Ensuring the Safety of America's Drug Supply Chain

A GiveWell Review of The Pew Charitable Trusts' Influence Over Title VII of FDASIA

(Tamara Mann, Ph.D. prepared this report)

Table of Contents:

I: Project Description

This report evaluates The Pew Charitable Trusts' influence over drug supply chain safety legislation in 2012. In a 2014 report distributed to GiveWell, Pew lists as an accomplishment (level green on their internal scorecard) the passage of legislation to "increase inspections of overseas drug plants." This legislation was included in Title VII of the 2012 FDA Safety and Innovation Act (FDASIA).[1]

This report aims to assess Pew's claim of impact over Title VII of FDASIA. In this report, I distinguish between mechanistic impact—how Pew accomplished its goals—and humanitarian impact—the broader human consequences of this achievement.

To fully understand Pew's strategic approach to drug safety legislation, this report also looks at how Pew's work on Title VII set the stage for further legislative accomplishments in FDASIA and later in the 2013 Drug Quality and Security Act.

[1] For more details on Title VII see, http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/ucm366058.htm.

II: Sources and Process:

This report relies on oral interviews and three kinds of written sources: articles regarding FDASIA in the popular press and trade journals, articles regarding FDASIA published by PEW and accessible on the PEW website, and books on the U.S. Food and Drug Administration (FDA) and drug safety.

I conducted six interviews. Two of the individuals I interviewed worked within Pew on FDASIA and the other four individuals worked within the government or industry between 2011 and 2013. One of those four, Elizabeth Jungman, recently moved from the Senate HELP (Health, Education, Labor and Pensions) Committee to a position at Pew. Despite this close connection with Pew, I found her comments to be detailed, honest, and thoughtful about Pew's relative impact on Title VII.

As this was a limited literature review, I focused my attention on the articles and books that were both easily accessible (through the web, ProQuest, and an academic library) and provided the largest amount of relevant information. I found all of the sources, including the articles produced by Pew, to be reliable. While the sources produced by Pew seek to explain and applaud Pew's accomplishments, they were written by veteran journalists and contain valuable information on how Pew influenced FDASIA.

While I took into consideration the agendas of both the oral and written sources, it was clear from the outset that there was broad agreement about the relative causal weight of Pew in Title VII.

There are voices missing from this narrative, including major stakeholders such as Heather Bresch, the CEO of Mylan (see stakeholder section) and representatives from consumer groups. If GiveWell were interested in pursuing this research further, I would extend interviews to them as well as to relevant parties that worked in the White House and the FDA.

III: FDASIA and PDUFA

On July 9th, 2012, the President signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA). This bill reauthorized the Prescription Drug User Fee Act (PDUFA), which continues and expands the fees private industry pays the FDA to ensure a safe and speedy review process. User fees currently account for almost half of the FDA budget and are crucial to the FDA's ability to evaluate new drugs and medical devices.[2] FDASIA also incorporated a number of other provisions, including giving the FDA, in

[2] Several additional FDA user-fee agreements are renewed on the same five-year cycle.
For a recent breakdown of the FDA budget request and user fees *see* (http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM388309.pdf).

Title VII of the bill, the ability to "address the challenges posed by an increasingly global drug supply chain."[3]

A. Important Policy Background on PDUFA

By 1990, years of budget cuts and scandal had left the FDA defanged. According to the health and science reporter Philip J. Hilts in his book *Protecting America's Health*, "…the FDA was in desperate shape, an organizational disaster waiting to happen." This, at the same time that the "industries the FDA regulated were booming…." The grim situation and the growing lack of public faith in the Administration began to concern companies within the pharmaceutical industry, who relied on the FDA for domestic and international credibility.[4]

The FDA, industry representatives, and key congressional committees came up with a solution to bolster the FDA's credibility and speed up review times—user fees. Likened to fees paid by national park visitors, the user fee law required companies to "pay a fee for each drug submitted for approval." The funds would then "go to hire medical officers to review drugs."[5] Enacted in 1992, the resulting law, the Prescription Drug User Fee Act (PDUFA), had a sunset clause.[6] Every five years the law must be renewed. Since user fees are crucial to the FDA's basic operations, PDUFA is considered 'must pass' legislation.[7]

The PDUFA renewal cycle can open a legislative window for stakeholders. FDA and industry representatives negotiate the user fee agreements and then send it to Congress. Congress then has the option of passing the user fees without riders or attaching additional policies.[8] Since the pharmaceutical industry prefers a "clean bill," stakeholders, notes the former Senior Health Policy Advisor to the U.S. Senate, Elizabeth Jungman, "have to push to get policy."[9]

While it is up to the stakeholders to urge Congress towards enacting additional policy, once that policy is on the table, the renewal cycle might start to favor stakeholders since any delays in the renewal cycle puts the FDA, and, in turn, the pharmaceutical companies, at risk. As one former Republican staffer on the Senate HELP Committee

[3] Public Law 112–144—JULY 9, 2012, (www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf).
[4] Philip Hilts, *Protecting America's Health: The FDA, Business, and One Hundred Years of Regulation* (New York, Knopf, 2003); 256.
[5] Philip Hilts, *Protecting America's Health: The FDA, Business, and One Hundred Years of Regulation* (New York, Knopf, 2003); 279.
[6] See PDUFA Legislation and Background (http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm144411.htm).
[7] Must pass legislation is a "vitally important measure that Congress must enact, such as annual money bills to fund operations of the government. Because of their must-pass quality, these measures often attract "riders" (unrelated policy provisos). http://www.senate.gov/reference/glossary_term/must_pass_bill.htm.
[8] Interview with Elizabeth Jungman, June 9, 2014.
[9] Interview with Elizabeth Jungman, June 9, 2014.

notes, "If it's not timely reauthorized, the FDA has to lay off a huge number of drug center employees which substantially disrupts the pharmaceutical companies."[10]

B. The Stakeholders

Leading up to PDUFA, the major stakeholders interested in drug supply chain policy were the FDA, the Pharmaceutical Research and Manufacturers of America (PhRMA), Biotechnology Industry Organization (BIO), individual brand and generic companies, Rx-360 (an international pharmaceutical supply chain consortium), a spate of consumer groups, and Pew.[11]

There were also crucial individuals who would become instrumental policy advocates: In addition to the team at Pew, there was Deborah Autor, at the time the FDA's Deputy Commissioner for Global Regulatory Operations and Policy, Heather Bresch the CEO of Mylan (a leading company making generic pharmaceuticals), and Martin VanTrieste, co-founder of Rx360 and the SVP of quality at Amgen (a major biotechnology company).[12]

It is important to mention here that I did not interview Heather Bresch of Mylan for this report so the company is not mentioned as often as it should be. There is broad agreement that Mylan, directly and through its role in the Generic Pharmaceutical Association, was instrumental in getting the generic drug industry to provide the new user fees necessary to fund inspections overseas.

IV: The Pew Strategy

A. Articulating the Problem

The Drug Safety Project at Pew arose in response to the 2007-2008 heparin crises, where dozens of individuals were harmed and some died after receiving contaminated heparin, a blood-thinning drug.[13] The heparin had "been adulterated during its manufacture in China."[14] Oversulfated chondroitin sulfate, which cost $9 a pound had been added rather than heparin, which costs $900 a pound.[15] The U.S. Food and Drug Administration

[10] Interview with former Republican staffer on the Senate HELP Committee, June 12, 2014.
[11] Interview with Allan Coukell, May 27th, 2014. These facts were confirmed by my other interview sources.
[12] A list of stakeholders are featured in the articles "Broad Range of Stakeholders Agree: Bipartisan, Bicameral Drug Quality and Security Act Will Improve Drug Safety, Should be Enacted as Soon as Possible," *Congressional Documents and Publications*, September 28, 2013 and "Senate Passes Most Comprehensive Drug Safety Bill in 25 Years," *Congressional Documents and Publications*, November 18, 2013.
The particular stakeholders I list here were mentioned multiple times in the written literature listed below and/or during interviews.
[13] The Drug Safety Project (http://www.pewtrusts.org/en/projects/drug-safety-project).
[14] The exact language on the Pew website has changed since the writing of this report. For more information on the Drug Safety Project see http://www.pewtrusts.org/en/projects/drug-safety-project.
[15] Harris, Gardiner, "Heparin Contamination May Have Been Deliberate, F.D.A. Says," *The New York Times*, April 30. 2008. http://www.nytimes.com/2008/04/30/health/policy/30heparin.html?_r=0

(FDA) concluded that the adulteration "was an economically motivated act—a clear breach of the U.S. pharmaceutical supply chain."[16]

The heparin disaster reflected wider changes in the upstream supply chain, the path from raw materials to the manufacturer. The country's regulatory system was only designed to monitor "a domestic vertically integrated supply chain" not the "globalized outsourced supply chain" that currently existed. The process "was opaque not only to the regulator but to the manufacturer whose name was on the product."[17]

From 2001 to 2008, "the number of drug products made outside the United States doubled…with up to 80 percent of active ingredients and 40 percent of finished drugs used by U.S. patients being manufactured abroad."[18] In the United States, "you can expect an FDA inspector to visit every two or three years. If you run a similar plant overseas, you can expect an FDA inspector to visit maybe every nine years, the stated average. Some plants may never be inspected…."[19]

In 2009, Allan Coukell, who first came to Pew as a grantee investigating the challenges and opportunities in pharmaceutical policy, began by studying the drug landscape. Coukell, a former clinical pharmacist and health reporter, "developed a memo that looked at the potential problems and policy solutions associated with drugs from clinical safety, marketing, pricing issues, to information to patients." It was clear to him that issues surrounding drug supply chain safety were "important and timely."[20] This issue also fit nicely within the overall strategy of the Pew Health Group at the time, which was dedicated to "protecting consumers from hidden risks."[21]

The majority of American drugs were not fully regulated.[22] An increasingly globalized drug supply chain had become opaque not only to consumers, but to regulators and even manufacturers. As Coukell reflects, "several years after the disaster, Congress had not acted. After early hearings, legislative momentum fizzled. We were concerned that if we didn't get involved, we wouldn't really fix the system until we had the next disaster."[23]

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[16] The exact language on the Pew website has changed since the writing of this report. For more information on the Drug Safety Project see http://www.pewtrusts.org/en/projects/drug-safety-project

[17] Interview with Allan Coukell, May 27th, 2014.

[18] The exact language on the Pew website has changed since the writing of this report. For more information on the Drug Safety Project see http://www.pewtrusts.org/en/projects/drug-safety-project

[19] The exact language on the Pew website has changed since the writing of this report. For more information on the Drug Safety Project see http://www.pewtrusts.org/en/projects/drug-safety-project

[20] Interview with Allan Coukell, May 27th, 2014.

[21] Interview with Allan Coukell, May 27th, 2014.

[22] *See* Deborah M. Autor, Esq, Deputy Commissioner for Global Regulatory Operations and Policy Food and Drug Administration, Department of Health and Human Services. Testimony before the Committee on Health, Education, Labor and Pensions, United States Senate, September 14, 2011. Last modified on March 2, 2015. (http://www.fda.gov/NewsEvents/Testimony/ucm271073.htm). In this testimony she explains that "Nearly 40 percent of the drugs Americans take are made elsewhere, and about 80 percent of active pharmaceutical ingredients (APIs) used in drugs manufactured in the United States come from outside our borders—from more than 150 countries, many with less sophisticated manufacturing and regulatory systems than our own."

[23] Interview with Allan Coukell, May 27th, 2014.

B. Developing Expertise: After Heparin

The Pew Drug Safety team began by crafting a comprehensive report on the problem, which they titled After Heparin.

To craft the report, they conducted numerous interviews with supply chain experts.[24] The interviews, notes Coukell, "built our substantive expertise on the issue and helped us develop the policy solutions. It also gave us a network of people who would be very influential in moving policy forward."[25]

The report simultaneously solidified Pew's expertise on the subject and gave Pew productive introductions to all of the relevant stakeholders.

C. Building Support: Congress and Industry

While working on After Heparin, the team began to develop congressional and industry champions who could partner with Pew to advance drug safety legislation. These partnerships were crucial to getting drug safety on the legislative agenda in 2012 and in bringing stakeholders on board to ensure passage.

The team worked closely with champions in the House and the Senate, some of whom had a longstanding involvement with drug safety and supply chain issues. These included Congressman John Dingell (D-MI), Congressman Henry Waxman (D-CA), Senator Charles (Chuck) Grassley (R-IA), Senator Tom Harkin (D-IA), Chairman of the Senate Committee on Health, Education, Labor, and Pensions, which has jurisdiction of the country's health care policies, and his Republican counterpart Senator Mike Enzi of Wyoming. They also met with staff from the House Energy and Commerce Committee, which oversees the FDA and had been conducting a detailed investigation into the heparin adulteration. A relatively new Senator, Michael Bennet, the freshman Democrat from Colorado, would become an important champion. Pew worked closely to support the Senator on legislation he introduced in 2010 and 2011.[26]

In addition to politicians, Pew reached out to industry heads, including Martin VanTrieste, the Senior Vice President of Amgen, the world's largest independent biotechnology company. Amgen specializes in medicines that treat serious illnesses, for which there are limited or no effective treatment options.[27]

Like Pew, VanTrieste was horrified by the heparin crisis:

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[24] For more information on these experts download the *After Heparin* report (http://www.pewtrusts.org/en/research-and-analysis/reports/2011/07/12/after-heparin-protecting-consumers-from-the-risks-of-substandard-and-counterfeit-drugs) and see Appendix A.
[25] Interview with Allan Coukell, May 27th, 2014.
[26] Interview with Allan Coukell, May 27th, 2014 and interview with Elizabeth Jungman, June, 9 2014.
[27] Interview with Allan Coukell, May 27th, 2014.

> Looking at what happened with heparin, I quickly came to the conclusion that this was not a failure of someone to do their job or a failure of good manufacturing practices. Criminal elements had entered the pharmaceutical supply chain.[28]

VanTrieste collaborated with colleagues at a few other pharmaceutical companies to create Rx-360, an industry consortium dedicated to protecting patient safety by focusing on the integrity of the supply chain. He recalls, "We all got together and we said what happened to Baxter [the maker of the adulterated heparin] was unfortunate but was something that Baxter didn't see coming or prevent. We were fortunate it didn't come to our companies because we wouldn't be able to see it or prevent it."[29]

Pew reached out to VanTrieste while he was working on Rx-360 and drug safety manufacturing for Amgen. VanTrieste eventually became Pew's strongest industry ally throughout the Title VII process. Before being contacted by Pew, he had little to no policy experience.[30]

Pew had another strong industry ally in Heather Bresch of Mylan, an industry leader in generic drugs. Mylan, remarks Jungman, got "very involved because they viewed it as a leveling of the playing field. Companies in the U.S. were inspected more frequently than facilities overseas, they viewed it as fundamentally unfair and a public health issue."[31] Mylan is credited by my sources for convincing the generic drug industry to provide the new user fees necessary to fund factory inspections overseas.

D. Announcing Expertise: The After Heparin Conference and Report

In March of 2011, Pew held a major stakeholder conference on the current state of the drug supply chain. Trust Magazine reports:

> "We had a convening of every group out there, from the industry side to the FDA," said [then] health group managing director Shelley Hearne. "We listened to everybody, and everybody had a say in the recommendations. That document and the conference were really key to the process in which we could sit down and hammer out how those recommendations could be incorporated.[32]
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> Participants included the president of the nation's largest generic drug company, the director of a China-based pharmaceutical auditing company, representatives of pharmaceutical companies, wholesalers, pharmacists, and chain and independent drugstores. Also participating in the meeting

[28] Interview with Martin VanTrieste, June 16, 2014.
[29] Interview with Martin VanTrieste, June 16, 2014.
[30] Interview with Martin VanTrieste, June 16, 2014 and interview with Allan Coukell, May 27th, 2014.
[31] Interview with Elizabeth Jungman, June, 9 2014.
[32] The exact language on the Pew website has changed since the writing of this report. For more information on the Drug Safety Project see http://www.pewtrusts.org/en/projects/drug-safety-project.

> were representatives of physicians and consumers, AARP, the FDA and trade associations representing just about everyone along the supply chain.[33]

The conference was designed to accomplish several goals: vet the After Heparin report, bring stakeholders together, support political leaders (Senator Bennet spoke at the conference), demonstrate viable policy solutions, and announce this issue to the press.[34]

Structured around "a series of presentations laying out the problems and solutions," the conference offered concrete policies that could be discussed and evaluated by stakeholders across the pharmaceutical supply chain, including "generic companies, brand companies, wholesalers, chain pharmacies, small pharmacies, medical groups, and consumer groups."[35] According to my sources, congressional staffers from both sides of the aisle attended the conference and were impressed.[36]

As a former staffer to the Senate HELP Committee summarized, "The service that Pew did was not just bringing everyone around the table. Everyone in Washington does that. People love to show up at tables. They were the people that actually did the homework. That is how they had value."[37]

After the conference, Pew released the After Heparin report. Now every stakeholder, from industry representatives to congressional staff members, had a document they could use to fully understand and explain the issue. Together, the conference and the report, my sources agree, convinced stakeholders that drug safety reform was both needed and politically viable.[38]

According to Coukell, members of the Senate HELP Committee staff "took the paper away and they really became convinced by seeing the diverse stakeholders agree on what needed to be done, and that it wouldn't get bogged down over an endless fight over policy."[39]

As Sarah Despres, Director of Government Relations at PEW, recalls, "We had a great convening in March and then we had this strong report. So we educated the hill about the problem and potential solutions. It was great to see hill staff with the report all dog-eared and clearly heavily used."[40]

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[33] The exact language on the Pew website has changed since the writing of this report. For more information on the Drug Safety Project see http://www.pewtrusts.org/en/projects/drug-safety-project.
[34] Interview with Allan Coukell, May 27, 2014.
[35] Interview with Allan Coukell, May 27, 2014.
[36] Interview with former Republican staffer to the Senate HELP Committee, June 12, 2014. Allan Coukell, Sarah Despres, and Elizabeth Jungman reiterated this point.
[37] Interview with former Republican staffer to the Senate HELP Committee, June 12, 2014.
[38] Interview with former Republican staffer to the Senate HELP Committee, June 12, 2014. Allan Coukell, Sarah Despres, and Elizabeth Jungman reiterated this point.
[39] Interview with Allan Coukell, May 27, 2014.
[40] Interview with Sarah Despres, May 29, 2014.

Martin VanTrieste, from Amgen, who actually spoke at the conference, utilized the report to convince large pharmaceutical companies of the merits of Title VII. He recalls: "The Pew report provided me with a ton of data, fact based, footnotes with pictures, to show when I went on my road shows. Pew provided the research work when I met in the executive suites of the big PhRMA companies."[41]

The press also got on board. The head of regulatory affairs for the FDA knew the conference had been a success when he got a call from CNN. The reporter was asking him all about this issue of globalization and drug safety. Years later the same head of regulatory affairs for the FDA told Coukell, "That was the moment that I realized you guys were going to do this."[42]

With the After Heparin conference and report, Pew successfully exposed drug safety as a major public health issue, established themselves as experts on the topic, and demonstrated that a bipartisan coalition of diverse stakeholders agreed on actual policy. There is consensus among my sources that the After Heparin report and conference gave legislators the tools and impetus to craft drug safety policy.[43]

E: Deploying Pew Skills: Expertise, Political Pragmatism, Accessibility

Expertise

After the conference, Pew decided to utilize, in Sarah Despres' words, "the moving vehicle" of PDUFA. *Trust Magazine* summarizes:

> The success of the report and the conference also affirmed the health group's conclusion that its policy objectives on drug safety and reviving the antibiotic supply chain could be packaged with upcoming legislation to renew user fees for drug and medical-device manufacturers. A 1992 law—the Prescription Drug User Fee Act, or PDUFA—enabled the FDA to speed its reviews of new drug applications and stipulates the fees must be extended every five years, and the next renewal date was to occur in 2012.[44]

They had to craft the appropriate messaging to convince industry to support a rider to PDUFA. Despres explains, "They wanted a clean bill. We had to overcome that and say 'Well, look, if you are going to do nothing else, at least do this. We had a crisis several years ago and we have FDA interest, we have industry interest. So if nothing else do this.'"[45] Republican staff believed that Pew was assisted in this matter by PhRMA's

[41] Interview with Martin VanTrieste, June 16, 2014.
[42] Interview with Allan Coukell, May 27, 2014.
[43] All of the sources interviewed for this report agreed on this point. For a complete list of sources see the bibliography.
[44] "Becoming a Trusted Source in Drug Safety Law's Passage," *Trust* M*agazine*, (The exact language on the Pew website has changed since the writing of this report. For more information on the Drug Safety Project see http://www.pewtrusts.org/en/projects/drug-safety-project.
[45] Interview with Sarah Despres, May 29, 2014.

suffering reputation at the time. "PDUFA came right after health care reform where PhRMA generated a huge amount of ill will for itself. Their goal was just to get PDUFA reauthorized. In a scale from about 1 to 100, they cared about that to a 100 and didn't really care about many other things."[46]

At this stage, experts in Pew's Government Relations department stepped in. *Trust Magazine* reports:

> The health group, along with colleagues from Pew's Government Relations team, spent much of 2011 working with congressional staffers and lawmakers who had taken an interest in drug safety or antibiotics issues. The Government Relations staff has deep experience in how to work on Capitol Hill. Its members know, as Sarah Despres, a senior officer who was key in guiding Pew's efforts on the Hill, said: "By working with the Hill staffers directly, you earn their trust." Managing director Tamera Luzzatto noted that staffers "know what their bosses' impulses are, which issues their bosses will roll up their sleeves for." [47]

The team began with messaging. The language had to be nuanced. They didn't want to "scare people" about taking drugs but they had to stress the importance and urgency of the issue. One of the ways they did this was by emphasizing the dispassionate expert over the emotional consumer.[48] Despres recalls, "We became the technical experts on supply chain. If anyone had a question on supply chain, they knew who to call."[49]

This is an important moment of consensus among the sources.[50] It is clear that Pew presented itself to all of the stakeholders involved as a technical expert in an arena desperate for accurate information.

But Pew was never only a technical expert -- they also positioned themselves as an organization solely concerned with what is best for public health.

While at the Senate HELP Committee, Elizabeth Jungman found this stance "really helpful . . . Pew is rightly perceived as just being focused on public health. I would be able to say to my boss, who was very interested in the consumer and public health perspective, that Pew is with us…If Pew is with us we are doing something that was close to the right thing."[51]

While Pew refined its messaging and political strategy, members of the Senate HELP Committee, many of whom had attended the conference, created a working group. The

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[46] Interview with the former Republican staffer on the Senate HELP Committee, June 12, 2014.
[47] "Becoming a Trusted Source in Drug Safety Law's Passage," *Trust* M*agazine*, (www.pewtrusts.org/news_room_detail.aspx?id=85899418387#sthash.03YBpWNM.dpu)
[48] Interview with Sarah Despres, May 29, 2014.
[49] Interview with Sarah Despres, May 29, 2014.
[50] All of the sources interviewed for this report agreed on this point. For a complete list of sources see the bibliography.
[51] Interview with Elizabeth Jungman, June 9, 2014.

group, evenly balanced between Democrats and Republicans, decided to begin the legislative process by educating themselves. In addition to reading widely, they invited experts in to speak with them. Pew not only assisted in locating experts for the group but they were also invited in to speak.[52]

At this time, Pew wielded its influence by continuing to leverage its expertise, targeting specific politicians, coordinating with their industry partners, and keeping the issue in the press. When the Senate HELP Committee began crafting the language for Title VII, the Pew team became a key resource for Congressional staffers in developing and vetting language.

For Jungman, the Senior Health Policy Advisor for the Senate, Pew was an indispensable resource and instrumental in getting Title VII passed.

"They were spending all day thinking about these issues and I was not able to…I relied on Pew a lot on technical assistance…. They were able to explain the issues and give important and useful examples."[53]

"What was important to me," she continued, "I felt like I was never going to get caught in a situation where I told my boss or other stakeholders something that Pew told me that later was going to be wrong. I could always rely on what I was hearing."[54]

In addition to relying on Pew for general expertise, Jungman also relied on Pew for thoughtful opinions on the repercussions of certain policy language. "If I shot off an email about language they would respond that there are a couple of ways this could play out. They spent a lot of time thinking about how it played out on the ground. This came from having really invested deeply in the supply chain, knowing all the players, knowing how it worked."[55]

Political Pragmatism

Pew leveraged their expertise on this issue with carefully designed political pragmatism.

Going into their lobbying effort, Sarah Despres comments, "We had identified a suite of reasonable policy solutions and appreciated that some things had to drop away. We took a very pragmatic approach: how can we achieve the goal of improving the supply chain (and not) fall on our sword."[56]

Despres also took a pragmatic approach to how she would deploy Pew's political resources. She explains, "I was targeted. I saw ten offices over and over again. We also spent time at the White House and at HHS [Department of Health and Human Services]

[52] Interview with Allan Coukell, May 27, 2014
[53] Interview with Elizabeth Jungman, June 9, 2014.
[54] Interview with Elizabeth Jungman, June 9, 2014.
[55] Interview with Elizabeth Jungman, June 9, 2014.
[56] Interview with Sarah Despres, May 29, 2014.

to make sure that was a priority for them too. So they could back up the FDA in its efforts."[57] In addition to using their own staff, Despres encouraged partners, particularly industry partners to reach out to important contacts on the hill.[58]

As one of Pew's strongest industry allies, VanTrieste brought the other pharmaceutical companies on board. According to a former Republican staffer, this was crucial. He comments:

> There was a small, cuddly, feel-good coalition of Title VII folks from pharmaceutical manufacturers who concentrate in supply chain integrity matters. So there was this Rx360 coalition -- those are like pharmaceutical supply chain regulatory experts, they are not the pharma research and manufacturers of America, the trade association - PhRMA. To pass a drug regulatory law, barring a horrible safety tragedy, as a practical matter, you need to work with PhRMA, the trade association itself.[59]

In VanTrieste's words, "Allan does NGO and policy makers. I do a really good job bringing regulators and industry to the table. Either one of us would have had a harder time doing it. Working together we were able to bring everyone to the table to understand the problem. That combination was synergistic."[60]

PhRMA, he continued, "tolerated" Title VII because "we were able to convince their five largest members to do it."[61] He convinced these members by explaining how contamination could happen to any company. While VanTrieste played a significant role in securing the support of these five members, he used the After Heparin report to do so. Moreover, he continued to talk regularly with Pew to coordinate strategy. [62]

In addition to working closely with industry representatives, Pew kept productive relationships with congressional staffers from both parties.[63] Even those who saw Pew as more of an agenda setter than a legislative partner continued to rely on the Pew After Heparin report and believed that Pew was responsible for putting drug supply chain safety on the agenda. As one Republican staffer said:

> I can't stress enough. Pew was very influential. Getting it on the agenda is the whole name of the game. The main accomplishment is getting it on the agenda and having it be the chairman's priority. If something is the chairman's top priority it will get done.[64]

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[57] Interview with Sarah Despres, May 29, 2014.
[58] Interview with Sarah Despres, May 29, 2014.
[59] Interview with the former Republican staffer on the Senate HELP Committee, June 12, 2014.
[60] Interview with Martin VanTrieste, June 16, 2014.
[61] Interview with Martin VanTrieste, June 16, 2014
[62] Interview with Martin VanTrieste, June 16, 2014
[63] Interview with the former Republican staffer on the Senate HELP Committee, June 12, 2014.
[64] Interview with the former Republican staffer on the Senate HELP Committee, June 12, 2014.

The key, one staffer concluded, is not appearing to be non-partisan -- the key is simply being credible:

> Honestly, any time you are an NGO, rank Republicans are always going to think that everyone to the left of them is a left-winger. You can't control anyone's perceptions of you, but you can always be the most rigorous about the homework. That is why they are credible.[65]

Accessibility

At the conclusion of the legislative process, Pew made itself indispensable to both the House and the Senate. *Trust Magazine* reports:

> When the process reached its final stage—reconciling the House and Senate bills in June—Pew's effort went into overdrive…. In a period of a few weeks, we were reacting to a Senate committee draft, a House committee draft, a Senate final draft, a House final draft and then a conference draft…. We were going through them over and over and producing detailed analysis, and often responding on short notice to requests from one staff or another for elucidation, or additional analysis or talking points—sometimes on all three of those issues in the same day. We were also in that phase in closed-door sessions with the FDA and the industry over the [unrelated drug distribution] supply chain provisions. In the last, frantic days of negotiating, Pew's goal of being a trusted source had been met. "The Pew staff had to be available 24/7," Hearne said.[66]

Throughout the legislative process, Pew made it a point to be extremely responsive and accessible to all queries. Coukell and his colleague Gabrielle Cosel gave detailed readings on the language of the bills, made policy judgments, and wrote careful responses. Coukell said, "We gave really, really, detailed responses when they would put out a draft. They were seeking feedback but often we were giving them a level of detail and thoughtfulness that was helpful to them…. We were involved in every step of the way."[67]

F. Taking Advantage of Political Capital and Opportunities

Working on Title VII, the team developed a strategy that had legs.

Reflecting on Pew's legislative wins in this arena, Despres comments, "I would love to say that we sat down as a team and said 'this is what we are going to do,' but that is not

[65] Interview with the former Republican staffer on the Senate HELP Committee, June 12, 2014.
[66] "Becoming a Trusted Source in Drug Safety Law's Passage," *Trust Magazine*, (The exact language on the Pew website has changed since the writing of this report. For more information on the Drug Safety Project see http://www.pewtrusts.org/en/projects/drug-safety-project).
[67] Interview with Allan Coukell, May 27, 2014.

sure at all. It started with drug supply chain…. It was reauthorization that put this group on the map."[68]

With Title VII, Pew became acknowledged experts and then started seeing more opportunities for policy within FDASIA. Despres states:

> It wasn't a pre-planned strategy. When I came, Allan testified [before Congress] once or twice maybe, but once he testified we just leveraged the heck out of that. Allan and Gabey testified 7 times in 15 months. All through the process of reauthorization when they were looking for non-industry nongovernment voice…. Anytime there was an opportunity we took it and tried to create it to keep ourselves out there as the experts who were willing to come up with pragmatic solutions that would also improve the status quo. We didn't want to win to win. We wanted to make a difference.[69]

From drug supply chain safety, Pew was able to get legislation into FDASIA to incentivize the creation of new and needed antibiotics. And after antibiotics, remarks Despres, "people were begging us to get into medical devices."[70]

While working on FDASIA, Jungman recalls, "It was frustrating to me that there were areas where Pew was not involved. They were late in the game on devices. I needed that engagement. From an outsider's perspective, I didn't know why Pew could be so deeply helpful in some circumstances and no use at all in other perspectives. I know you know FDA, so why can't you talk to me about devices? But now that I am at Pew, I see the really strategic process that goes into every project decision."[71]

Eventually, the team got the green light to go into medical devices and Pew came to be seen as an authority on the majority of issues involved in FDASIA. As Despres says, "Pew was seen as an expert on a lot of issues that were in the mix. We filled a niche of a public interest group actively engaged in a lot of different issues in the user fee legislation. This bolstered our credibility and bolstered our reputation. From our standpoint these were three distinct bills with three distinct staff." From the outside, anyone "could just call me and they knew they could get an answer. It made us the go-to people. As a whole, to the outside, we looked like one big FDA policy shop."[72]

Pew had amassed enough good will and political capital through Title VII, antibiotics, and medical devices that when it came to track and trace, they were not only able to thwart mediocre policy but were also given a seat at the table to negotiate better legislation.

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[68] Interview with Sarah Despres, May 29, 2014.
[69] Interview with Sarah Despres, May 29, 2014.
[70] Interview with Sarah Despres, May 29, 2014.
[71] Interview with Sarah Despres, May 29, 2014.
[72] Interview with Sarah Despres, May 29, 2014.

Track and Trace

When FDASIA passed, the press picked up on the failure to implement a "track and trace program" – a program to require unique serial numbers on each package of drugs and a national system to track those drugs and detect counterfeits. Doctors writing in *JAMA* stated their concern and *Bioworld Today* ran a statement by Senator Burr: "Sen. Richard Burr (R-N.C.) took issue with rushing such a 'crucial piece of legislation' through Congress. In the haste he said, important provisions like a track-and-trace system for drugs were sacrificed."[73]

For Pew this was not a failure; it was a victory.

In the beginning of negotiating Title VII, Jungman and her colleagues entertained the notion of including legislation to monitor downstream supply chain issues, the path from the manufacturer to the pharmacy. "It was part of the Pew report and everyone was interested in doing both [upstream and downstream]," she said. The Senate Committee, however, quickly realized that they were not going to get a compromise on downstream.[74]

While the Committee (and Pew, for that matter) postponed working on downstream supply chain, the pharmaceutical industry began paying attention to a set of state laws, particularly in California, that when fully implemented, would have enforced rigorous requirements for monitoring the downstream supply chain.[75] As Jungman reflects, "Industry was going to have to change a lot to comply with California. That was the real driver."[76] Although Pew supported the California standard, they had two concerns 1) it would never get implemented and 2) there would be a confusing array of state standards rather than a national one. [77]

In 2012, recalls Coukell, "Industry came together with a strong desire to preempt California and other state laws and create a single national standard. They came up with a proposal late in the user fee cycle that they were pushing hard."[78] The proposal supplanted the strong California law with a weaker federal standard. According to Coukell, the policy, "sacrificed robustness by meeting the demands of different stakeholders, particularly retail pharmacies."[79]

When Senators Bennet and Burr tried to include a version of this legislation, Pew worked with their offices to strengthen the bill. Pew, along with FDA and some members of Congress, felt strongly that federal legislation should not preempt a strong state law

[73] Steinbrook, Robert (MD); Sharfstein Joshua M. (MD), "The FDA Safety and Innovation Act," JAMA, October 10, 2012; "Senate Passes PDUFA V; Next Stop President's Signature," *Bioworld Today*, June 27, 2012.
[74] Interview with Elizabeth Jungman, June 9, 2014.
[75] Interview with Allan Coukell, May 27, 2014.
[76] Interview with Elizabeth Jungman, June 9, 2014.
[77] Interview with Allan Coukell, May 27, 2014 and interview with Elizabeth Jungman, June 9, 2014.
[78] Interview with Allan Coukell, May 27, 2014.
[79] Written correspondence with Allan Coukell, July 7, 2014.

unless it achieved certain minimum advances for patient safety. [80] As Coukell recalls, "Industry created the momentum and, ultimately, we decided it simply didn't accomplish what it needed to."[81]

Pew had worked with the senators from California – and with the California Board of Pharmacy – to build support for strong federal standard. [82] Despres recalls, "Under Senate procedure, it is difficult to pass something if even one Senator objects." Senators Dianne Feinstein and Barbara Boxer wrote to Senator Harkin, laying down a marker that they would not allow this bill to move as it was written.[83]

"Committee leadership told the stakeholders, 'you have to come to a deal on this.' FDA hated it Pew didn't like it,"[84] Coukell recalls, "It became clear that it wouldn't pass without substantial changes."[85]

When negotiations for track and trace got started, Pew had a seat at the table. Despres recalls, "Essentially we were told to go into a room and see if we can figure out a deal…. Once you are at the table you are at the table… In order for the legislation to move it had to satisfy Pew, the industry coalition, and the FDA. We were one of three interests. We had leveraged our success in user fee reauthorization to be meaningful in this process."[86]

According to Jungman, Pew was asked to be in the negotiating room because, "they were respected on both sides of the aisle."[87]

Leading up to the user fee renewal deadline, there was a lot of momentum to get track and trace passed.

Jungman recalls, "When the House passed their bill, we were doing three meets a day." It was the negotiating parties, the FDA, the Pharmaceutical Distribution Security Alliance industry coalition, and Pew. "It was incredibly intense. This was everybody's full time job for a while. We were really trying to get it down."[88]

"There was extreme time pressure. In 60 days, pink slips would go out to FDA employees if we couldn't pass user fees. We also knew a Supreme Court decision on the ACA would come down." Once that decision went "we wouldn't be able to get a health measure off the floor because everyone would want to stack ACA stuff to it."[89]

[80] Interview with Allan Coukell, May 27, 2014.
[81] Interview with Allan Coukell, May 27, 2014.
[82] Correspondence with Allan Coukell, August 25, 2014.
[83] Correspondence with Allan Coukell, August 25, 2014.
[84] Interview with Sarah Despres, May 29, 2014.
[85] Interview with Allan Coukell, May 27, 2014.
[86] Interview with Sarah Despres, May 29, 2014.
[87] Interview with Elizabeth Jungman, June 9, 2014.
[88] Interview with Elizabeth Jungman, June 9, 2014.
[89] Interview with Elizabeth Jungman, June 9, 2014.

"Ultimately, the stakeholders left the room and negotiations continued and we hit the closest we could come to a compromise. Sent it out to stakeholders. Can everyone live with this? And we got a resounding no from a lot of sides including Pew. The bill passed without it. We took three or four days off and got right back into the room. It was a long haul but we got there."[90]

Although the negotiations failed in 2012, the momentum to get track and trace persisted. The threat of California motivated industry, and the desire for a strong national standard kept the FDA and Pew involved. In Jungman's estimation, "California was holding this coalition of people together. We had to get this done before California became effective or the window of opportunity for national legislation would have passed."[91]

The Pew strategy was to persuade one or two of the pharmaceutical companies to get behind a strong track and trace bill. Despres relates, "What we knew at the time was that there were strong differences of opinion. The drug industry wanted preemption more than anything and they were willing to accept higher requirements under federal law because they were facing higher requirements under state law. We just needed to find one or two companies who were willing to speak out in support of strong federal standards."[92]

To do so the team looked for a substantial industry partner. They found one in EMD Serono, the biopharmaceutical subsidiary of Merck, a global pharmaceutical and chemical group. According to Dave Nichols, the company's Senior Director of Federal Government Affairs, EMD Serono became the pivotal example that showed other pharmaceutical companies that unit-level tracking and accountability across the supply chain was possible.

In Nichols' assessment, "Pew was absolutely necessary. It wouldn't have happened without them. They had been working on this issue longer than we had. They were at the table when we started getting involved as a company. What they didn't have was a real time, real life, example of a company that thinks that this can be done. It was Pew on one side before we got involved and all the PhRMA companies on the other side. They said we can't do it. Pew said 'I think you can.' But we were the example of one that could."[93] Pew also identified and served as a conduit for numerous small technology companies that were selling pharmaceutical tracking technology and services. Pew helped them deliver a message to the Hill that the proposed policies were feasible, even if sometimes they were unable to speak publicly for fear of offending their major pharmaceutical industry clients.

On November 27, 2013, President Obama signed into law The Drug Quality and Security Act. Title II of the bill, the Drug Supply Chain Security Act, established a track and trace program.

[90] Interview with Elizabeth Jungman, June 9, 2014.
[91] Interview with Elizabeth Jungman, June 9, 2014.
[92] Interview with Sarah Despres, May 29, 2014.
[93] Interview with Dave Nichols, June 18, 2014.

And that was not Pew's only legislative success in this arena for that year. In addition to track and trace, Pew helped shape legislation to ensure oversight of sterile compounding. This issue became particularly salient after a steroid injection caused fungal meningitis in approximately 700 patients. Here too, Pew's expertise proved invaluable. Coukell comments, "Because we were already established as an expert in drug safety and supply issues, we were in a position to help shape that legislation and push it along. We didn't know compounding was ahead of us. We were able to be opportunistic when it did happen."[94]

Despres agrees, explaining, "Between October 2012 and January 2013, we brought together a number of stakeholders, hospital pharmacists, hospital groups, other groups, and FDA to hammer out what would be the right regulatory framework for sterile compounding. Because we were already there on track and trace it was the same staff. One of our legislative strategies is that we are always around, you can't get rid of us."[95]

V: What Pew Wanted and What Pew Got

Between 2012 and 2013, Pew had four major policy accomplishments. As Coukell summarizes, "in 2012 we had Title VII of FDASIA and we also had the GAIN Act (Generating Antibiotic Incentives Now), and we had some medical device positions. Both Title VII and GAIN *were* Pew priorities and huge wins. In 2013 we had the Drug Quality and Security Act, which contained both track and trace legislation and compounding legislation. Four important measures in two years."[96]

In terms of Title VII of FDASIA, Pew not only accomplished its legislative agenda, but also used the win to further its policy goals.

Comparing Pew's initial policy recommendations in the After Heparin report and the final law finds 16 of 26 recommendations fully realized and five partially included. Five were not included.[97] For example, FDASIA requires the FDA to use a comprehensive risk assessment framework to prioritize drug manufacturing plant inspections, creates a single risk-based framework for foreign and domestic plants, and outlines criteria to be included in risk assessments. Another Pew recommendation included in the law was granting FDA the authority to bar importation of a drug if the site at which it was manufactured refuses or delays an FDA inspection. FDASIA also made explicit that Good Manufacturing Practices for drug producers include an obligation to control the quality of the ingredients and raw materials they use in their drugs, a further Pew recommendation.[98]

While FDASIA did not give FDA the power to subpoena documents from drug manufacturers to support oversight and investigations (a Pew recommendation), it did

[94] Interview with Allan Coukell, May 27, 2014.
[95] Interview with Sarah Despres, May 29, 2014.
[96] Interview with Allan Coukell, May 27, 2014.
[97] This information comes from an internal Pew report.
[98] Correspondence with Allan Coukell, October 7, 2014.

give the agency the authority to access documents outside of a physical plant inspection. Similarly, Pew advocated that FDA have the authority to require a drug recall. While that was not granted, FDASIA does give FDA the power to administratively detain drugs.[99]

In a few cases FDASIA did not accept Pew's recommendations. For example, the law does not require drug companies to name specific employees responsible for signing off on product quality, as is required by European regulators and as Pew recommended. Nor did it establish new whistleblower protections for drug manufacturer employees.[100]

As Coukell summarizes, "We didn't get everything we wanted in Title VII but we got the lion's share of it."[101] It is important to note that Pew, from the outset, established moderate policies that they believed would inspire actual political action.

VI: Mechanistic Impact, Humanitarian Impact, and Conclusion

Mechanistic Impact

It is clear to me that the Pew team dived into this issue area with a clear value system, a careful political strategy, and the flexibility to leverage success. These assets coincided with a social and political context that made policy change viable. There was a serious drug safety catastrophe, an industry worn down by bad publicity, a legislative window with PDUFA, and powerful individuals within and outside of Pew invested in getting new policy.

Saying that, I do not believe drug safety legislation would have been passed without Pew's involvement.

Pew put drug supply chain safety concerns on the legislative agenda in 2011 and actively built the coalition that ensured its passage in 2012. The team also assisted with and vetted the language of the 2012 bill and made sure that weak policy proposals did not supplant strong ones. Pew accomplished these goals largely by capitalizing on their expertise and by deploying the multi-pronged strategy listed above. Pew did not act alone. It had the assistance of strong industry partners, FDA officials, and key congressmen and senators.

Pew's causal weight in this issue area should not be underestimated. They became the single most important non-government and non-industry player in the field. They brought the stakeholders together, gave them the necessary information to pursue the topic, and demonstrated the viability of actual policy.

Humanitarian Impact

There are two major reasons assessing humanitarian impact is difficult at this time.

[99] Correspondence with Allan Coukell, October 7, 2014.
[100] Correspondence with Allan Coukell, October 7, 2014.
[101] Interview with Allan Coukell, May 27, 2014.

- It is challenging to account for crises averted rather than crises solved.
- It is too soon to fully evaluate the effects of the legislation, particularly when key parts of the legislation are still being implemented.

Saying that, Pew is staying on top of the FDA and issues concerning drug supply chain safety. As Coukell relates, "We are aware when key guidances have to be issued. Last week we issued a report on compounding. We will comment on FDA guidance. We will continue to stress and remind people of the safety problems and remind people why the legislation was passed."[102] Pew is also starting to look at the unintended consequences of the legislation as well as how federal legislation is playing out in the states.

VanTrieste recently attended a large three-day conference of the peripheral drug association. Pew was "very active in that conference, providing information and leading discussions." In his estimation, Rx-360 and Pew are keeping "up the heat on the FDA."[103]

According to all six of the individuals I interviewed, the FDA is on track with Title VII.

While Pew and Rx-360 are starting to assess the humanitarian impact of the law, there are some guiding questions that would be useful to keep in mind if GiveWell pursues this further.

- Is the FDA doing what it is supposed to do?
- Are the enforcements happening on the ground in the way they were intended to happen?
- Have any breaches in the supply chain been discovered and averted?
- Did this legislation have an impact on public health that one could assess?

Conclusion

Pew's success in this arena demonstrates the value of a trustworthy and responsive expert with the patience to wait for a political window and the strategic resources to build the coalition that can turn that window into actual policy.

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4. Jungman, Elizabeth - Director, Drug Safety and Innovation, Pew (former Senior Health Policy Advisor, U.S. Senate Committee on Health, Education, Labor and Pensions; worked as the lead Democratic committee staffer on FDASIA).

5. Nichols, Dave - Senior Director of Federal Government Affairs, EMD Serono

6. VanTrieste, Martin - Senior Vice President for Quality Control, Amgen