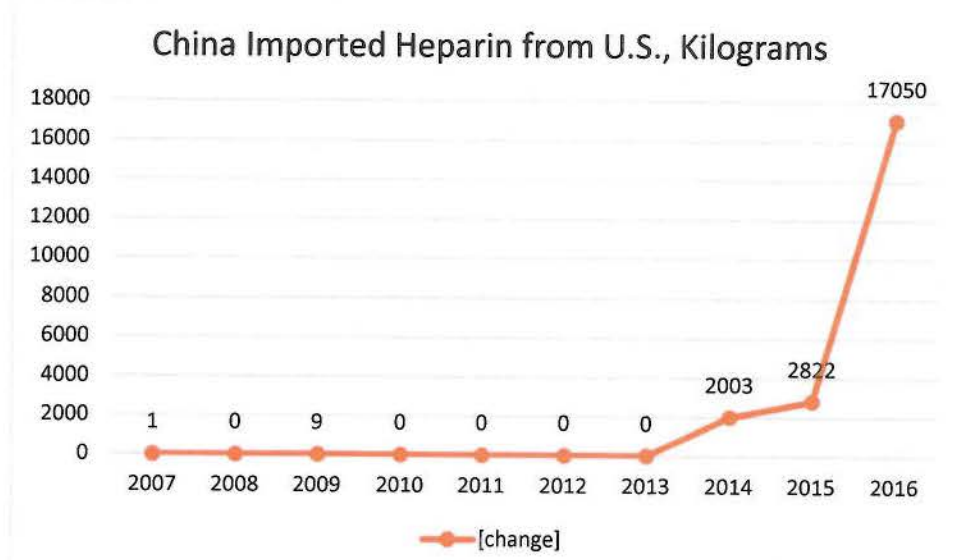


Source: China Customs data downloaded by Global Trade Atlas, as reported to staff by Congressional Research Service.

Further, in recent years, the United States has emerged as the leading importing foreign country to China for heparin imports—meaning that the United States is the largest exporter to China for heparin. This is particularly interesting given the U.S. dependency on China for heparin and the limited U.S. heparin supply. Between 2007 and 2013, the U.S. either had zero exports or exports to China in the single digits. In 2014, the U.S. exported 2,003 kilograms of heparin to China, and in 2015, the U.S. exported 2,822 kilograms of heparin to China. In 2016, the U.S. exported 17,050 kilograms of heparin to China, by the far the leading exporter of heparin that did not originate in China and with the greatest value of imports at \$11,634,209. The heparin exported by the United States constituted about 44 percent of the value of all Chinese heparin imports in 2016.<sup>20</sup> This volume also surpassed the 15,557 kilograms of heparin directly imported from China to the U.S.—the first time it has been known that the volume of U.S. exports of heparin to China is more than direct imports of heparin from China to the U.S. However, the U.S. still receives additional heparin imports from other countries where the heparin was sourced from China. See Exhibit 6.

<sup>20</sup> For heparin exported from China and then later reimported to China, China Customs lists such shipments as imports from China. Most Chinese heparin imports are listed as being from China. As reported by the Congressional Research Service in consultation with GTA, imports report the country of origin of the goods being imported or the country that created the goods being imported. This means that it is possible for a country to import goods that were created within their own country that have been exported and then reimported back into their country *without significant change in form* and report that trade as an import from itself.

Exhibit 6



Source: China Customs data downloaded by Global Trade Atlas, as reported to staff by Congressional Research Service.

This increase in imports is consistent with a similar trend in the Chinese pork industry. Since 2007 China has begun to import significant quantities of pork for the first time to make up for the domestic supply shortage.<sup>21</sup> From 2007 to 2014, China's pork imports have increased substantially, with an annual average growth rate of 150 percent.<sup>22</sup> Further, Chinese entities have acquired control over key pig or heparin supplies in the U.S. In 2013, a Chinese holding company acquired the largest pork producer in the U.S., Smithfield Foods and Shenzhen Hepalink acquired Scientific Protein Laboratories.

China's pork industry is still facing supply pressures due to pig diseases, rising feed costs, labor costs, environment pollution, and food safety concerns.<sup>23</sup> In 2007, the Chinese central government established a national pork reserve to deal with pork shortages and volatile pork prices in the same year. Further complicating assessment of the Chinese pig supply is that official agricultural statistics for China are subject to major inconsistencies and have been questioned by researchers.<sup>24</sup> One analyst concluded: "China's self-sufficiency in pork is not sustainable in the long run."<sup>25</sup>

Another indicator of Chinese pig supply issues impacting heparin production is the increased use of frozen intestines based on FDA documents provided to the Committee. Numerous instances of this practice were identified in recent FDA inspections of Chinese heparin manufacturers:

<sup>21</sup> Hanming Fang, China's Astounding Appetite for Pork: Recent Trends and Implications for International Trade, Research: Inside Penn Wharton PPI, 5 Issue Brief No. 3 (April 2, 2015).

<sup>22</sup> *Id.*

<sup>23</sup> *Id.*

<sup>24</sup> Xiaohua Yu and David Abler, Where Have All the Pigs Gone? Inconsistencies in Pork Statistics in China, 30 China Economic Review 469 (September 2014). <http://dx.doi.org/10.1016/j.chieco.2014.03.004>

<sup>25</sup> Fang, *supra* note 15.

- A February 2014 inspection of a crude heparin supplier to a major heparin API (Active Pharmaceutical Ingredient) manufacturer found documented use of imported unauthorized frozen intestines to manufacture crude heparin. The imported intestines were frozen and produced in Denmark. The reasons given for purchasing imported frozen intestines were to reduce cost and increase profit. The supplier stated it purchased 200,000 imported frozen intestines. Two months after the incident, the supplier continued to use imported frozen intestines for crude production, and the API manufacturer terminated the supply contract. However, the FDA inspectors were told the supplier then sold to another supplier who sold to another Chinese heparin API manufacturer for the U.S. market, but a 2015 FDA inspection of this firm did not show that FDA followed up on whether frozen intestines were being provided to this firm by the crude supplier.
- A January 2015 inspection revealed the unauthorized use of frozen intestines by a crude heparin supplier who then tried to cover it up. The quality assurance manager for the heparin API manufacturer claimed she audited the supplier and frozen intestines processing was included in an audit report shown to FDA inspectors in a previous inspection.
- A March 2014 inspection found that a crude heparin workshop owned by a heparin API manufacturer had a batch of frozen intestines in the casing workshop, a deviation of its written agreement with a heparin API firm customer. The FDA inspectors could not verify the source of the batch of frozen intestines and observed that the practice was not as rare as suggested by the manager of the workshop.
- A December 2014 inspection of a heparin casing company found four workers uploading frozen intestines and intestine skins from an independent trailer type cold room into a small blue truck.
- An August 2014 inspection of a crude heparin manufacturer found that once more than about 10,000 pig intestines were accumulated, a non-refrigerated truck would pick up the frozen intestines for transport to the manufacturing site. The FDA inspectors found there was no monitoring of the temperature of the intestines during the 12-hour or 2-day delivery time of the frozen intestines from the slaughterhouse to the factory in a non-refrigerated truck. No temperature monitoring instrumentation or recording of temperature were observed.

In addition to the use of frozen pig intestines, other factors further raising uncertainty about the capacity of the Chinese pig and heparin supply include:

- Differing yields of heparin depending on the species and age of pigs. A recent study found a surprising absence of heparin in intestinal mucosa of baby pigs.<sup>26</sup>
- U.S. Pharmacopeia revision in 2009 in response to the heparin crisis increased the minimum specifications of heparin sodium activity from 140U/mg to 180U/mg, which

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<sup>26</sup> Yanlei Yu, et al., Surprising absence of heparin in the intestinal mucosa of baby pigs, 27 *Glycobiology* 57 (2017).

had the effect of increasing the number of pig intestines needed to make one kilogram of heparin API for those Chinese heparin manufacturers that were producing heparin API at 160U/mg or lower.

- While the Chinese heparin supply has increased since the heparin crisis of 2008, global heparin API demand has nearly doubled during the same time frame, from 23.6 trillion units of heparin API demand to an estimated 44.3 trillion units in 2015.<sup>27</sup>
- Continued growth of the low molecular weight heparin market.<sup>28</sup>
- China's requirement in 2015 that all heparin come from pigs.<sup>29</sup>
- Growth in China's domestic demand for heparin.<sup>30</sup>

In light of these concerns, we would appreciate FDA providing the Committee by March 2, 2018 with a contingency response plan in the event of a heparin shortage. If you have any questions regarding information in this letter or about this request, please contact Alan Slobodin with the Majority Committee staff at (202) 225-2927.

Sincerely,



Greg Walden  
Chairman



Joe Barton  
Vice Chairman

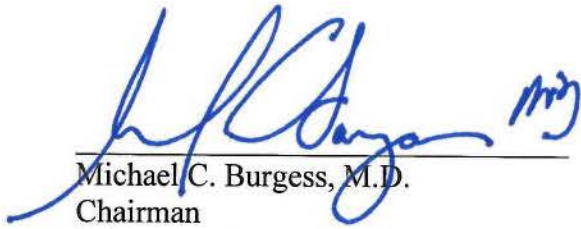
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<sup>27</sup> Nanjing KingFriend IPO Prospectus 2016, 1-1-106 citing Huicong Pharmaceutical Industry Net, [www.pharmacy.hc360.com](http://www.pharmacy.hc360.com) (site has malware).

<sup>28</sup> Jawed Fareed et al., *Biological Profile of the Hyper/Oversulfated Chondroitin Sulfate Contaminant Isolated from Recalled Heparin*, 34 SEMINARS IN THROMBOSIS & HOMEOSTASIS 119 (2008), available at <http://www-heparin.rpi.edu/main/files/papers/460SemThrombHemostas08%20copy.pdf>. "The supply and demand ratio for heparin and heparin-related products has become imbalanced in the past few years due to the expanded use of low molecular weight heparin."

<sup>29</sup> Change in the Chinese Pharmacopeia in 2015 to require 100 percent porcine heparin was noted in the Committee's letter to FDA, March 29, 2016, *supra* note 13.

<sup>30</sup> "With the explosive population of cardio-cerborvascular sufferers in China, the market share of heparin drugs keeps increasing year by year." China Pharma-Intelligence.com, "China Heparin Industry Report 2010". This trend correlates with China's aging society. The number of senior citizens over 65 in China was 104 million in 2006, and is predicted to reach 332 million in 2050. J. Hu, Y. Dai, and K. Gu, *Pharmaceutical Supply Chain in China: Challenges and Opportunities*, 8 (CAPS Research, March 2010). Summary of Powerpoint Presentation by Tao Jianhong, Deputy Director, of the SFDA's Southern Pharmaceuticals Economic Research Institute and Editor-in-Chief, *Medicine Economic News*, (2011) (translated by CRS): The domestic (Chinese) demand for heparin raw materials in 2010 was 15.9 billion units, or 60.69 percent of the global demand. Domestic demand is forecast to grow to 34.56 billion units in 2015, accounting for 78.02 percent of the global total.

A handwritten signature in blue ink, appearing to read "M. Burgess" with a flourish at the end.

Michael C. Burgess, M.D.  
Chairman  
Subcommittee on Health

A handwritten signature in blue ink, clearly legible as "Gregg Harper".

Gregg Harper  
Chairman  
Subcommittee on Oversight  
and Investigations

cc: The Honorable Frank Pallone, Jr., Ranking Member

The Honorable Gene Green, Ranking Member  
Subcommittee on Health

The Honorable Diana DeGette, Ranking Member  
Subcommittee on Oversight and Investigations