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6 EXAMINING THE ROOT CAUSES OF DRUG SHORTAGES:

7 CHALLENGES IN PHARMACEUTICAL DRUG SUPPLY CHAINS

8

9 THURSDAY, MAY 11, 2023

10

11 House of Representatives,

12 Subcommittee on Oversight and Investigations,

13 Committee on Energy and Commerce,

14 Washington, D.C.

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18 The subcommittee met, pursuant to call, at 10:31 a.m. in
19 Room 2123, Rayburn House Office Building, Hon. Morgan
20 Griffith [chairman of the subcommittee] presiding.

21

22 Present: Representatives Griffith, Duncan, Palmer,
23 Lesko, Crenshaw, Rodgers (ex officio); Castor, Schakowsky,
24 Tonko, Ruiz, Peters, and Pallone (ex officio).

25

26 Staff Present: Kate Arey, Digital Director; Sean
27 Brebbia, Chief Counsel; Lauren Eriksen, Clerk; Peter Kielty,

28 General Counsel; Emily King, Member Services Director; Karli
29 Plucker, Director of Operations (shared staff); Gavin
30 Proffitt, Professional Staff Member; John Strom, Counsel;
31 Michael Taggart, Policy Director; Joanne Thomas, Counsel;
32 Austin Flack, Minority Junior Professional Staff Member;
33 Waverly Gordon, Minority Deputy Staff Director and General
34 Counsel; Tiffany Guarascio, Minority Staff Director; Liz
35 Johns, Minority GAO Detailee; Will McAuliffe, Minority Chief
36 Counsel, Oversight and Investigations; Christina Parisi,
37 Minority Professional Staff Member; Greg Pugh, Minority Staff
38 Assistant; Harry Samuels, Minority Oversight Counsel; Andrew
39 Souvall, Minority Director of Communications, Outreach, and
40 Member Services; and Caroline Wood, Minority Research
41 Analyst.

42

43 *Mr. Griffith. The Subcommittee on Oversight and
44 Investigations will now come to order.

45 The chair recognizes himself for five minutes for an
46 opening statement.

47 Good morning, and welcome to today's hearing. This
48 morning's hearing will examine the very serious and growing
49 problem of prescription drug shortages.

50 Americans need more reliable access to lifesaving drugs.
51 According to the American Society of Health-System
52 Pharmacists, we currently have over 247 active drug
53 shortages. Between 2021 and 2022, drug shortages increased
54 by almost 30 percent. It is unbelievable that in our great
55 country there is a shortage of drugs to treat childhood
56 cancer, and that is just one example. It is even more
57 galling when you consider that most shortages are in the
58 generic drug space, where there should be competition. The
59 median price of a drug in shortage between 2013 and 2017 was
60 less than \$9 per treatment dose.

61 Generic drugs account for 90 percent of all
62 prescriptions, but only 17 percent of drug spending.
63 Generics are perhaps the only significant segment of our
64 health care industry where costs have not increased faster
65 than inflation. The generic pharmaceutical industry is
66 plagued with a myriad of issues leading to drug shortages.

67 We have an economic environment so unappealing to

68 manufacturers that lifesaving drugs are produced by one or,
69 at most, two companies worldwide, often at unsustainably
70 artificially low prices. There is a broad consensus that the
71 root cause of drug shortages is a profound market failure
72 caused by economic forces unique to the drug market.

73 Middlemen such as Pharmaceutical Benefit Managers, PBMs,
74 or Group Purchasing Organizations, GPOs, do not care to look
75 for ways to mitigate shortages. By one count, for every \$100
76 spent on a generic prescription drug, \$44 goes not to the
77 manufacturer, not to the producer, but to a middleman. The
78 three largest Pharmaceutical Benefit Managers control around
79 80 percent of the commercial drug sales.

80 The 4 largest Group Purchasing Organizations control 90
81 percent of the medical supply market, and have massive market
82 power. They could help end drug shortages by prioritizing
83 generic drugs' availability and quality. Instead, they use
84 their market power to force a race-to-the-bottom pricing
85 without consideration for quality or availability. Their
86 contracts with generic drug manufacturers consist of a take-
87 it-or-leave-it approach, leaving the generic manufacturer
88 with the option of either complying or losing access to the
89 market. Many of them choose to lose that access and just go
90 out of business.

91 Over the past 10 years, the United States has seen
92 dozens of generic drug manufacturing facilities close, and

93 this shortage problem isn't limited to just closings. The
94 typical generic drug has just two manufacturing facilities.
95 We currently do not fully utilize the factories that we have.
96 As Professor Sardella notes, we only use about half of our
97 current generic manufacturing capabilities. We now have
98 fewer manufacturing facilities both in the U.S. and globally,
99 and our supply chain has proven to be fragile and vulnerable
100 to disruption. Forty percent of generic drugs are made at a
101 single facility, thus even a temporary shutdown of a single
102 facility triggers a shortage.

103 We are also far too dependent on foreign countries for
104 generic drugs and active pharmaceutical ingredients, or API,
105 especially China and India. Our dependance on China
106 represents a serious national security risk. China's new
107 interpretation of its national security law may actually make
108 FDA's already anemic inspection program in that country a
109 crime.

110 As we are holding this hearing, FDA Commissioner Califf
111 is appearing before our Health Subcommittee. All too often
112 his agency has made drug shortages worse, and left us more
113 vulnerable. The FDA's response to shortages is to allow for
114 foreign-made generics and API to come unfettered to the U.S.
115 market. The FDA claims to be focused on collecting
116 information, but it does not effectively use the information
117 that it already has.

118 We need an FDA that prioritizes applications from U.S.
119 manufacturers and gives companies the flexibility to address
120 shortages with resources based here. Solving drug shortages
121 is going to require an all-of-the-above approach. Purchasers
122 of generic drugs must incentivize quality and reliability in
123 generic drugs, and we must always keep in mind the human toll
124 of drug shortages.

125 I look forward to hearing from our witnesses today who
126 are working in innovative ways to help solve drug shortages.

127 [The prepared statement of Mr. Griffith follows:]

128

129 *****COMMITTEE INSERT*****

130

131 *Mr. Griffith. I thank you all for being here, and I
132 yield back. I now recognize the gentlelady from Florida, Ms.
133 Castor, ranking member of the subcommittee, for her five-
134 minute opening statement.

135 *Ms. Castor. Well, thank you, Mr. Chairman, and thank
136 you for calling this critical hearing on the root causes of
137 drug shortages.

138 These drug shortages are becoming more prevalent due to
139 a warped marketplace. And as a witness Professor Laura Bray
140 in her testimony stated, no patient should have to hear the
141 words, "We do not have medicine to treat you."---

142 Drug shortages in America are at a 5-year high. In 2022
143 we experienced a 30 percent jump in the number of drugs in
144 shortage. FDA has documented 136 drugs on its shortage list,
145 and health care providers suspect the actual number is far
146 higher. These shortages can last years, and some critical
147 drugs have been in shortage for over a decade. The impacts
148 of these shortages on our neighbors receiving cancer care,
149 children and their caregivers, are incredibly upsetting
150 because when drugs are in short supply lifesaving care can be
151 delayed, can be canceled, patients may be placed on
152 medication that is less effective or more expensive.

153 The cascading impacts of not receiving appropriate
154 medicine can impair a person's ability to live a full life,
155 to attend school, to work. Plus, it can lead to increased

156 costs of care and more serious health complications like
157 adverse drug reactions, increased hospitalizations, or even
158 death.

159 Children and their providers can be hit particularly
160 hard by drug shortages. Children's hospitals often
161 frantically respond to these shortages by scrambling for
162 necessary and appropriate drugs. They have to devote
163 additional staff time and resources to finding ~~a~~-appropriate
164 replacement drugs and determine the appropriate dosage for
165 the replacement drug. Is it safe for children? It takes
166 children's hospitals 50 percent longer to address shortages
167 than other hospitals because of the time needed to compound
168 replacement products into pediatric dosage forms. And it is
169 so costly. One drug in shortage alone can cost a children's
170 hospital north of \$50,000 in labor and substitute products.

171 So we have got to get ahead of these shortages before
172 they happen so that our neighbors and providers are not
173 blindsided and left scrambling to find workarounds.

174 This past winter's triple epidemic of the flu, RSV, and
175 COVID-19 were exceedingly difficult because shortages of
176 basic medicine like Tylenol and ibuprofen ultimately got so
177 severe that retailers began imposing purchase limits at the
178 counter, sending parents searching multiple locations for
179 medication to take care of their families. FDA took the
180 action it could within its limited authority to ensure that

181 more products were available for consumers, but the current
182 haphazard approach of addressing crisis episode by episode is
183 not working to give American families the certainty and the
184 quality of care they need and deserve.

185 So together we need to require greater transparency from
186 manufacturers about where they source raw materials for
187 drugs. We know that 72 percent of manufacturers supplying
188 the U.S. market with active pharmaceutical ingredients, or
189 API, are overseas, mostly in India and China, and the
190 percentage of APIs manufactured in those countries by volume
191 may be higher. I sit on the Select Committee on the
192 Strategic Competition between the U.S. and the Chinese
193 Communist Party, and API manufacturing is another example how
194 over-reliance on raw materials from China creates real-life
195 risks to the well-being of Americans.

196 Greater transparency will help us better understand
197 where we need to shore up the domestic production and invest
198 in new technologies. But the need to address shortages
199 doesn't end with manufacturers. We need to make sure that
200 the anti-consumer behavior by intermediaries like PBMs and
201 GPOs does not create affordability barriers for patients that
202 magnify the effects of drug shortages for families in need.

203 And we have a model, Mr. Chairman, for action, for
204 bipartisan action. When faced with a semiconductor shortage,
205 Congress acted to adopt the CHIPS and Science Act and invest

206 in Americans and our supply chains. Drug shortages will also
207 require a coordinated approach across government, but with
208 manufacturers, providers, and payers to create domestic
209 production, ~~to~~ shore up supply chains, and revitalize
210 scientific research that hopefully will strengthen our
211 economy and our health care system.

212 I hope that our witnesses today can help us better
213 understand the reasons why shortages occur and persist, and
214 how better and smarter tools would improve insight into the
215 supply chain to better guide strategies to strengthen it. By
216 better understanding the root causes of these shortages,
217 Congress and our public health institutions can enact
218 policies to address them.

219 I am really looking forward to our witnesses today and
220 covering this topic. So thank you all for being here.

221 [The prepared statement of Ms. Castor follows:]

222

223 *****COMMITTEE INSERT*****

224

225 *Ms. Castor. And I yield back my time.

226 *Mr. Griffith. I thank the gentlelady for yielding
227 back, and now recognize the chairwoman of the full committee,
228 Mrs. McMorris Rodgers, for her five minutes of opening
229 statement.

230 *The Chair. Good morning. Our goal today is to examine
231 the complex challenges and root causes that lead to drug
232 shortages.

233 Just last November, in September -- in Spokane parents
234 were shocked that Amoxicillin, a common antibiotic, wasn't
235 readily available at pharmacies. Parents had to contact
236 multiple pharmacies and talk to the doctor to get
237 alternatives, which is no small effort when your child is
238 sick.

239 Our committee has exposed the harmful consequences of
240 consolidation, Federal programs, and malincentives that
241 distort the market and make it more difficult for patients to
242 get lower cost medication. Sometimes it is because these
243 medications are not on pharmacy or hospital shelves, or
244 because they are not covered by insurance. These market
245 distortions hinder the adoption of quality generic drugs and
246 weaken the drug supply chain.

247 The FDA has not been an effective partner in combating
248 drug shortages. Even after Congress provided FDA new
249 authority in 2020 to get more information regarding where

250 American prescription drugs are made, we still do not have
251 good data on where either finished medications or active
252 pharmaceutical ingredients, or APIs, are sourced.

253 FDA last testified that around 80 percent of API
254 facilities and 60 percent of finished dosage facilities are
255 overseas, including India and adversarial countries like
256 China. These are countries who limit our foreign drug
257 inspection program's ability to operate adequately. It is an
258 enormous problem if we cannot properly inspect the quality of
259 the ingredients in common drugs Americans rely on.

260 This situation not only raises concerns over drug
261 quality, but it also poses a significant threat to national
262 security. If adversarial countries were to cut off the
263 supply of necessary APIs to manufacturers, American patients'
264 lives could hang in the balance.

265 Further, the COVID-19 pandemic taught us that we cannot
266 rely on the Chinese Communist Party, which blocked the export
267 of PPE and other critical supplies, lied about positive case
268 numbers, and has refused to cooperate into any meaningful
269 investigation into the origins of COVID-19.

270 As we strive to strengthen our supply chain, we must
271 encourage American innovation, increase domestic
272 manufacturing capabilities, and promote the adoption of
273 quality generic drugs. And we need a system that
274 acknowledges and rewards such innovation.

275 In 2019 HHS programs accounted for 40 percent -- 41
276 percent of all prescription drug spending. Yet those
277 programs may have unintended consequences leading to
278 unsustainably low prices or incentivizing middlemen to get
279 the best deal at the expense of a secure supply chain. We
280 should look at all Federal programs this committee oversees
281 to help create a more secure and reliable drug supply chain
282 for our nation.

283 We have gathered a diverse group of witnesses with
284 expertise into the pharmaceutical drug supply chain to help
285 us start to dig into these complex programs and challenges
286 and what potential solutions there are, whether in American
287 manufacturing or in trying to innovate around middlemen in
288 the system.

289 We will also hear from Laura Bray on why this work to
290 stop shortages is so important. Laura has heard many times
291 what no parent wants to hear, that there is a shortage of
292 medicine needed to treat her doctor's -- or her daughter's
293 cancer.

294 As I close, I want to note that I am encouraged by the
295 bipartisan approach to this hearing. This is a critical
296 issue that transcends political party lines, and I am
297 confident that by working together we can help ensure more
298 people like Laura's daughter get the lifesaving care and
299 medicines that they need when they need it. Thank you.

300 [The prepared statement of The Chair follows:]

301

302 *****COMMITTEE INSERT*****

303

304 *Mr. Griffith. I thank the gentlelady for yielding
305 back. I now recognize the ranking member of the full
306 committee, Mr. Pallone, for his five-minute opening
307 statement.

308 *Mr. Pallone. Thank you, Mr. Chairman.

309 Today we are examining the root causes of drug
310 shortages, which negatively impact the health and well-being
311 of so many Americans. Drug shortages are not a new issue,
312 but unfortunately, they are currently at a five-year high.
313 Shortages can last anywhere from a year to over a decade,
314 with 15 critical drugs in shortage for over 10 years. This
315 past -- this past year alone, we have seen harmful
316 disruptions in the availability of children's pain medication
317 and medication to create or to treat conditions like ADHD.
318 And these shortages can result in delayed care, ineffective
319 treatment, increased hospitalizations, and even death.

320 So we need to do more to prevent these drug shortages,
321 including building a robust and resilient drug supply chain.
322 This is not only critical to the health and well-being of
323 Americans, but also to our national security. However, we
324 cannot effectively tackle the challenges associated with drug
325 shortages without more information about the current supply
326 chain. Key gaps remain in our understanding of how drugs are
327 manufactured and brought to market.

328 The Administration for Strategic Preparedness and

329 Response has shared that there can be up to 20 key materials
330 per pharmaceutical. However, our public health agencies
331 currently do not know which materials are used in the
332 production of each drug, and in what quantity. We also do
333 not know the quantity of active pharmaceutical ingredients
334 used in drugs for the U.S. market that is manufactured
335 overseas. And while we know that 72 percent of active
336 pharmaceutical ingredient manufacturers serving the U.S.
337 market are overseas, we do not know the actual volume of the
338 ingredients that they manufacture, and that number is likely
339 much higher than the 72 percent.

340 So FDA has some limited tools to examine the supply
341 chain. Recently, as part of the CARES Act, Congress took
342 bipartisan action to start addressing drug supply chain
343 information gaps. The law included a requirement that
344 manufacturers develop risk management plans and annually
345 report to FDA on the amount of each drug they make available
346 for commercial distribution. This is a step in the right
347 direction, providing us more information than we had before.
348 And while it has been useful, it is not enough to fully
349 address drug shortages caused by supply chain issues.

350 FDA has repeatedly told us that, with its limited tools,
351 it is simply not capable of using its existing authorities to
352 directly prevent or mitigate a shortage. For example, FDA's
353 current reporting requirements don't allow the agency to

354 determine which suppliers of active pharmaceutical
355 ingredients manufacturers rely on. This makes it difficult
356 to predict how a disruption with one supplier would affect a
357 manufacturer's ability to produce their drugs.

358 FDA's tools are even more limited when it comes to
359 forecasting and anticipating changes in demand. We have seen
360 how sudden spikes in demand for certain drugs can cause a
361 shortage, most recently in the market for Adderall and
362 children's pain medication. However, manufacturers are not
363 required to report those demand surges to FDA, which means
364 FDA may lack the information it needs to foresee a shortage.
365 Without that information, FDA can't take the necessary action
366 to identify new manufacturers, expedite additional
367 inspections, or review new products that can fill gaps.

368 So giving FDA these tools will allow the agency to
369 understand why these shortages occur so that we can take
370 action to predict and address them. I would like to hear
371 from our witnesses how greater visibility into the supply
372 chain will help alleviate challenges that drive disruptions
373 in drug availability. And most importantly, I look forward
374 to discussing how more reliable access to important drugs
375 would improve the lives of patients and their families.

376 So I am pleased the subcommittee is also hearing from
377 experts about what we can do to increase pharmaceutical
378 manufacturing efficiency for greater domestic production.

379 I especially want to thank Professor Muzzio from Rutgers
380 University in my congressional district for being here today.
381 Dr. Muzzio directs Rutgers Center for Structured Organic
382 Particulate Systems, and he is a national leader in the
383 development of continuous manufacturing methods and
384 technologies, which will help us improve drug manufacturing
385 efficiency and quality.

386 Dr. Muzzio was also instrumental in supporting passage
387 of my legislation, the National Centers of Excellence in
388 Advanced ~~and~~ Continuous Pharmaceutical Manufacturing Act,
389 which President Biden signed into law last year. And that
390 law empowers the FDA to partner with universities around the
391 country to further develop continuous manufacturing
392 technology, which will, hopefully, strengthen domestic
393 pharmaceutical manufacturing and help prevent future drug
394 supply chain shortages.

395 So thank you for being here today, Dr. Muzzio.

396 Thank you to all the witnesses.

397 [The prepared statement of Mr. Pallone follows:]

398

399 *****COMMITTEE INSERT*****

400

401 *Mr. Pallone. And with that, Mr. Chairman, I yield
402 back.

403 *Mr. Griffith. I thank the gentleman for yielding back.
404 That concludes the members' opening statements.

405 I remind all members that, pursuant to committee rules,
406 the members' opening statements will be made a part of the
407 record.

408 We want to thank all of our witnesses for being here
409 today and take the time to testify before our subcommittee.

410 Each witness will have the opportunity to give an
411 opening statement, followed by a round of questions from
412 members.

413 Our witnesses today are Dr. Alex Oshmyansky, CEO/founder
414 of the Mark Cuban Cost Plus Drug Company; Anthony Sardella,
415 chair, API Innovation Center; Laura Bray, founder, Angels for
416 Change; and Fernando Muzzio, distinguished professor of
417 chemical and biochemical engineering at Rutgers University,
418 which I learned is in Mr. Pallone's district.

419 We do appreciate you all being here today, and we look
420 forward to hearing from you on this important issue. And
421 thank you so much for taking your time.

422 As you know, and as you are aware, this committee is
423 holding an oversight hearing, and when doing so we have the
424 practice of taking our testimony under oath. Do any of you
425 have an objection to testifying under oath?

426 Seeing that no one has objected, we will proceed.

427 Further, you are advised that you are entitled by
428 counsel -- you are entitled to have counsel present with you,
429 pursuant to House rules. Do any of you wish to have your
430 counsel present with you today?

431 All right, seeing that none have desired to have their
432 counsel with them, would you all rise and raise your right
433 hand, please?

434 [Witnesses sworn.]

435 *Mr. Griffith. Recognizing that all responded in the
436 affirmative -- and you all can be seated, thank you --
437 recognizing that all have responded in the affirmative, I
438 would say that you are now sworn in and under oath, subject
439 to the penalties set forth in title 18, section 1001 of the
440 United States Code.

441 All right. We got through all the legal mumbo jumbo
442 that we needed to get through. We will now recognize Alex
443 Oshmyansky for his five-minute opening statement.

444 *Dr. Oshmyansky. Alex is fine.

445 *Mr. Griffith. All right.

446 *Dr. Oshmyansky. First, thank you so much to the
447 subcommittee.

448 *Mr. Griffith. Yes, we need you to turn on the mike
449 and --

450 *Dr. Oshmyansky. Hear me?

451 *Mr. Griffith. Yes, maybe pull it up a little bit so
452 you are loud enough. We could hear you, but then nobody at
453 home --

454 *Dr. Oshmyansky. Oh, but no one else. Got you.

455 *Mr. Griffith. -- or on C-SPAN can hear you.

456 *Dr. Oshmyansky. Okay.

457

458 TESTIMONY OF ALEX OSHMYANSKY, MD, PHD, CEO/FOUNDER, MARK
459 CUBAN COST PLUS DRUG COMPANY; ANTHONY SARDELLA, CHAIR, API
460 INNOVATION CENTER, ADJUNCT LECTURER & SENIOR RESEARCH
461 ADVISOR, CENTER FOR ANALYTICS & BUSINESS INSIGHTS, WASHINGTON
462 UNIVERSITY IN ST. LOUIS; LAURA BRAY, FOUNDER, ANGELS FOR
463 CHANGE; AND FERNANDO MUZZIO, PHD, DISTINGUISHED PROFESSOR OF
464 CHEMICAL & BIOCHEMICAL ENGINEERING, RUTGERS UNIVERSITY

465

466 TESTIMONY OF ALEX OSHMYANSKY

467

468 *Dr. Oshmyansky. Well, first off, thank you so much to
469 the committee and the subcommittee for inviting me to speak
470 today. It's an honor and a privilege.

471 As I speak here today, there are approximately 200 drug
472 products listed as in shortage on the U.S. FDA shortage
473 database. Many of these medicines are critical lifesaving
474 medications such as albuterol, the treatment for an acute
475 asthma attack. Several chemotherapeutic drugs for cancer are
476 in shortage.

477 The rates of morbidity and mortality for pediatric
478 cancers in the U.S. have gone up in recent years, as the
479 medications necessary to treat them are increasingly
480 unavailable. The majority of these medications are
481 relatively simple to make, and have been available for
482 decades. How is it that they are unavailable in the United

483 States, the wealthiest country in the history of human
484 civilization?

485 The root underlying causes are complex and multi-
486 factorial. However, Mark Cuban Cost Plus Drug Company is
487 working diligently in the background to try to address drug
488 shortages through a combination of innovative technologies
489 and business model innovation.

490 We have constructed an advanced pharmaceutical
491 manufacturing plant in Dallas, Texas. The facility utilizes
492 robotic fill finish technology optimized by AI machine vision
493 systems that are designed to incorporate single use
494 disposable components. The robotic manufacturing systems
495 installed at our manufacturing facility can transition
496 between making batches of different types of medication
497 within hours, rather than months, with full FDA cGMP
498 compliance. This allows us to very rapidly pivot from making
499 one drug type to another in order to address pharmaceutical
500 drug shortages as they arrive.

501 In principle, we can have a new manufacturing line up in
502 four hours. In combination with a regulatory strategy as a
503 503(b) compounding site, we are very rapidly able to pivot
504 from making a shortage drug product with full compliance with
505 FDA regulations.

506 In addition, within the next few months, we will be
507 launching Mark Cuban Cost Plus wholesale, which will enable

508 independent pharmacies, clinics, and hospitals to get access
509 not just to our products, but products from any
510 pharmaceutical manufacturer at a true, transparent price.
511 This will enable us to ensure distribution of products
512 outside of the conventional distribution oligopolies.

513 Our pilot manufacturing facility is currently completing
514 its validation process, and is expected to begin commercial
515 sales later this year. It has an estimated capacity of
516 between one and two million sterile doses of medication a
517 year, either pre-filled vials or syringes. Initial products
518 will include pediatric chemotherapy agents, lidocaine, and
519 essential ICU medications. However, we will be nowhere near
520 meeting the national demand for these products.

521 Mark Cuban Cost Plus has also drafted preliminary
522 designs for a much larger facility, based on similar
523 technologies, that would hopefully be able to alleviate the
524 majority of acute drug shortage issues in the United States.
525 We believe such a facility would cost approximately \$300
526 million to construct, based on current estimates. We believe
527 that through a private-public partnership or otherwise,
528 through government investment, we will be able to build the
529 infrastructure necessary to ensure pharmaceutical drug
530 shortages no longer affect the health of Americans.

531 Thank you so much.

532

533 [The prepared statement of Dr. Oshmyansky follows:]

534

535 *****COMMITTEE INSERT*****

536

537 *Mr. Griffith. Thank you.

538 And we now recognize Mr. Sardella for his five-minute
539 opening statement.

540

541 TESTIMONY OF ANTHONY SARDELLA

542

543 *Mr. Sardella. Good morning. I'd like to thank
544 Chairman Griffith, Ranking Member Castor, and the
545 distinguished members of the committee for holding this
546 meeting. And it's a privilege to speak with you. My name is
547 Tony Anthony Sardella. I'm an adjunct professor at the Olin
548 Business School at Washington University. I'm also the
549 university's senior analyst for their Center for Analytics
550 and Business Insights, and also chair a new non-profit that
551 is dedicated to the reshoring of API to the United States,
552 the API Innovation Center.

553 The economic viability of the generic pharmaceutical
554 industry, which represents over 90 percent of the medications
555 prescribed in the United States, is diminishing and
556 contributing to supply disruptions, drug shortages, with
557 significant negative implications for U.S. health security.
558 Economic conditions indicate that this environment will only
559 worsen, further jeopardizing the quality and the stability of
560 our nation's pharmaceutical supply chain.

561 COVID-19 revealed the country's over-reliance on foreign
562 production of essential drugs. My research revealed that the
563 United States has no domestic-based supply for approximately
564 83 percent of the top 100 generic medicines prescribed in
565 America. These are highly prescribed medicines such as

566 cardiovascular, atorvastatin, and lisinopril that many
567 patients leverage and rely on every single day.

568 The principal driver to strengthen our health security
569 and keep our nation's drug supply chain secure is economics,
570 not just logistics. We must address the economic instability
571 of the generic pharmaceutical market. We must expand public
572 and private partnerships, and incentivize domestic drug
573 manufacturing.

574 Generic drugs are commodity products, and because they
575 are substitutable, price becomes the dominant factor in any
576 type of market competition. Since 2016, the generic industry
577 has experienced price erosion greater than 50 percent. An
578 average high-volume 30 count bottle of medicine is now less
579 than \$1.50, the equivalent of \$0.05 per tablet.

580 But there is a high cost to low prices. The
581 implications are significant. Reduced earnings lead to cost
582 cutting and reduced ability to invest in new product
583 development, factory maintenance, and innovation. The
584 economic pressures facing generic manufacturers are
585 contributing to increased quality and compliance risks, as
586 they are unable to expend capital to address FDA warning
587 letters, evidenced by greater than 1 in 4 prescriptions in
588 the U.S. are filled by a company that has received an FDA
589 warning letter in the last 26 months.

590 No single entity can solve this complex problem and

591 challenge to strengthen our domestic manufacturing. It
592 requires a coordinated approach between the public and
593 private sector. It involves, first, the de-risking of the
594 adoption of advanced manufacturing technologies that will
595 make the U.S. manufacturing globally competitive.

596 Second, it involves leveraging existing available
597 generic manufacturing infrastructure. In September last year
598 I published a study that revealed that, of the 37 U.S.
599 generic manufacturing sites surveyed in my research, they
600 were producing at just half of their annual production
601 capacity. And by repurposing the existing auto manufacturing
602 base, 57 percent of the U.S. manufacturing sites could be
603 operational in 1 year, and 86 within 2 years, which equates
604 to 30 billion capsules and doses of essential and critical
605 medicines within a 2-year period.

606 Third, several market-based solutions exist to foster
607 industry investment in domestic manufacturing, and ensure a
608 long-term, sustainable U.S.-based supply. The driver of
609 price erosion for generics is the inability to differentiate
610 on product quality, a dimension of market competition in
611 virtually every other market.

612 Quality price trade-offs can be addressed by creating
613 transparent quality scores that enables competition on a
614 dimension beyond only price, while incentivizing
615 manufacturers with strong quality.

616 Leveraging the buying power of the Federal Government,
617 which accounts for approximately 34 percent of total health
618 care spending in the United States, with sourcing policies
619 that favor and incentivize domestic manufacturing or
620 manufacturers with strong compliance records -- which is a
621 practice already employed in Germany, Brazil, India, and
622 China -- is another important instrument to incentivize U.S.-
623 based manufacturing.

624 Improving provider reimbursements for U.S.-made generics
625 and realigning preferred drug list formularies can also drive
626 incentives.

627 I'd like to thank the committee for your time and the
628 opportunity to share my research, data, and perspective
629 pertaining to the pharmaceutical supply chain and drug
630 shortages.

631 [The prepared statement of Mr. Sardella follows:]

632

633 *****COMMITTEE INSERT*****

634

635 *Mr. Griffith. Thank you for yielding back.

636 I now recognize Ms. Bray for her five-minute opening
637 statement.

638

639 TESTIMONY OF LAURA BRAY

640

641 *Ms. Bray. Good morning. I'm Laura Bray, chief change
642 maker at Angels for Change, a volunteer-supported
643 organization on a mission to end drug shortages. I
644 appreciate the opportunity to speak here today and represent
645 the patient voice.

646 Thank you for your leadership and bipartisan work to
647 prevent and end drug shortages.

648 Four years ago my husband Mike and I were sitting in a
649 hospital room when our child, Abby, was diagnosed with
650 leukemia. At that moment we became caretakers while our
651 child began to fight for her life. We were told we were
652 lucky that this leukemia, unlike many other pediatric
653 cancers, has a cure: a miracle protocol, a cocktail of drugs
654 given in certain timeframes, but leading to very successful
655 treatment.

656 The doctors used these success numbers -- above 90
657 percent -- to provide assurances, but also to alert us that
658 compliance was the single most effective thing, as her
659 parents, we could do every day for her survival. With our
660 trusted physicians, nurses, care team, and child life
661 specialists we became a team using every tool available to
662 ensure our child's compliance of this cocktail.

663 When a child doesn't want to take her meds anymore, when

664 they can't take the pain of being poked and prodded again,
665 when they lose their hair, when it's just too much, we all
666 focus on the importance of the medicine for their survival.

667 I was sitting in a hospital room with Abby when I first
668 heard the words, "We don't have the drug needed today. It's
669 on shortage.'`

670 My Abby, our fierce middle child, caught it right away,
671 and said, "I thought I needed this. Does this mean I die?''

672 Before that moment I didn't know our pharmaceutical
673 supply chain was broken. I had the same questions she had.
674 I told her the only thing I could. "We're going to try to
675 find it.'`

676 With no experience, using my background as a business
677 professor, the help of friends and family and Google, we
678 successfully found the medicine. But it didn't end there.
679 Abby's protocol was impacted by a drug shortage again and
680 then again, three lifesaving shortages in nine months,
681 different drugs, different root causes. It wasn't enough
682 that my nine-year-old had to consider her mortality because
683 of cancer. She also had to consider it again because our
684 supply chain was not making enough medicines of the drugs I
685 told her would save her.

686 This experience haunted me, and I began to ask questions
687 about how common it was for patients to experience something
688 like this. I was surprised by how easy it was to find the

689 answers. Twenty years of research outlining this drug
690 shortage crisis. There had been calls to actions. There had
691 been hearings like this going back many, many years.

692 If we had these answers, why did my child and our family
693 have to go through this? It was such a cruel place to find
694 ourselves. I knew no patient should have to go through a
695 search again alone.

696 So with my friends and family joined in the mission, we
697 launched Angels for Change in 2019, becoming the only patient
698 advocacy organization with a mission to end drug shortages in
699 the United States. And almost immediately, patients began to
700 call. Eventually, hospitals began to call, too. I connected
701 with members of the supply team, the supply chain. We
702 learned from each other. I asked the members to become
703 change makers with me.

704 The patients stuck in the drug shortage, they are our
705 purpose. But it was the people that make up the supply chain
706 that stepped up and took on collaborative, patient-focused
707 work with us that gave me hope. To date, we have helped
708 patients and hospitals find hundreds of courses of medicine
709 stuck in this broken supply chain during three dozen
710 different drug shortages.

711 Proactively, we foster stakeholder collaboration to
712 build resiliency, convening members at our summit and helping
713 to launch the End Drug Shortages Alliance, which now has 162

714 supply chain members ready to do this work. These
715 collaborative spaces have led to innovative pilot programs
716 like our Project Protect.

717 Through Prediction, a small manufacturing incentive
718 grant of \$100,000, we created gap supply of 2 essential
719 medicines. Those medicines went short, and it was accessed
720 650,000 times last year for patients in need. This type of
721 multi-stakeholder resiliency work must be supported and
722 scaled.

723 Building a resilient supply chain will take more
724 transparency, redundancy, and connectivity. Our pathway
725 forward is built on six principles. I've outlined them in
726 our written testimony. Every stakeholder will need to do
727 their part, but together we can ensure no child will ask
728 their parent, "Will I die if I don't get my medicine?"`

729 Thank you.

730 [The prepared statement of Ms. Bray follows:]

731

732 *****COMMITTEE INSERT*****

733

734 *Mr. Griffith. Wow, thank you.

735 Dr. Muzzio, your five-minute opening statement. Thank
736 you.

737 *Dr. Muzzio. Thank you. Can you hear me?

738

739 TESTIMONY OF FERNANDO MUZZIO

740

741 *Dr. Muzzio. So, Chairwoman Rodgers, Chairman Griffith,
742 Ranking Member Pallone, Ranking Member Castor, members of the
743 subcommittee, my name is Fernando Muzzio, I'm a distinguished
744 professor of chemical and biochemical engineering at Rutgers
745 University. And I'm the director of CSOPS, which is an NSF
746 engineering research center focused on developing
747 pharmaceutical products and processes. I greatly appreciate
748 the opportunity to appear in this hearing to talk about the
749 root causes of drug shortages, and also share some views on
750 how advanced manufacturing could help mitigate this problem.

751 I want to make two facts, and I appreciate that my
752 testimony may be a little different than the other witnesses.

753 The first fact is that we know that the proximate cause
754 of more than 60 percent of shortages is quality issues,
755 whether those quality issues are caused by economic reasons
756 or something else, but quality issues cause the majority of
757 the shortages.

758 The second fact is that advanced manufacturing methods
759 can improve quality and quality control, and therefore may
760 help reduce the incidence of some of these issues. Let me
761 explain why.

762 In the traditional batch manufacturing approach, a
763 manufacturer takes a large amount of ingredients, say 500

764 kilograms, puts that into a process unit, implements the
765 process, then the material moves to another piece of
766 equipment, and another piece of equipment, and after several
767 steps over many hours to make a large number of product
768 units, let's say a million tablets or a million vials. And
769 then they take 10 to 30 samples from that million tablet
770 batch, send them to the lab, get results, assume that those
771 results are representative of the whole batch, and make the
772 decision to release the product based on those results.

773 The process is time-dependent. Things are changing as
774 you are going through this particular traditional process,
775 and that can affect the quality of the product over time.
776 And this provides also a very limited opportunity to observe
777 product quality. In contrast, continuous manufacturing is
778 capable of much better quality control.

779 First of all, the ingredients come into the process at a
780 fixed ratio. They move gradually, but continuously from
781 process unit to process unit, but we keep the process very
782 close to steady conditions so that every portion of material
783 experiences the same process. There is only a small amount
784 of materials in the process at any time, but for every small
785 portion of material, we monitor quality in real time. And
786 this allows us to diagnose quality issues in real time,
787 exclude faulty material from what's going to be dispensed to
788 patients, and minimize quality failures.

789 Where are we in implementing this? Well, we started 17
790 years ago in our center. There were other efforts at the
791 same time. We established a full ecosystem of industry,
792 government, and academia, attracted over \$120 million in
793 funding for this work, and we built and demonstrated the
794 first continuous manufacturing line that operated in a full
795 state of control, and then supported Johnson and Johnson and
796 other companies in commercially implementing these
797 technologies.

798 In more recent developments -- and I want to give credit
799 to the FDA for this -- the FDA emerging technology teams has
800 accepted 42 proposals for continuous manufacturing review.
801 They have, actually, as of March, approved 13 continuous
802 manufacturing applications.

803 Direct compression, which is the most common type of
804 continuous manufacturing, has now graduated as an emerging
805 technology. They led the approval by the International
806 Conference on Harmonization of what is called Q13, the global
807 guidance in continuous manufacturing, and we have
808 collectively built widespread consensus, including the U.S.
809 Government through multiple administrations, that advanced
810 and continuous manufacturing could be part of the solution.

811 Now, this also produces an important opportunity for our
812 country. Given the advantages of continuous manufacturing,
813 we expect that there will be hundreds of billions of dollars

814 manufactured by continuous manufacturing. We can agree that
815 we would like that manufacturing to happen in the U.S. Now
816 this is feasible, and it can be done in a sustainable manner
817 because continuous manufacturing requires less unskilled
818 labor, which, because that kind of labor is cheaper in other
819 countries, has been one of the reasons why manufacturing
820 moved to those other countries.

821 However, it's important to recognize that implementation
822 of these technologies requires knowledge, requires training,
823 and requires access to infrastructure.

824 We expect other developments in the next few years. For
825 example, we expect that we will be able to implement what we
826 would call advanced batch manufacturing, where we will use
827 many of the techniques developed for continuous
828 manufacturing, now adapted for batch, to be able to inspect
829 100 percent of the product stream so that every single
830 product unit is analyzed in real time, and faulty product is
831 sent to scrap.

832 We also expect that we're going to expand continuous
833 manufacturing to generics, over-the-counter products,
834 manufacture of active pharmaceutical ingredients and
835 intermediates, as well as injectables, including biologics,
836 and that we will use similar methods to create other advanced
837 technologies such as distributed manufacturing.

838 All of this is possible, but to achieve this we really

839 need centers of excellence that will work in a sustained
840 manner in re-energizing the partnership between government,
841 regulators, and academia so that we can create places where
842 all of the workforce can be trained, the know-how is
843 available, and we can support industry, continue to move
844 forward.

845 As in Public Law 117-328, these centers would also make
846 possible to implement a national strategy in workforce
847 development that is needed to facilitate this.

848 So in concluding, I would request please that my full
849 written testimony be included in the record, and I will be
850 happy to answer any questions that I may. Thank you.

851 [The prepared statement of Dr. Muzzio follows:]

852

853 *****COMMITTEE INSERT*****

854

855 *Mr. Griffith. Thank you very much for your testimony.
856 Thank you to all the witnesses. At this point, we will begin
857 the questioning process, and I will begin with five minutes
858 of questioning.

859 Dr. Sardella, can you repeat for us -- I think this was
860 in your testimony -- what percentage of the generic drugs are
861 manufactured in facilities that have received an FDA warning
862 letter?

863 Yes, turn your mike on.

864 *Mr. Sardella. One out of four prescriptions in the
865 United States over the last twenty-six months.

866 *Mr. Griffith. So roughly 25 percent.

867 *Mr. Sardella. Correct.

868 *Mr. Griffith. In over how many months?

869 *Mr. Sardella. Twenty-six, the last twenty-six months.

870 *Mr. Griffith. And some of those FDA warning letters
871 stay open for years, do they not?

872 *Mr. Sardella. That is correct. And the industry is
873 less able, due to low margins, to be able to address them.
874 And so their options are shutter, not comply, or continue to
875 operate. And --

876 *Mr. Griffith. Let's talk about non-compliance, because
877 while some of these warning letters may be on things that
878 folks back home might think are trivial and so forth, but
879 there was an open warning letter on the New England

880 Compounding Company at the time that they produced a sterile
881 injection which cost -- I believe it was 38, 40 lives,
882 several of whom were in my area. My district was impacted by
883 that outbreak. And that was a warning letter because people
884 were trying to cut costs.

885 And so I want folks back home -- and I think you would
886 agree with me that when you have 25 percent of your generic
887 medicines being manufactured under a warning letter, most of
888 it is not going to be a big deal, but some of it might be a
889 big deal, and this is a concern that we need to take, as a
890 nation. Would you agree?

891 *Mr. Sardella. I agree, Chairman. In that spectrum
892 there are very much warning letters that don't imply any type
893 of safety issue, but there's also those that do, and those
894 are significant, and have dire consequences.

895 *Mr. Griffith. Yes, and that is my concern here, is
896 that, you know, in our race to save a few pennies here and
897 there, we are sacrificing both availability that Ms. Bray
898 talked about and quality.

899 All right, back to my real questions, the ones that I
900 had prepared in advance. In your white paper, Dr. Sardella,
901 you wrote that it is unrealistic to fully move our API
902 sourcing and manufacturing onshore. Instead, you propose the
903 U.S. API industry should achieve a minimum level of
904 self-sustainability. Explain that for me.

905 *Mr. Sardella. We've done some research that estimates
906 the cost to bringing the top 40 prescribed medicines and the
907 top 40 essential medicines. We feel this would begin to
908 stabilize the U.S. supply chain, reshoring those productions
909 to the United States.

910 Our estimates are that that would cost less than \$2
911 billion, which is less than 1 percent of our total spend on
912 pharmaceuticals for those generics, and allow us to have
913 greater certainty and control of our drugs, knowing that the
914 APIs are the clinical part of the drug that allows it to be a
915 great therapeutic. So --

916 *Mr. Griffith. And would you agree with me that it is
917 likely, if we were to do something like that, that then that
918 would also encourage other folks to maybe make some APIs that
919 weren't in the top 40?

920 *Mr. Sardella. That's exactly correct. If we can think
921 of them -- we use at the API Innovation Center the construct
922 of critical and essential. If one -- critical being ones
923 that are critical to our national security. Those
924 cardiovasculars that we take, patients take every single day,
925 they're not in shortage, but they're core to our national
926 security.

927 The ability to incentivize production of those drugs
928 here in the United States will allow for capability to
929 produce the essentials in the United States and, therefore,

930 solving two of the issues, national security and our drug
931 shortage for our essential medicines.

932 *Mr. Griffith. All right. You also talked about supply
933 chain challenges and how that is exacerbated by inflexible
934 regulations. Could you expand on that?

935 And are there lessons we can learn from our experience
936 in moving up the speed on COVID-19 that we should look to
937 extend?

938 *Mr. Sardella. Yeah. Well, I think on COVID-19 there
939 are some efforts to allow for greater inspections of
940 different facilities to allow for better quality to be
941 produced. I think a couple of the key things that we've
942 learned is any type of expedited approvals or processing
943 allow for faster time to market, allowing companies to have a
944 quicker return on their investment on their capital.

945 *Mr. Griffith. I have got one more question for you --
946 and I had some for the others, so I apologize, but I am
947 running out of time -- Group Purchasing Organizations are
948 considered the price setters for generic medications in our
949 pharmacy supply chain, and they seem to create marketing
950 efficiencies. What role have they played in creating current
951 -- the current environment where we have shortages, and what
952 accountability is there for GPOs when shortages occur?

953 *Mr. Sardella. The GPOs are contributing significantly
954 to the aggregation of profits to them versus the

955 manufacturers. They're putting the manufacturers out of
956 business, first.

957 The second -- I would caution -- as we develop policy to
958 address GPOs, recognize that any redistribution of those
959 profits would go to foreign manufacturers, not U.S., because
960 that's where they're getting their supply. If the goal is to
961 create a sustainable, strong economic, U.S.-based supply,
962 that -- those incentives have to be established before the
963 addressing the GPOs concentration of profits.

964 *Mr. Griffith. All right. I appreciate it. My time is
965 up, and so I will now recognize the ranking member of the
966 subcommittee, Ms. Castor, for her five minutes of
967 questioning.

968 *Ms. Castor. Well, thank you, Mr. Chairman.

969 Professor Bray, I am so proud that a working mother from
970 the Tampa Bay area of three children who grappled with a
971 pediatric cancer diagnosis for her young daughter used her
972 business acumen to start a non-profit to help solve the drug
973 supply shortage. It's a remarkable story, and your voice is
974 very important in this discussion.

975 So you explained your daughter went to one of the
976 premier children's hospitals in America, Saint Joseph's
977 Children's Hospital in Tampa. And yet they are grappling
978 constantly with shortages of lifesaving drugs. What did you
979 - what did you learn as you dug into it as to the root causes

980 of the -- of the drug shortages, and why is it impacting
981 children especially?

982 *Ms. Bray. Thank you. Thank you for addressing me, and
983 thank you for having this meeting today.

984 So first, pediatrics are uniquely vulnerable to drug
985 shortage because we're a smaller patient population. And
986 when you have a broken marketplace, the smaller samples will
987 always fall out.

988 And then pediatric cancer is even a smaller niche of
989 that small, broken place. And what we found is that,
990 actually, pediatric cancer is 90 percent more likely to go
991 into shortage, their drugs, and they stay short 30 percent
992 longer. But it's -- compounds because their treatment is
993 multi-layered, and relies on many different drugs and very
994 specific protocols. So one or two drugs, in short, can have
995 drastic problems to their -- to a pediatric cancer diagnosis.

996 What we have found, both, you know, initially, when we
997 navigated the supply chain for my own child, but then as
998 chief change maker at Angels for Change, we navigate this
999 crisis for patients and hospitals all the time. I like to
1000 say, you know, the four P's, we're stuck here at the bottom.
1001 That's the physician, the pharmacist, the purchaser, and the
1002 patient. We're the consumer of these goods, and we do not
1003 have a lot of power during a time of disruption. And so
1004 together we can navigate this crisis a little bit better and

1005 be a unified voice.

1006 And so one thing we have found is that collaboration
1007 during a time of drug shortage would really help. This
1008 marketplace is deeply fragmented. Everyone, I think, talked
1009 about transparency today. We do need transparency. There's
1010 gaps in knowledge. And until we have a clear picture, we
1011 can't address the right solutions for the right problems.
1012 And those are the redundant solutions that are -- my other
1013 wonderful panelists have talked about.

1014 No one solution is going to fix this. It will be
1015 multi-layered and redundant. But to do that we have to be
1016 connected as an entire supply chain. All members must be at
1017 the table. There is a space for all of us, especially the
1018 patient.

1019 *Ms. Castor. So you did this. You mentioned in your
1020 testimony you actually initiated something called Project
1021 Protect, where you just dived in and tried to actually create
1022 a certain supply chain for certain drugs and shortages. How
1023 did -- how did that work?

1024 Why did -- why was it -- why was it left to you, without
1025 much help from government agencies that should be helping?

1026 *Ms. Bray. Well, I think there's a role for scalability
1027 of innovative programs that have been working already, for
1028 sure.

1029 So Project Protect, it was -- there's a lot of

1030 discussion about whether prediction can ever fix this, and I
1031 believe it can. Any healthy supply chain -- we're in the
1032 world of blockchain and AI, that's the stuff I talk about in
1033 my business classes and, you know, why wasn't this supply
1034 chain, you know, in the new millennia of supply chain
1035 management?

1036 And so I was like, we've got to start with prediction.
1037 So we got to we got to prove that. So we used prediction and
1038 said, what drugs do we think might go short? We picked two.
1039 There's a lot of work underway on prediction. I encourage
1040 that work to be scaled.

1041 And we then went to a small onshore manufacturer, a
1042 503(b), like Alex talked about, and said, what would it cost
1043 you and how much time would it take to ensure this for the
1044 American people if it did go short?

1045 They surprised me by saying about 60 days and \$100,000.
1046 I said, "Each?" And they said no, for both. So I wrote a
1047 grant, and signed an agreement with them, and told them be
1048 ready to supply if this -- if it goes short. It did go
1049 short, and --

1050 *Ms. Castor. And these drugs were?

1051 *Ms. Bray. Pardon?

1052 *Ms. Castor. Name the drugs.

1053 *Ms. Bray. It was potassium chloride and sodium
1054 chloride, and it was accessed 650,000 times last year during

1055 a time of shortage. So it didn't stop the disruption. What
1056 it was was gap supply, efficient, flexible gap supply that
1057 was incentivized by the marketplace and a private -- public-
1058 private partnership.

1059 I think this is a model that can be duplicated over and
1060 over and over again to protect the American people during a
1061 time of disruption. And then we do need to do all the work
1062 to help eliminate some of this disruption that the rest of my
1063 colleagues have talked about.

1064 *Ms. Castor. Thank you, Professor.

1065 *Ms. Bray. Thank you.

1066 *Mr. Griffith. The gentlelady yields back. I now
1067 recognize the chairwoman of the full committee, Mrs. McMorris
1068 Rodgers of Washington, for her five minutes of questioning.

1069 *The Chair. Thank you, Mr. Chairman. I wanted to start
1070 with Dr. Alex.

1071 In your written testimony you describe how a PBM will
1072 negotiate rebates, and then keep a percentage of the rebate
1073 negotiated. How do these negotiated rebates distort the drug
1074 market?

1075 And specifically, can you explain how rebates negotiated
1076 by PBMs contribute to high drug prices, shortages of
1077 essential medicines, or the race-to-the-bottom pricing that
1078 undermines our drug supply chain, and the impact that this
1079 has on patients, providers, and pharmacies?

1080 *Dr. Oshmyansky. Sure thing. So, you know, the PBMs, I
1081 kind of think of them in my head as payment processors, sort
1082 of similar to Visa or MasterCard. And many years ago they
1083 realized, hey, we're processing all the payments, we can
1084 negotiate for drug prices on behalf of the people we're
1085 processing payments for.

1086 And the way they decided to go about it was to negotiate
1087 a rebate. They wouldn't charge you for this service of
1088 negotiation, they would just take a cut of the rebate back
1089 off of a list price. And it soon became very readily
1090 apparent that the biggest way to make this cut of the rebate
1091 as big as possible was to make the rebate as big as possible.
1092 So the standard rebate on a generic drug product now is
1093 between 85 and 88 percent. And where else in life do you get
1094 an 88 percent discount? Like, something's a little off.

1095 So -- and they capture, you know, let's say 10 percent
1096 for the sake of talking, percent of that rebate. That serves
1097 to, you know, increase the cost of the actual drug by 60 to
1098 100 percent, with none of that actually going to the
1099 manufacturer itself.

1100 One of the big misconceptions we have at Cost Plus is
1101 that we're able to somehow better negotiate the price of
1102 these medications, or we get a better price. We don't. We
1103 actually pay more. Manufacturers like working with us,
1104 because we're a small entity, as opposed to one of these big

1105 purchasing conglomerates. So they -- we actually pay them
1106 marginally more than the competition, and yet we're able to
1107 still save patients significant amounts of money.

1108 And that 88 percent discount, let's say, that can be
1109 just an average. We've seen much more extreme discounts --
1110 or rebates, rather. Imatinib, the chemotherapy agent, has a
1111 list average wholesale price, the generic, of \$10,000 for a
1112 month's supply. Meanwhile, we sell it at our website with --
1113 and again, paying more than other suppliers -- for \$30, about
1114 \$30, for that same month supply. And the actual adjudicated
1115 cost, so the actual price patients pay, we see at the counter
1116 at, like, CVS or Walgreens is 2,000, \$3,000 for a month
1117 supply. And that's not going to the manufacturer. So it's
1118 just extreme distortions in the way drugs are paid for.

1119 *The Chair. Thank you. Thank you for that. And I
1120 don't think that there is a single, all-encompassing solution
1121 for shortage problems.

1122 Would you speak to how transparency, additional
1123 transparency, might help?

1124 *Dr. Oshmyansky. Oh, sure. You know, I think if
1125 patients, providers, payers just know what these medications
1126 actually cost, and what percentage are going to
1127 intermediaries in the supply chain, you know, I think if
1128 patients learned that most of the money they were spending on
1129 insulin went not to the insulin manufacturer, but to the

1130 intermediaries in the supply chain, you know, I think that
1131 would incentivize, you know, a change in the way the supply
1132 chains work to have, you know, as my colleagues have been
1133 saying, more of the revenue going to the people that do the
1134 actual hard work of the manufacturing itself.

1135 And forgive me, I didn't answer your last question
1136 entirely as to, you know, what are the dynamics that lead to
1137 only a few manufacturers getting contracts. Because of the
1138 oligopolies at the levels of the purchasers, the sourcing
1139 programs, rebate aggregators, GPOs, all of these subsidiary
1140 entities of the big purchasing conglomerates, only a couple
1141 companies can win that battle for the contract. And say
1142 there's 12 manufacturers. If only two or three win the
1143 contracts, you know, the others have no incentive to keep
1144 their supply chains open.

1145 *The Chair. Thank you.

1146 *Dr. Oshmyansky. So if we just create an open
1147 marketplace where, you know, the manufacturers themselves can
1148 compete on quality --

1149 *The Chair. Thank you. I am going to -- I am running
1150 out of time here. I had -- and I wanted Dr. Sardella -- I am
1151 going to have to ask others -- to address you.

1152 I wanted to give -- Ms. Bray, you started talking about
1153 the potential of public-private partnerships, and I just
1154 wanted to give you my remaining time to talk -- just hear

1155 some more about the potential to help meet -- solve this
1156 problem.

1157 *Ms. Bray. Thank you. And I just realized I never
1158 mentioned Abby is doing great. She's thriving. She's 13
1159 today, and entered survivorship this spring.

1160 *The Chair. Oh, that is great to hear.

1161 *Ms. Bray. So just -- since I never mentioned that.

1162 You know, any healthy, you know, important supply chain
1163 relies on partnership, and every member will need to have a
1164 place at this table, especially when we talk about
1165 incentivizing the right motives.

1166 The FDA's 2019 root causes, possible solutions report
1167 stated in the executive summary, "Enduring solutions will
1168 take multi-stakeholder efforts and re-thinking business
1169 practices.'" That's basically all I've been doing since we
1170 founded.

1171 How do I collaborate with as many people as possible in
1172 the supply chain? It includes the FDA, it includes the
1173 supply chain members, it includes the manufacturers and the
1174 hospitals.

1175 How do we align our incentives to get as many patients
1176 the needed drugs that they deserve? And that's, you know,
1177 the one message I want to say: we need to be connected and
1178 collaborate, but then there needs to be tools of connectivity
1179 so we can scale.

1180 *The Chair. Thank you.

1181 *Ms. Bray. Thank you.

1182 *The Chair. Thank you very much, thanks for being here.
1183 I yield back.

1184 *Mr. Griffith. The gentlelady yields back. I now
1185 recognize the ranking member of the full committee, Mr.
1186 Pallone, for his five minutes of questions.

1187 *Mr. Pallone. Thank you, Mr. Chairman. I am still
1188 concerned that FDA lacks the information it needs about how
1189 pharmaceutical products are produced, and real-time data
1190 regarding changes in supply and demand for drugs and their
1191 key ingredients, so let me ask Dr. Muzzio.

1192 What gaps remain when it comes to our knowledge of the
1193 pharmaceutical supply chain, in your opinion?

1194 *Dr. Muzzio. I'm sorry, I didn't hear you.

1195 *Mr. Pallone. Let me get closer to the mike here. Dr.
1196 Muzzio, what gaps remain when it comes to our knowledge of
1197 the pharmaceutical supply chain?

1198 *Dr. Muzzio. Well, there are many. In addition to the
1199 ones I have mentioned, I want to point out that there is an
1200 additional factor that I'm very concerned about, which is in
1201 reading all the government reports on this issue, you know,
1202 on the last couple of years, there is only barely a mention
1203 of the chemical building blocks that are needed to make the
1204 drug substances.

1205 So the discussion is, you know, who makes the finished
1206 product, or who makes the drug substance, but then it turns
1207 out that, to make the drug substance, you need to have access
1208 to pieces of that molecule. And there is very, very limited
1209 knowledge of where those pieces come from, except to say
1210 that, for many APIs made in India, which we consider a
1211 friendly nation, in many cases the building blocks also come
1212 from China.

1213 So we might have to go earlier upstream the supply chain
1214 to ensure that we are able to actually make things in
1215 friendly shores, including our shore. So I think that's a
1216 big gap in our understanding of how -- you know, where
1217 shortages come from. There's been instances where key
1218 starting materials were found to be contaminated, and that
1219 triggered a whole sequence of events, then bringing other
1220 problems as we go -- as we went down the supply chain. So I
1221 think that those are important issues.

1222 I am aware of efforts at USB, for example, to create a
1223 substantial map of the entire supply chain. I don't think
1224 they are unique. There is another organization doing
1225 something similar. I don't recall their name right now. I
1226 think that's a very important effort that also needs to be
1227 supported, and strengthened and, you know, completed.

1228 And we need tools that will allow us to update the model
1229 of the supply chain dynamically. One important thing is to

1230 realize that it's not a static object, that once you describe
1231 it, it remains like that forever. It changes all the time.
1232 So we need not only to inventory the pathways, we also need
1233 to create methods to update the model of the supply chain
1234 very rapidly every time the conditions change. Otherwise, we
1235 would be fighting last year's war, so to speak.

1236 *Mr. Pallone. All right, thank you. So let me go to
1237 Professor Bray.

1238 Where have you seen FDA work most effectively in its
1239 response to drug shortages, and how could additional
1240 visibility into the supply chain strengthen that work?

1241 *Ms. Bray. Thank you for asking. I believe the Office
1242 of Drug Shortage at CDER is doing a lot of great, patient-
1243 focused work, and it's actually led by people who were our
1244 health care providers. And I think they're doing great work,
1245 we work together often. They're open to communication and
1246 feedback, and I'm very appreciative for the work that they do
1247 during a time of crisis.

1248 Where we could get better is a lot of the approaches are
1249 reactive, and there is missing gaps of information, just like
1250 everybody has said. So I would like to do a mindset shift on
1251 drug shortages as a crisis, and that mindset shift is to
1252 change from a focus of mitigation to ending. And so when you
1253 think about the fact that our current strategy for drug
1254 shortages is a word called "mitigation," mitigate means what

1255 do we do with available supply? And when you ask that
1256 question, the answers and next questions are who gets it, and
1257 who doesn't. And all you get is disparity and plays for
1258 mistrust and power.

1259 The question we need to be asking, it's a full dynamic
1260 shift, and it is, how do we end drug shortages? When we ask
1261 that question, it's how much supply do we need for the
1262 American people? How do we ensure that we have access to
1263 that supply, and how do we make sure that supply gets to the
1264 people when there's disruption?

1265 And you can see how quickly that mindset shift gets to
1266 very different solutions. One is potentially reactive that
1267 is repeated over and over again for 20 years, and one is
1268 proactive that can work to secure the supply chain for all
1269 patients and make a more resilient supply chain. Thank you.

1270 *Mr. Pallone. Well, thank you both, and thank you, Mr.
1271 Chairman.

1272 *Mr. Griffith. The gentleman yields back. I now
1273 recognizes the gentleman from South Carolina, chair of our
1274 Energy Subcommittee, Mr. Duncan, for his five minutes of
1275 questioning.

1276 *Mr. Duncan. Thank you, Mr. Chair.

1277 Dr. Sardella, your white paper does a great job in
1278 outlining the current state of U.S. API infrastructure and
1279 its potential effects on national security. Your paper

1280 discusses the vulnerabilities of U.S. pharmaceutical supply
1281 chain. In particular, you highlight our reliance on foreign
1282 sources for the active ingredients in our pharmaceutical
1283 drugs. Can you please share with the committee the potential
1284 risk or consequences that such a dependency poses to U.S.
1285 health care system?

1286 *Mr. Sardella. Two real risks that we experienced
1287 during COVID.

1288 The over-reliance on foreign manufacturers leave us
1289 vulnerable not just to demand shocks like COVID, but also
1290 supply shocks due to geopolitical tensions. During COVID,
1291 India had to stop any export in order to ensure the safety of
1292 their own population, which -- and, in fact, cut off supplies
1293 to the United States for critical medicines that we required.

1294 Second, the chief economist in Beijing -- we don't have
1295 to think it might happen -- intimated that our drug supply
1296 chain was, in fact, a lever to ensure that we cooperated as a
1297 country on geopolitical issues ranging from trade to Taiwan.

1298 So we've experienced the risks of being over-reliant
1299 already, from a geopolitical perspective as well as from a
1300 supply to citizens.

1301 *Mr. Duncan. It points to the need to onshore both
1302 pharmaceuticals, microchips, energy sources, because in a
1303 time of war or a pandemic like we saw, when the United States
1304 of America is reliant on sources for any of those things from

1305 overseas, then systems stop and the ability to provide the
1306 medication that our constituents need is important. So the
1307 need to onshore that is important.

1308 But when we talk about drug shortages, you have got to
1309 keep in mind that in many instances making generic drugs is
1310 simply not profitable. So let's shift to generic. In those
1311 situations, the manufacture does not have the resources or
1312 economic incentive to invest in the manufacturing of those
1313 products to keep them on the market, especially if it's a
1314 loss leader.

1315 So could you speak -- with the passage of the Inflation
1316 Reduction Act, which is a misnomer, is it possible that brand
1317 products selected for negotiation have generics in
1318 development?

1319 And if a drug selected for negotiation makes it harder
1320 or less profitable for generics to come to market, could we
1321 see an increase in the shortages?

1322 *Mr. Sardella. Well, first, in regards to the shortages
1323 from over-reliance, the strategy should not be to just move
1324 the same type of manufacturing to the United States to
1325 produce them at economic low profitability or losses. It
1326 should be to leverage the advanced technologies, technologies
1327 that Fernando mentioned such as continuous flow, that allow
1328 for significant cost reductions.

1329 The API Innovation Center is focused on a series of

1330 oncology drugs. We took a crisis in oncology, the drug
1331 called Lomustine, built a consortium of innovators who had
1332 developed new, novel techniques to produce it using
1333 continuous flow, existing manufacturers with capacity to
1334 produce it here in the United States on behalf of the
1335 Glioblastoma Foundation.

1336 It also engaged with critical entities such as Emerson
1337 that makes the control systems. It took numerous
1338 stakeholders. The impact of that is a 90 percent cost
1339 reduction on a drug that now, all of a sudden, becomes
1340 feasible to manufacture in the United States for the
1341 Glioblastoma Foundation.

1342 So it requires very much technology to do that, to
1343 compete long-term. It also requires changing to incentivize
1344 that U.S.-based manufacturer, allowing for changes in
1345 formularies and preferred drug lists to, in fact, allow for
1346 that manufacturer with advance technologies that are more
1347 environmentally favorable, less footprint, as well as
1348 economically more favorable, to be chosen in the formulary.

1349 *Mr. Duncan. Is the hang-up to do that the FDA?

1350 *Mr. Sardella. There's numerous instruments that can be
1351 brought to bear that wouldn't require significant legislative
1352 change in regards to allowing it. So there's an ability to
1353 designate on those formularies what the requirements are for
1354 preferred drug. And it could be U.S.-made, made from a

1355 facility that has no warning letter. And third, using even
1356 advanced technologies, which would allow for more energy
1357 efficiency, lower environmental footprint, and as well,
1358 higher quality standards, as Fernando had indicated.

1359 This is within our grasp, very reasonable grasp.

1360 *Mr. Duncan. Thank you so much.

1361 Chairman, I yield back.

1362 *Mr. Griffith. The gentleman yields back. I now
1363 recognize the gentleman from New York, Mr. Tonko, for his
1364 five minutes of questioning.

1365 *Mr. Tonko. Well, I thank the chair and ranking member
1366 for the opportunity today, and welcome the witnesses.

1367 Getting ahead of drug shortages will allow us to
1368 increase access to lifesaving medications for patients when
1369 they need them most. As we have seen this past year,
1370 shortages can happen because of unanticipated spikes in
1371 demand for drugs. I am thinking today about parents of sick
1372 children who couldn't obtain children's Tylenol during this
1373 year's confluence of RSV, COVID-19, and influenza, or people
1374 with ADHD who could not consistently obtain important
1375 medications because of an anticipated surge in demand due to
1376 a sharp increase in prescriptions through the pandemic.

1377 One of my constituents from Saratoga Springs shared how
1378 she could no longer find her daughter's medication. And she
1379 said, "As a mother, I can't believe this, that a child that

1380 needs medication can't get it."11 It is a sentiment of both
1381 shock and outrage I share along with many of my constituents.

1382 My understanding is that, without more drug information
1383 about the demand for drugs, we don't know how much production
1384 is required to meet that need. For example, a study in 2022
1385 from Brandeis University found that there was a shortage of -
1386 - shortage of naloxone, a critical drug used to reverse
1387 overdose in nearly every U.S. state. The study found that
1388 the shortage was in part created because there was no
1389 comprehensive data on how much naloxone was needed, and who
1390 was using it. So I want to be sure our agencies have all the
1391 tools they need to be able to accurately gauge demand
1392 fluctuations so that we know where we need to fill in gaps.

1393 You noted in your testimony, Professor Bray, that FDA
1394 currently has limited visibility into spikes in demand for
1395 pharmaceutical drugs. Why is having greater visibility into
1396 that demand for prescription drugs so important, and what
1397 would having that information allow FDA to do?

1398 *Ms. Bray. Thank you for asking. Well, I think we've
1399 spent a lot of time talking about the supply-side issues of
1400 this crisis, but there are demand-side issues. And just
1401 because we fix the supply-side issues doesn't mean patients
1402 are going to get equal and disparity-free access. So we at
1403 Angels for Change spend a lot of time making sure available
1404 supply onshore is in the right place at the right time,

1405 instead of stuck somewhere in the supply chain.

1406 So it does -- we are blind a lot when we don't know
1407 what's happening with spikes of demand. The entire supply
1408 chain is. And so when we throw in a potential solution based
1409 on old information, what happens is that solution actually
1410 works, but then a spike of demand makes it fail, and then it
1411 builds additional distrust in the entire supply chain.

1412 So I do think -- I often am flying blind about what's
1413 going on with the demand, and where the actual drug is, and
1414 it is a very laborious non-economies of scale process built
1415 on a painstaking network of American people who care. Like,
1416 emails and phone calls, "What are we doing? Where is it?"
1417 This is unnecessary. We could have, you know, not -- but
1418 it's not just the information, it's what are we going to do
1419 with it? What's the tool we're going to do to make sure
1420 people have access?

1421 And then you got to the beginning -- the beginning part
1422 of your question was actually about Adderall and amoxicillin.
1423 You know, it's the information before then. Those were
1424 predictable. There were people who are subject matter
1425 experts who knew those things were happening, who tried to
1426 ring those bells well ahead. And some of us put in some
1427 safeguards because of them. And so we need data that leads
1428 to prediction so that we don't have disruption, and that's
1429 the key.

1430 And just like my colleague said, there is amazing work
1431 being done. We have many times worked with USP and their
1432 medicines supply map. They are doing unbelievable work
1433 mapping the entire global supply chain. It isn't effective
1434 until it's used to solve it for the American people.

1435 *Mr. Tonko. Thank you.

1436 And Dr. Oshmyansky, you, in your testimony, share that
1437 the manufacturing systems used in your facility can
1438 transition between making batches of different medications
1439 within hours, when it usually takes months. How would
1440 collecting greater insights into unanticipated demand allow
1441 facilities like yours to respond in a nimble and agile way to
1442 a shortage?

1443 *Dr. Oshmyansky. Oh, sure. So the longest lead time
1444 item for our manufacturing is not really switching over to
1445 supply lines. It's sourcing the active ingredient.

1446 So our plan is to have a portfolio of active ingredient
1447 of the drugs we anticipate will go into shortage, send them
1448 to independent laboratories for quality and safety testing.
1449 That process takes a few months. Once we've done that
1450 process, we don't need to repeat it. But if we can
1451 anticipate what the drug shortages are predicted to be ahead
1452 of time, we can have that API in our portfolio ready to go.

1453 *Mr. Tonko. Thank you so much.

1454 And with that, Mr. Chair, I yield back.

1455 *Mr. Griffith. I thank the gentleman for yielding back.
1456 I now recognize the gentleman from Texas, Mr. Crenshaw, for
1457 his five minutes of questioning.

1458 *Mr. Crenshaw. Thank you, Mr. Chairman. Thank you for
1459 this hearing, and thank you to our witnesses for being here
1460 today. It is an important subject.

1461 You know, in the Houston area, just outside my district,
1462 Texas Children's Hospital, 80 percent of their patients are
1463 impacted by drug shortages. That is the whole hospital.
1464 They currently have 101 medications on back order, 350
1465 medications on allocation, where they are limited in the
1466 quantity that they can produce. Eight of these are
1467 chemotherapy agents that are used in first-line treatment of
1468 pediatric cancer.

1469 So I want to, in as little time as possible, because
1470 this is a much longer conversation, but Mr. Sardella, I want
1471 to figure out how this supply chain looks with active
1472 pharmaceutical ingredients to the -- in the best way that we
1473 can. Eighty-five percent of APIs are from foreign countries.
1474 Sixty percent of our finished dose forms are from foreign
1475 countries. And, you know, a lot of people wonder why.

1476 So what is in an API? Just a variety of other
1477 chemicals? Is there -- are there -- is there, like, a top
1478 three chemicals that are in APIs? Can you describe that
1479 really quickly?

1480 *Mr. Sardella. Yeah, and you bring up an excellent
1481 point. The API itself is the chemical that produces the
1482 medicinal effect. It is the most important element in that
1483 capsule tablet, in that drug.

1484 *Mr. Crenshaw. But the --

1485 *Mr. Sardella. The remaining elements are elements that
1486 allow for either the transport through your digestive system
1487 or other type of elements to allow it to survive and be
1488 effective.

1489 And quite interesting, what you bring up is something
1490 that we've seen. It's API, even we've heard capsules or the
1491 caps of a bottle will be in shortage and have a supply chain
1492 challenge which may prevent -- we always think of just the
1493 active -- but all these other areas, the excipients, et
1494 cetera.

1495 *Mr. Crenshaw. But I want to focus on APIs for a
1496 second. So an API is a chemical, but it is a chemical made
1497 up of other chemicals.

1498 *Mr. Sardella. Correct?

1499 *Mr. Crenshaw. Right? And where do those other
1500 chemicals come from?

1501 *Mr. Sardella. Oh, yeah.

1502 *Mr. Crenshaw. You know, and --

1503 *Mr. Sardella. So --

1504 *Mr. Crenshaw. Go ahead.

1505 *Mr. Sardella. Yeah. So we are reliant on what would
1506 be called starter materials. And these are the original
1507 chemicals that allow us to make those APIs. The majority of
1508 them are carbon-carbon, carbon-nitrogen, carbon-oxygen bonds.
1509 They're the foundational elements.

1510 To build a sustainable API, we need to also allow for
1511 the creation of starter materials here in the United States.

1512 *Mr. Crenshaw. And this is -- I do have a point to
1513 this. So those starter materials are widely available in the
1514 United States.

1515 *Mr. Sardella. Mm-hmm.

1516 *Mr. Crenshaw. Right? They are generally derived from
1517 petrochemicals. So, like, benzene, which is like a natural
1518 gas-derived chemical, is used to make ibuprofen.

1519 *Mr. Sardella. Mm-hmm.

1520 *Mr. Crenshaw. I didn't know that. We have a lot of
1521 natural gas and benzene. Like, these are easy base chemicals
1522 to get. So we are exporting these base chemicals to other
1523 countries so they can make the APIs, so they can send back
1524 those APIs to us to make the more advanced drugs, the final
1525 product, and then we complain about our supply chains.

1526 What is stopping us from cutting out that middleman? Is
1527 it a policy issue? Is it a market issue? What is happening
1528 there?

1529 *Mr. Sardella. It would be having economically viable

1530 domestic API manufacturers that can be the purchasers of
1531 those starter materials.

1532 *Mr. Crenshaw. Okay.

1533 *Mr. Sardella. That would be the key to its consumption
1534 and use here in the United States.

1535 *Mr. Crenshaw. Nobody just -- nobody has had that
1536 business idea?

1537 *Mr. Sardella. Well, the APIs, a majority of the
1538 generic ones, are not economically viable to produce in the
1539 United States. And so they've been offshored. And so that
1540 demand, that U.S. domestic demand --

1541 *Mr. Crenshaw. Why aren't they economically viable?
1542 What do they state as their reasons for not opening up shop?

1543 *Mr. Sardella. Yeah, they'll cite lower labor costs as
1544 one reason. They'll cite economies of scale, government
1545 incentives that these other countries have received to build
1546 their facilities. Even right now, India is subsidizing new
1547 facilities being built so that they wouldn't be reliant on
1548 China --

1549 *Mr. Crenshaw. Well, in a very short amount of time we
1550 did we did get a lot out of you, so I appreciate it, but I
1551 want to I want to move on, please, to Laura Bray.

1552 Thank you for being here with Mother's Day coming up,
1553 and the problem we have with especially cancer drugs for
1554 kids. So real quick, what roadblocks are currently in place

1555 at the FDA that really create the problem you are trying to
1556 solve? What would be your top three? Or one.

1557 *Ms. Bray. So, I mean, I think part of the problem here
1558 is this is a very, very large risk solution for any one
1559 member to take on, right? So there are a lot of barriers
1560 everywhere. There's not just barriers in one member, there
1561 is a lot of risk of any one member taking --

1562 *Mr. Crenshaw. I totally get that. But I -- you know,
1563 we have to focus on one thing, and I like to focus on the
1564 FDA. So, like, from your perspective, what would change at
1565 the -- what would be a better way the FDA would do business
1566 that would help what you are trying to accomplish?

1567 [No response.]

1568 *Mr. Crenshaw. It is okay if you are not -- if it is --

1569 *Ms. Bray. I -- you know, I think we all have -- every
1570 member needs to come to this table because it is so multi-
1571 faceted, and there are true and real reasons for every single
1572 policy that has been put in place. But we're -- keep putting
1573 policies on top of policies of broken marketplace. And so I
1574 think we all need to be at the table saying, here's the
1575 solution, here's what my part can do, here's what my part can
1576 do.

1577 And so to pick one thing from one member to do, as my
1578 colleague said, it's such a dynamic marketplace, it would
1579 quickly become extinct, right?

1580 *Mr. Crenshaw. Yes.

1581 *Ms. Bray. We need to all be at the table.

1582 *Mr. Crenshaw. We need solutions. You know, and --

1583 *Ms. Bray. So the --

1584 *Mr. Crenshaw. -- so, you know, one of the things I
1585 would point out --

1586 *Ms. Bray. So the solutions are we've got a six-point
1587 plan.

1588 It's first, align the incentives and motives. Everybody
1589 needs to be at the table, aligning those motives.

1590 It's employing prediction and forecasting, followed by
1591 being ready to supply the American people.

1592 Then we have to empower the collaboration of this multi-
1593 faceted supply chain.

1594 Patients need to be at the center of the solution, so
1595 we're ending shortages instead of mitigating them.

1596 And we need to establish an entrance and exit ramp so
1597 that the marketplace can evolve without patients getting left
1598 behind.

1599 That's the steps. And it's multi-layered.

1600 *Mr. Griffith. The gentleman --

1601 *Mr. Crenshaw. I appreciate it, I yield back.

1602 *Mr. Griffith. -- yields back, but we may very well
1603 have some what we call QFRs, questions after the hearing, and
1604 we will get an opportunity to answer at that time.

1605 I now recognize the gentlelady from Arizona, Mrs. Lesko,
1606 for her five minutes of questioning.

1607 *Mrs. Lesko. Thank you, Mr. Chair, and thank you for
1608 all of you being here. I apologize, I had to go to another
1609 committee hearing and come back here.

1610 Mr. Sardella, a key role of the FDA's mission to ensure
1611 drug safety, effectiveness, and ultimately, availability
1612 includes its foreign and domestic drug manufacturing facility
1613 inspections program. While the COVID-19 pandemic effectively
1614 halted nearly all overseas inspections for 2020 and part of
1615 2021, the number of inspections conducted both in the U.S.
1616 and overseas has been precipitously declining since 2016.

1617 In 2019, in its 2019 report of FDA inspection data, the
1618 GAO identified FDA's inability to oversee the global supply
1619 chain as a high-risk issue, and concluded with
1620 recommendations to the agency to increase the number of
1621 inspections of foreign drug establishments.

1622 Unfortunately, GAO's 2022 follow-up report on FDA's
1623 inspection capabilities did not conclude that the agency is
1624 in any better off -- is any better off in conducting timely
1625 and reliable foreign inspections. In fact, GAO found that
1626 the share of foreign facilities that have not been inspected
1627 in over five years has increased from 30 percent in 2020 to
1628 nearly 80 percent in 2022.

1629 Furthermore, GAO shared that the FDA inspected just 6

1630 percent of facilities overseas in 2022. Given that most U.S.
1631 drugs and APIs are manufactured in foreign facilities, this
1632 raises serious concerns with FDA's ability to ensure the
1633 quality and availability of human medical products
1634 manufactured overseas.

1635 So my question to you is, how critical are timely and
1636 effective inspections of both domestic and foreign
1637 manufacturing facilities for ensuring the security of our
1638 drug supply chain?

1639 *Mr. Sardella. They're absolutely essential for us
1640 ensuring the quality and the safety of the medicines that
1641 U.S. citizens consume.

1642 They're also extremely important in ensuring the
1643 stability of the market because, through those inspections,
1644 the ability to understand which manufacturers are complying,
1645 which manufacturers are delivering on quality manufacturing
1646 processes.

1647 And then the next element there is incentivizing that,
1648 rewarding those that don't have any warning letters for
1649 decades and decades, as opposed to those who, in fact, would.
1650 The ability to make that distinction on quality is to have a
1651 robust inspection, auditing process that allows us to make
1652 those distinctions, both to ensure the market is stable and
1653 to allow for safety of the medicines.

1654 *Mrs. Lesko. I agree, and I think most U.S. people

1655 would be surprised at the low number of inspections that are
1656 going on for the drugs that they are taking each and every
1657 day, and foreign drug makers.

1658 This past December the President authorized \$10 million
1659 for a pilot program to increase the number of foreign
1660 inspections at the FDA. However, the agency has cited
1661 challenges in the agency's ability to recruit and retain
1662 investigators as a major factor in the delay or dereliction
1663 of timely foreign inspections.

1664 Again, Mr. Sardella, how confident are you that this
1665 pilot program will close the gap in the share of overseas
1666 establishments that remain uninspected, while there remains a
1667 fundamental challenge within FDA to retain investigators and
1668 prioritize foreign inspections?

1669 *Mr. Sardella. Yeah, I feel FDA is no dissimilar to any
1670 organization in its struggles to develop talent, recruit
1671 talent to conduct its efforts. I feel they, like all
1672 organizations, will be challenged to be able to allow for the
1673 right workforce that enables them to go overseas as well as
1674 globally to do their inspections.

1675 I also feel that there's other opportunities to allow
1676 for understanding the quality of medicines that are more
1677 technical in nature versus only inspection in nature.

1678 Modernizing the monitoring systems. Fernando had talked
1679 about the new emerging advanced manufacturing technologies,

1680 control systems that monitor the productions every second as
1681 these medicines are produced. Those will allow inspection
1682 and observation without being at the facility, only through
1683 data transport in real time, every second. Those will be
1684 very transformational capabilities that we should look into
1685 and enable the FDA to utilize and leverage.

1686 *Mrs. Lesko. Thank you, and I yield back.

1687 *Mr. Griffith. I appreciate the gentlelady yielding
1688 back. I now recognize Dr. Ruiz of California for his five
1689 minutes of questioning.

1690 *Mr. Ruiz. Thank you, and thank you all for your
1691 testimony today.

1692 Drug shortages have serious impacts on quality and
1693 safety of patient care in this country. Before Congress I
1694 practiced as an emergency physician at Eisenhower Medical
1695 Center in California. I have seen firsthand the effects that
1696 drug shortages can have on patients, their providers, and
1697 their families by causing delayed care or second-choices
1698 treatments, especially when I want to intubate a patient and
1699 we don't have sSuccinylcholine, ~~and~~ I have to use another
1700 paralytic that is not used very often. Okay?

1701 Professor Bray, how have you seen shortages play out for
1702 patients seeking emergency care?

1703 *Ms. Bray. Thank you for asking. There is severe
1704 patient impact happening every day, and not just in missing,

1705 skipping, or changing doses. Ninety percent of oncologists
1706 state that drug shortages have led to patient harm up to
1707 death.

1708 We also can't forget the emotional trauma that you're
1709 putting on a family in a medical crisis. Patients deserve
1710 access to these medicines. The patient -- the physicians and
1711 nurses and care team who are trying to solve these crises and
1712 save them deserve easy and equal access to these medicines.

1713 *Mr. Ruiz. Thank you. Generic drugs are particularly
1714 vulnerable to shortages: 40 percent of drugs -- 40 percent
1715 of drugs -- have only one manufacturer, and most generic
1716 drugs have only one competitor per drug. Having limited
1717 sources for essential drugs or medical supplies is dangerous,
1718 particularly when an emergency strikes.

1719 So, for example, when Hurricane Maria devastated Puerto
1720 Rico in 2017, a major saline manufacturer was damaged. This
1721 caused a shortage for hospitals throughout the country of
1722 this very basic and critical lifesaving medical supply.

1723 Dr. Muzzio, can you -- how can the government support
1724 more diversified drug manufacturing that is less susceptible
1725 to supply chain disruptions?

1726 *Dr. Muzzio. Thank you for the question. We've been
1727 looking at this very carefully because, as my colleagues
1728 mentioned, there are a number of economic constraints. And
1729 we have also a 30-year history now of offshoring and losing

1730 manufacturing shares. So the reversal of that process is
1731 going to take sustained plan over many years with, you know,
1732 a lot of insight into not only how to make it profitable
1733 again, but also how to regain the know-how that we have lost,
1734 and how to build better systems that are more nimble, able to
1735 do more flexible manufacturing of a larger number of
1736 products. I'm very encouraged by some of the things that
1737 I've been hearing.

1738 One way the government can do it is by recognizing the
1739 following. There are reasons why the generic manufacturers
1740 are having trouble implementing the newer technologies,
1741 right? They cost a lot of money, they take a long time, and
1742 they don't have access in-house to people with the knowledge.
1743 So this is the perfect opportunity to create, again, centers
1744 of excellence, places where we have the knowledge, we have
1745 the people, and we have the equipment needed to implement the
1746 solutions, working closely with contract manufacturers that
1747 can then very rapidly pick up the required manufacturing
1748 tasks --

1749 *Mr. Ruiz. Thank you.

1750 *Dr. Muzzio. -- like 503(b)s or other manufacturers.
1751 It will take a network --

1752 *Mr. Ruiz. Thank you.

1753 *Dr. Muzzio. -- to solve the problem.

1754 *Mr. Ruiz. Center of Excellences [sic].

1755 Mr. Sardella, in its July 2021 Report on Supply Chain
1756 Resiliency, the White House proposed several recommendations
1757 to strengthen the generic market. The report recommended
1758 providing greater predictability in production costs,
1759 pricing, and volume sold to manufacturers, as well as
1760 increasing government and private sector flexibility in
1761 contracting and sourcing. How would enacting these
1762 recommendations help strengthen the generic market and help
1763 prevent future shortages?

1764 *Mr. Sardella. The ability to have certainty in your
1765 demand, from a business perspective, would drive economic
1766 investment and production of these.

1767 A common instrument of contracting in the United States
1768 government is what's called the IDIQ, Indefinite Demand,
1769 Indefinite Quantity. There's no ability to have certainty in
1770 your investments if you have an indefinite demand or an
1771 indefinite quantity. Solidifying those quantities, the years
1772 of demand, will allow for businesses to make investments and
1773 understand their return to their shareholders or to their
1774 owners.

1775 *Mr. Ruiz. Thank you.

1776 So drug shortages caused severe adverse health outcomes,
1777 and are an urgent problem. We need to support policy and
1778 resources that help address supply chain vulnerabilities so
1779 that shortages are less frequent and can be quickly

1780 addressed. Stat.

1781 I yield back.

1782 *Mr. Griffith. I thank the gentleman for yielding back.

1783 I now recognize Mr. Palmer of Alabama for his five minutes of
1784 questions.

1785 *Mr. Palmer. Thank you, Mr. Chairman. Thank you for
1786 holding the hearing, and for the witnesses' testimony today.

1787 Dr. Sardella, one of the things that I am concerned
1788 about is the FDA's role in the shortages. And in your
1789 testimony you mentioned the expensive and complex compliance
1790 challenges that so many drug companies face.

1791 In a previous Congress, we had had a number of hearings
1792 related to drug manufacturers and the massive increase in
1793 cost, and one of the things that we discovered was how
1794 regulations had forced a lot of companies either out of
1795 business or into being sold to other companies so that the
1796 company that bought them basically became the sole
1797 manufacturer. We saw that with drugs like insulin and
1798 EpiPens, things like that.

1799 I just want your thoughts, a little more clarity from
1800 what you said in your testimony about how this is impacting
1801 the cost and availability of these drugs.

1802 *Mr. Sardella. Yeah. So, as a manufacturer, if we
1803 start with the understanding that their profitability is
1804 already low, when they have a warning letter from the FDA

1805 there is therefore an expense that they have to incur to
1806 bring the facility up to standards to meet that. Sometimes
1807 the businesses cannot afford -- their return on their capital
1808 is so low already, less than five percent -- I mean, in
1809 business school we teach if you're anywhere below 20 percent
1810 you should be out of business.

1811 So then when you couple the request to have to comply,
1812 the facility will shutter. They will not make the
1813 investment. Only 4 percent in recent data, from numbers in
1814 the 2020s, only 4 percent of the FDA warning letters are now
1815 being addressed, a drastic drop, and that's a result of their
1816 inability economically to resolve them. So the facilities
1817 shut down. Akorn, a facility, just recently shut down.

1818 *Mr. Palmer. Right, I saw that.

1819 *Mr. Sardella. Nesher, as well.

1820 *Mr. Palmer. Yes. And then, when you combine that with
1821 the need to upgrade the manufacturing processes with newer
1822 equipment and things like that, and the stranded cost that's
1823 involved in that, plus for newer drugs the stranded costs
1824 involved in that, it really becomes an economic issue in many
1825 respects that we have to address.

1826 And again, listening to your testimony and reading your
1827 testimony, you make excellent points about the order of
1828 magnitude increases in drug production if we -- if the
1829 companies had the ability to upgrade their equipment.

1830 Would you think that incentives or tax credits, things
1831 like that, would be helpful to companies?

1832 *Mr. Sardella. Incentives, very much. One we are -- we
1833 have an example.

1834 The API Innovation Center is working with the State of
1835 Missouri. The State of Missouri is funding the de-risking of
1836 their adoption of new technology. So what we've done, as a
1837 non-profit, we've procured the new advanced manufacturing
1838 technology, developed it, and are placing it in existing
1839 Missouri manufacturing, manufacturers that have been there,
1840 some for 100 years, some new ones for 30 years, and some for
1841 just 10 years. And that now is being able to bring supply
1842 for cancer drugs like Lomustine and a suite of an additional
1843 six.

1844 In some respect, those incentives de-risk the adoption,
1845 very effective. The one element of the tax incentive is when
1846 you have an industry with such low profitability, tax
1847 incentives are less effective than creating certainty of
1848 demand by changing formularies.

1849 *Mr. Palmer. Well, you set me up perfectly for where I
1850 want to go with this.

1851 And this is a little different direction, Mr. Chairman,
1852 because in 1996 the Clinton Administration repealed section
1853 936 of the U.S. Internal Revenue Code, which provided tax
1854 incentives for drug manufacturers, and it had a devastating

1855 impact on the pharmaceutical industry in Puerto Rico. And
1856 what people don't realize is that, of U.S. territories,
1857 including the States, Puerto Rico even today still
1858 manufactures more pharmaceutical products than any state,
1859 including Indiana.

1860 But after the repeal of 936 we saw an exodus of drug
1861 manufacturers to other countries. In a number of respects I
1862 remember Horizon Pharma out of Chicago moved enough of their
1863 production and headquarters to Ireland because if they
1864 reached a certain percentage of foreign ownership they were
1865 not subject to U.S. taxes, and their tax went down to 12-and-
1866 a-half percent.

1867 So what do you think about reinstating section 936, and
1868 particularly in how it would impact our ability to produce
1869 the drugs that we need?

1870 *Mr. Sardella. Yeah, I don't know the regulation or
1871 legislation well enough to comment, but I do believe tax in
1872 that case would be a strong instrument to incentivize
1873 manufacturing in the U.S.

1874 *Mr. Palmer. Well, it was a huge industry in Puerto
1875 Rico. It was -- obviously, the problems were compounded with
1876 Hurricane Maria years later. I think it was eight years
1877 later, that.

1878 Mr. Chairman, I think that is something that we need to
1879 explore. We might not be the right committee for that since

1880 it is a tax issue, but I do think it is part of the solution.

1881 I yield back.

1882 *Mr. Griffith. I thank the gentleman for yielding back.

1883 Seeing no further members wishing to ask questions, I
1884 would like to thank each of our witnesses for being here
1885 today. Thank you all so much.

1886 In pursuance of committee rules, I remind members they
1887 have 10 business days to submit additional questions for the
1888 record -- that is the QFR, questions for the record -- and I
1889 ask that witnesses submit their responses within 10 business
1890 days upon receipt of those questions.

1891 Without objection, this committee is adjourned.

1892 [Whereupon, at 12:09 p.m., the subcommittee was
1893 adjourned.]