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4 ``FDA USER FEES 2012: HEARING ON ISSUES RELATED TO
5 ACCELERATED APPROVAL, MEDICAL GAS, ANTIBIOTIC DEVELOPMENT,
6 AND DOWNSTREAM PHARMACEUTICAL SUPPLY CHAIN''
7 THURSDAY, MARCH 8, 2012
8 House of Representatives,
9 Subcommittee on Health
10 Committee on Energy and Commerce
11 Washington, D.C.

12 The Subcommittee met, pursuant to call, at 10:15 a.m.,
13 in Room 2322 of the Rayburn House Office Building, Hon. Joe
14 Pitts [Chairman of the Subcommittee] presiding.

15 Members present: Representatives Pitts, Burgess,
16 Shimkus, Murphy, Gingrey, Latta, Lance, Cassidy, Pallone,
17 Dingell, Schakowsky and Waxman (ex officio).

18 Staff present: Andy Duberstein, Deputy Press Secretary;

19 Nancy Dunlap, Health Fellow; Paul Edattel, Professional Staff
20 Member, Health; Debbie Keller, Press Secretary; Ryan Long,
21 Chief Counsel, Health; Carly McWilliams, Legislative Clerk;
22 Chris Sarley, Policy Coordinator, Environment and Economy;
23 Brett Scott, Staff Assistant; Heidi Stirrup, Health Policy
24 Coordinator; Alli Corr, Democratic Policy Analyst; Eric
25 Flamm, FDA Detailee; Karen Lightfoot, Democratic
26 Communications Director, and Senior Policy Advisor; Karen
27 Nelson, Democratic Deputy Committee Staff Director for
28 Health; and Rachel Sher, Democratic Senior Counsel.

29 Mr. {Pitts.} This Subcommittee will come to order.

30 The Chair recognizes himself for 5 minutes for an
31 opening statement.

32 Today we are taking a more in-depth look at several
33 issues related to the FDA user fee programs. First, we will
34 hear about FDA's Accelerated Approval process for certain new
35 drugs that treat serious or life-threatening illnesses and
36 provide a greater therapeutic benefit over existing drugs and
37 therapies. Accelerated Approval has been successful in
38 speeding cancer and HIV/AIDS drugs to market, and I am
39 particularly interested in how the process can be better
40 utilized for rare diseases.

41 Earlier this week, Representative Stearns, along with
42 Representatives Bilbray and Towns, introduced the Faster
43 Access to Specialized Treatments, the FAST Act, to help
44 expedite new drugs through the approval process.

45 We will also hear about FDA's regulation of medical gas
46 and the need for targeted regulations for these substances,
47 due to their differences from most drugs.

48 Representative Lance has introduced H.R. 2227, the
49 Medical Gas Safety Act, which would reform the current FDA
50 regulation of medical gases to create an appropriate process
51 for medical gases to be approved. It would also remove the

52 current regulatory uncertainty for medical gases by
53 establishing targeted regulations that take into account the
54 unique characteristics of medical gases. Representative
55 Lance's bill is bipartisan. It is cosponsored by members of
56 the Full Committee from both sides of the aisle.

57 Next, we will address the lack of new antibiotics in the
58 pipeline and how Congress and FDA can act to incentivize new
59 antibiotic development.

60 Dr. Gingrey's Generating Antibiotic Incentives Now Act,
61 or the GAIN Act, H.R. 2182, targets this problem. This bill
62 would extend the exclusivity period for new prescription
63 antibiotics and add an additional 6-month period of
64 exclusivity for a manufacturer if the new antibiotic
65 identifies a companion diagnostic test. The GAIN Act also
66 has bipartisan support, including eight Democrats and 15
67 Republicans from the Full Committee.

68 Finally, the Subcommittee will hear about the dangers
69 and weaknesses to the current pharmaceutical supply chain
70 from manufacturers, to distributors, to pharmacies, and how
71 best to ensure that counterfeit, adulterated or stolen drugs
72 do not end up in the hands of patients.

73 Representative Bilbray and Representative Matheson are
74 currently working in this area, and Dr. Cassidy's Online
75 Pharmacy Safety Act, H.R. 4095, aims to educate the public

76 about which Internet pharmacies are known to be safe and
77 legitimate.

78 We have three panels today. I would like to thank all
79 of our witnesses for being here. I look forward to their
80 testimony.

81 [The prepared statement of Mr. Pitts follows:]

82 ***** COMMITTEE INSERT *****

|
83 Mr. {Pitts.} So at this time I recognize the ranking
84 member of the Subcommittee on Health, Mr. Pallone, for 1
85 minute--oh, 5 minutes. I am sorry.

86 Mr. {Pallone.} Thank you, Chairman Pitts.

87 Today we are holding another hearing to examine
88 important FDA-related issues that could be considered as a
89 part of the user fee agreements, or the UFA legislation.
90 These include changes to the current expedited approval
91 process for new drugs, the regulation of medical gases,
92 antibiotic drug development, and the downstream
93 pharmaceutical supply chain. It is my hope that our
94 witnesses that will help the Subcommittee examine the ways in
95 which these issues can be or should be addressed in our
96 upcoming legislation.

97 Accelerated Approval is one of the processes by which
98 the FDA approves certain New Drug Applications that offer
99 meaningful therapeutic benefit over existing treatments for
100 serious or life-threatening diseases. This process has been
101 responsible for the great strides in medicine to treat HIV
102 and cancer, and has provided patients with speedier access to
103 important new medicines.

104 According to the FDA, over 80 new products have been
105 approved under Accelerated Approval since the program was

106 established including 29 drugs to treat cancer, 32 to treat
107 HIV, and 20 to treat various other conditions. There are
108 also two other programs that help expedite the approval of
109 certain promising investigational drugs known as Fast Track
110 and Priority Review.

111 Some have stated the accelerated approvals may be
112 working for certain conditions but it had limited success in
113 developing medicines to treat other rare diseases. As such,
114 we will examine different proposals today that would clarify
115 and improve some of FDA's authorities. While I am open to
116 such proposals, it is important to note that any changes we
117 make must not lower the safety of effectiveness standards by
118 which FDA approves new medicines.

119 Today we will also discuss the regulation of medical
120 gases. Medical gases are among some of the most widely
121 prescribed drugs and have been in use since before the
122 enactment of the Federal Food, Drug and Cosmetic Act in 1938.
123 Many of these, for example, oxygen, are often used with other
124 medical products such as a device. As I understand it, most
125 of these core gases have been marketed for many years without
126 an approved New Drug Application. According to the industry,
127 medical gases are different than other traditional drugs and
128 should be treated as such. Therefore, they have proposed a
129 new regulatory system for dealing with medical gases that

130 would cover things like good manufacturing practices,
131 labeling, distribution, registration, listing and product
132 tracking requirements. I believe there is a great value to
133 this conversation so that members can understand the issues
134 involved. However, I wonder whether an entirely new
135 regulatory system is the answer.

136 Development of antibiotic drugs is a critical public
137 health issue. As Chairman of this Subcommittee last
138 Congress, we held a hearing on the increasing of antibiotic
139 resistance and its threat to public health. Unfortunately,
140 the Nation's ability to counter this threat could be limited
141 because of the lack of antibiotics being developed.
142 Antibiotics were among the most impactful medical innovations
143 of the 20th century. A routine treatment to combat bacterial
144 infections, they are one of the main contributors in the
145 decline of infectious diseases. But bacteria are living
146 organisms, and as such, as they can and will mutate with time
147 to be able to resist the drugs that have been developed to
148 combat them. We now find ourselves in a situation where our
149 triumph over infectious disease is in jeopardy. More and
150 more bacteria are proving to be resistant to the antibiotics
151 currently on the market.

152 I am eager to hear from FDA and witnesses today about
153 the proposed legislation that would create financial

154 incentives for companies to develop more antibiotics drugs
155 and spur advancement of these products, particularly whether
156 that approach will help solve the issues our system faces but
157 also what would be the shortfalls of that approach. For
158 example, how do we limit the uses of these new antibiotics so
159 that we don't see the same type of resistance we are seeing
160 now with old medicines?

161 And one of the more complicated but critical issues is
162 the downstream safety of the U.S. drug supply chain. In
163 order to ensure that we do not have counterfeit stolen drugs
164 entering the supply chain and harming patients, this
165 Committee has heard for a long time about the call for
166 greater oversight of the drug supply chain. The need to set
167 up a system that would track and trace the movement of drugs
168 once they enter the marketplace has been the common theme.
169 Just last month, we saw a counterfeit version of the cancer
170 drug Avastin found in the United States. The counterfeit did
171 not contain the medicine's active ingredient, proving to be
172 ineffective, and this is dangerous and in some cases life
173 threatening.

174 I think we can all agree that Congress needs to get
175 serious about securing the supply chain and that a national
176 system is necessary to prevent these drugs from reaching
177 patients. Some States are beginning to pass their own laws.

178 California, for example, has a law that will go into effect
179 in 2015.

180 I am interested to hear about the different approaches
181 being proposed, specifically, the positives, negatives and
182 feasibility of each. However, as we contemplate moving
183 forward, we must not rush to legislation. These are really
184 complicated and dense processes, and if we are looking at
185 setting a national standard, it is critical that it be a
186 strong, robust standard that is most beneficial to the
187 consumer.

188 So just let me close, Mr. Chairman, by thanking
189 everyone. I look forward to our panels today. Your
190 testimony and insight will remain useful in the months ahead.
191 Thank you.

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

193 ***** COMMITTEE INSERT *****

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194 Mr. {Pitts.} The Chair thanks the gentleman and yields
195 5 minutes to Dr. Gingrey from Georgia.

196 Dr. {Gingrey.} Mr. Chairman, thank you for yielding to
197 me. I am going to confine my remarks to the shortages of
198 antibiotics, and of course, that is the bill that the
199 Chairman referred to.

200 Mr. Chairman, again, I appreciate you holding this
201 hearing and the three panels of witnesses. The need for new
202 antibiotics is well established and beyond question.
203 Antibiotic resistance is a threat to global public health as
204 well as United States national security. Drug-resistant
205 bacteria like those featured in the movie Contagion threaten
206 American patients and troops in much the same way. Whether
207 transmitted from person to person or contracted from
208 biological weapons, the overall threat is the same. As a
209 physician, I understand how important it is that medical
210 providers use antibiotics judiciously, but no matter how
211 judiciously we use the current supply of drugs we have or
212 will have in the coming years, we need more. To quote the
213 testimony of Dr. Janet Woodcock of the FDA, the United States
214 is, and I quote her, ``at a critical juncture with regards to
215 drug development. We are in urgent need of new therapeutic
216 options to treat the resistant bacteria that we currently

217 face and we will need new therapeutic options in the
218 future.' ' This critical juncture requires immediate action
219 if we are to prevent a public health disaster from hitting
220 our shores in the next decade.

221 I want to thank Dr. Woodcock for being here today, and I
222 personally thank Dr. Margaret Hamburg for her leadership on
223 this important issue as the Director of the FDA.

224 To Dr. Woodcock's testimony, antibiotic resistance
225 cannot be solely solved by the development of new drugs but
226 it also be solved without them. In fact, we can answer every
227 other problem with regard to antibiotic resistance, but if we
228 fail to address the lack of incentives for drug companies and
229 research and development experts and new antibiotic drug
230 development, let me say this emphatically, we will lose this
231 fight.

232 As a group of bipartisan Members of Congress, my
233 coauthors and I have forwarded H.R. 2182, the Generating
234 Antibiotic Incentives Now, or GAIN Act, to encourage new drug
235 development. The legislation is product of years of
236 thoughtful consideration, and it strikes a balance between
237 the need for drug companies' incentives and the needs and
238 requirements of good public health policy. That balance is
239 attested to in the nearly 50 organizations that currently
240 support our effort. Their testimonials, which I will be

241 entering into the record shortly, underscore the potential
242 that the GAIN Act holds to ensure patients will continue to
243 have the lifesaving medications that they need. Among those
244 we count public health leaders like the Pew Charitable Trust,
245 patient organizations including Kids v. Cancer, medical
246 providers like St. Jude's Children's Hospital in Tennessee,
247 and organizations representing 2.5 million veterans and
248 wounded warriors, among others.

249 The legislation as drafted focuses incentives on a list
250 of unmet needs and life-threatening pathogens from which
251 infections arise. These pathogens were identified by the
252 Infectious Disease Society of America as looming threats to
253 public health because little or no treatment currently exists
254 to combat the infections that they cause. The legislation
255 also includes, and this is most important, Mr. Chairman. The
256 legislation also includes the ability for the FDA to update
257 this list to meet new and emerging threats so that we
258 continue to encourage the therapeutic options that FDA will
259 testify are needed.

260 To be clear, drug researchers and manufacturers in early
261 development focus their efforts on identifying products that
262 work against as an identified pathogen as an example
263 including their ability to kill a specific or variety of
264 deadly bacteria. Only after a compound is identified as

265 working against a specific pathogen do the societies then
266 focus on infection sites in the body in order to measure the
267 efficacy of that potential drug.

268 Some have questioned the need to be so specific with
269 regards to the types of killer bacteria that we are focusing
270 on in the GAIN Act. To that issue, let me read to you a
271 sentence from one of the many support letters we have
272 received. ``The GAIN Act definition ensures that unmet
273 medical needs get the attention they deserve in an industry
274 where other therapeutic areas often hold greater commercial
275 promise.'' However, the incentives for development decrease
276 dramatically if we are unable to know with a high degree of
277 certainty that a product would qualify for the incentives in
278 the GAIN Act in early phase development. In short, our
279 ability to demonstrate to companies the incentives in the
280 GAIN Act as early in the drug development process as possible
281 is the foundation upon which our efforts rest.

282 Mr. Chairman, I have gone over time. I will go ahead
283 and submit the rest of my comments for the record, and I look
284 forward to the testimony of the three panels of witnesses.

285 [The prepared statement of Dr. Gingrey follows:]

286 ***** COMMITTEE INSERT *****

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287 Mr. {Pitts.} The Chair thanks the gentleman and
288 recognizes the gentlelady from Illinois, Ms. Schakowsky, for
289 5 minutes for an opening statement.

290 Ms. {Schakowsky.} I really have just about a minute to
291 say this, but I wanted to put it on the record.

292 I wanted to say that I strongly support the development
293 of drugs to enhance therapeutic options for patients with
294 rare diseases. There is no question that both patients and
295 their families must cope with unusual and unique issues when
296 they have a rare disease. I can appreciate the desire on the
297 part of patient groups and their families as well as industry
298 to create an accelerated approval for drugs to treat rare
299 diseases. I both understand and support that goal, but I
300 also want to ensure that in seeking to accelerate drug
301 approval that we do not expose patients to unnecessary and
302 unacceptable risks. While I am committed to efforts to
303 accelerate the development of rare-disease drugs, I want to
304 make sure we maximize drug safety efforts and that we do not
305 encourage expedited FDA approval if doing so would jeopardize
306 that goal.

307 So I am looking forward to hearing you, Dr. Woodcock, on
308 how best to address this issue, and I will yield back my
309 time.

310 [The prepared statement of Ms. Schakowsky follows:]

311 ***** COMMITTEE INSERT *****

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312 Mr. {Waxman.} Will the gentlelady yield to me?

313 Ms. {Schakowsky.} Of course.

314 Mr. {Waxman.} Thank you very much for yielding to me.

315 We have all the Subcommittees scheduled at the same time, and

316 I was trying to get up as quickly as possible, and I am

317 pleased to have this opportunity to make an opening statement

318 because we are going to be looking at some important

319 proposals today, and we haven't yet seen the legislative text

320 but the proposed list of user fee add-ons is long, and as

321 each day passes I am increasingly concerned about whether we

322 will have time to get to a bipartisan agreement on such an

323 ambitious package of bills.

324 The policies we will be discussing today involve complex

325 public health issues. For us to do a responsible job on

326 these proposals, we need time and we need bipartisan

327 agreement. We should not rush this work. We should

328 prioritize getting it right, not just getting it done, and if

329 we are able to come to a bipartisan agreement in the time

330 available, it makes sense to move them along with the other

331 bills. Otherwise, I hope we can all agree it will be better

332 to wait so that we do not jeopardize the passage of the

333 underlying user fee bills.

334 Let me turn to some specific proposals. We have learned

335 in a series of hearings this Subcommittee held in 2010 that
336 the problem of antibiotic resistance is a dire public health
337 threat and our arsenal of effective antibiotics is running
338 dangerously low. So clearly we need to look at ways to
339 incentivize the development of new antibiotics. The GAIN Act
340 is a good first step at achieving this goal. However, we
341 should ensure that the bill is narrowly tailored to drugs
342 that treat dangerous infections for which we don't have
343 adequate treatments. Otherwise, we risk worsening the
344 problem of resistance. We also need to ensure that the bill
345 mandates that FDA and other agencies involved take steps to
346 ensure that the efficacy of these newly developed antibiotics
347 is preserved once they are on the market.

348 We will also hear today about FDA's Accelerated Approval
349 system. We can all agree that we want the most effective,
350 innovative medicines to be available at the earliest possible
351 time. So if there are improvements that could be made in the
352 way FDA reviews these medicines, we should consider them.
353 But I am concerned that some of these proposals are driven by
354 unsubstantiated claims that FDA has become too demanding of
355 drug companies, requiring too much data, and thereby
356 allegedly keeping drugs from patients and driving innovation
357 and jobs abroad.

358 As we have heard at previous hearings, there is

359 apparently no reliable data to back up these claims. To the
360 contrary, as the testimony of Friends of Cancer Research and
361 FDA has shown, FDA actually approves novel drugs faster than
362 its counterparts in Europe or anywhere else in the world. In
363 the past, the National Organization for Rare Diseases has
364 also testified about its study showing that FDA is quite
365 flexible in its requirements for approving orphan drugs.

366 We want drugs approved as quickly as possible but we
367 want the FDA to do its job, and it is a difficult one. We
368 want to give you the tools and we want you to have the
369 flexibility to do that job as quickly as possible while
370 meeting the requirements of the law.

371 I am open to considering whether legislation can help
372 FDA work with companies to get more breakthrough medicines to
373 patients more quickly. However, we need to ensure that any
374 adjustments don't alter FDA's approval standards.

375 Today's hearing will also examine efforts to improve the
376 integrity of our drug supply chain. This is an important
377 issue. There is a regulatory void at the federal level
378 because the United States does not currently have laws
379 requiring the tracking and tracing of pharmaceuticals.
380 Consequently, some States have stepped in and enacted their
381 own laws, and we are going to hear today about California,
382 which currently has a law that would mandate one of the most

383 robust pedigree systems in the country. Many have suggested
384 that there is a need for a single federal system that would
385 preempt these State laws. I believe having a system at the
386 federal level could make sense if done correctly but I would
387 have grave concerns about preempting a strong State law,
388 especially in California.

389 Thank you, Mr. Chairman.

390 [The prepared statement of Mr. Waxman follows:]

391 ***** COMMITTEE INSERT *****

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392 Mr. {Pitts.} The Chair thanks the gentleman. That
393 concludes our opening statements.

394 Our first panel will have just one witness, Dr. Janet
395 Woodcock, Director of the Center for Drug Evaluation and
396 Research at the FDA. We are happy to have you with us today,
397 Dr. Woodcock. You are recognized for 5 minutes for your
398 opening statement.

|
399 ^STATEMENT OF JANET WOODCOCK, M.D., DIRECTOR, CENTER FOR DRUG
400 EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

401 } Dr. {Woodcock.} Thank you, Mr. Chairman, and good
402 morning.

403 Mr. Chairman and members of the Subcommittee, I am Janet
404 Woodcock. I am Director of the Center for Drug Evaluation
405 and Research at the FDA, and I really appreciate the
406 opportunity to testify on these important issues that are
407 before the panel.

408 The mission of the drug program at FDA is to make sure
409 that medicines are of high quality, safe, effective and
410 available. The quality of the United States drug supply has
411 long been taken for granted by, I think, the health care
412 community but the drug supply can be threatened by poor
413 manufacturing practices, by economically motivated
414 substitute, as we saw in the heparin problem, and by
415 counterfeit drugs, all problems that we have observed in the
416 last several years and that are increasingly. The FDA must
417 continue to be vigilant to maintain the quality of drugs in
418 this country, and we must have the property tools to maintain
419 a high-quality medicine supply.

420 At the same time, health professionals and patients

421 continue to rely on FDA standards for safety and efficacy so
422 that the benefits and risks of medicines are studied and that
423 they are described in the drug label at the time of approval
424 and that we remain vigilant for unexpected side effects once
425 the drugs are marketed. In considering new steps to enhance
426 FDA regulations, we should not diminish the historic
427 protective standards for safety and efficacy that have served
428 our patients so well.

429 And finally, drugs should be available. The current
430 drug shortage crisis has highlighted how important a reliable
431 drug supply really is. The drug user fee proposals FDA has
432 delivered to Congress are targeted to strengthen the
433 availability of drugs for Americans.

434 The prescription drug user fee program that Congress has
435 authorized four times already has really assured that the
436 United States is the leader in developing and introducing new
437 important drugs to the public so that Americans have access
438 to that cutting-edge science and to drugs that will treat
439 life-threatening conditions.

440 The new generic drug user fee proposal is intended to
441 strengthen our generic drug review program that provides
442 access to affordable, high-quality drugs and also addresses
443 FDA oversight of drug quality around the world. And FDA's
444 biosimilars program is intended to provide access to more

445 affordable biologic drugs.

446 While these FDA programs are strong and successful, it
447 is clear there are continuing challenges in drug regulation,
448 many of which will be discussed at this hearing. I look
449 forward to working with you to find solutions that will
450 benefit our public that we serve mutually. Thank you.

451 [The prepared statement of Dr. Woodcock follows:]

452 ***** INSERT 1 *****

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453 Mr. {Pitts.} The Chair thanks the gentlelady, and I
454 will begin the questioning and recognize myself 5 minutes for
455 that purpose.

456 Dr. Woodcock, what can we do to expand Accelerated
457 Approval to further help patients including those with rare
458 diseases?

459 Dr. {Woodcock.} First, let me say that the Accelerated
460 Approval program has been very successful and has brought
461 access, early access to lifesaving drugs to patients with
462 HIV, patients with cancer, and to many patients with orphan
463 and rare diseases. However, we believe more could be done as
464 far as clarity of use of this proposal. We have found that
465 both in the industry, in the academic community and even
466 sometimes within the FDA itself there is confusion about the
467 use of Accelerated Approval. So we believe that additional
468 clarity in the use of this would be very beneficial. We also
469 plan to issue guidance that will also clarify the use of
470 Accelerated Approval and will explain our evidence standards
471 more clear.

472 Mr. {Pitts.} Thank you. Despite the success of
473 Accelerated Approval for cancer drugs, I have talked with
474 patients and innovators and investors, and they indicate that
475 some in FDA intend to limit the use of the Accelerated

476 Approval pathway for cancer drugs. This is very concerning
477 to me. As you know, if FDA goes down this path, patient
478 access to important new cancer drugs will be decreased.
479 Investment in new cancer therapies will continue to drop.
480 That would be unacceptable. Rather than limiting the use of
481 Accelerated Approval in cancer, shouldn't we be looking for
482 ways to expand it? Would you please comment on this?

483 Dr. {Woodcock.} Certainly, and I believe we are looking
484 for ways to expand the use of Accelerated Approval in cancer.
485 For example, we will soon issue a draft guidance on the use
486 of a new surrogate called pathologic complete response, which
487 would be used in high-risk breast cancer as a mechanism to do
488 Accelerated Approval. So I believe that we have been
489 successful in cancer, and in fact, over the last year we have
490 approved cancer drugs using Accelerated Approval, sometimes
491 using what are called historical controls, which means that
492 the drug is treated in patients and their response is
493 compared to what would have happened if they had had standard
494 therapy.

495 So we are not really backing away from that. However,
496 we have had discussions about the magnitude of the response.
497 What does that mean? That means that if you see in a
498 historically controlled trial, maybe you see a 5 percent
499 response rate or a 10 percent response rate, you really don't

500 know the amount of benefit to the patients, and so that is
501 the level of disagreement that is going on. It is very
502 technical and it is within the oncology community. But
503 please be assured, we are not backing off with Accelerated
504 Approval for cancer. In fact, we would like to find more
505 endpoints we could use for Accelerated Approval.

506 Mr. {Pitts.} Okay. Thank you. We all agree that it is
507 important to prevent counterfeit drugs from reaching our
508 Nation's patients. What steps is the agency taking to
509 prevent this?

510 Dr. {Woodcock.} We have for a long time had extensive
511 effort on counterfeits. We are working with our foreign
512 counterparts around the globe to try and identify gaps in the
513 supply chain and inspection coverage and so forth, have early
514 notification between all regulatory authorities when
515 counterfeits are discovered. Our Office of Criminal
516 Investigations also handles a lot of investigations into
517 counterfeit drugs. However, we do believe that additional
518 authorities are necessary for us to be able to stem this
519 tide.

520 Mr. {Pitts.} All right. Now, you mention in your
521 testimony that a system to track and trace prescription drugs
522 through the supply chain would help ensure the integrity of
523 our drug supply. Do you believe the most effective track-

524 and-trace system would involve a uniform standard throughout
525 the country, and what are the elements of a cost-effective
526 system?

527 Dr. {Woodcock.} Because drugs are shipped all around
528 the country and across State lines, we believe uniform
529 standards are important and we are developing elements of
530 standards that we would publish suggested standards that
531 could be used. The most important features of track and
532 trace are the following. Number one, that you can identify
533 the product as it moves through the supply chain and
534 particularly in real time so that patients aren't being
535 exposed to counterfeits before you discover that they have
536 entered the system, so that is one point. Another point is
537 that modern drug manufacturing makes lots of drugs, in other
538 words, batches, but it isn't like you might think of, you
539 know, what you might compound or whatever. A batch may be a
540 million pills or tablets or more. And so instead of a batch
541 moving through the supply chain on a pallet, okay, a batch
542 would be a lot, would be broken up and go all over the
543 country in different--so a lot--tracking to the lot level is
544 not that helpful, would not be that helpful if we wanted
545 real-time detection, say, drugs that have been stolen from
546 that lot and then diverted and reentering the supply chain or
547 a copy had made of that lot number and then put back into the

548 supply chain at some point. We would not be able to detect
549 that unless we are tracking that lot as it goes along by
550 unit, not by whole lot.

551 So we recognize that there are tradeoffs between cost of
552 these systems and the benefits that they would provide, but
553 if we want out patients not to get counterfeit drugs, which
554 has happened even recently--they have been administered to
555 cancer patients--we are going to need a system that tracks to
556 the unit level and identifies the movement of the drugs in
557 real time.

558 Mr. {Pitts.} The Chair thanks the gentlelady.

559 The Chair recognizes the Ranking Member, Mr. Pallone,
560 for 5 minutes for questions.

561 Mr. {Pallone.} Thank you, Mr. Chairman.

562 Dr. Woodcock, I wanted to ask you a question about the
563 GAIN Act and then a couple of questions about medical gases.
564 I think we can all agree that we need to find ways to
565 encourage and facilitate development and approval of
566 important new antibiotics. The GAIN Act is one attempt to
567 achieve that goal. However, I know FDA and others have had
568 concerns about the current definition of which drugs would be
569 eligible for the incentive. I believe that IDSA and others
570 have suggested that GAIN should be limited to new antibiotic
571 for treating serious infections for which there is an unmet

572 medical need. I think the focus on treating serious
573 infections has not been controversial but I wanted to know
574 your views on the other two components, that the antibiotics
575 should be a new chemical or molecular entity and that it
576 should meet an unmet medical need, if you could just tell me
577 your views on that, and then I am going to get to the medical
578 gases. Go ahead.

579 Dr. {Woodcock.} A new chemical entity is simply an
580 attempt to make sure that this incentive applies to new drugs
581 that are being developed and not to re-studying older drugs.
582 So I think that particular provision is really up to Congress
583 as far as how that--but what we really need is new molecular
584 entities or new chemical entities that have new mechanisms of
585 action that will be put against these threats.

586 Now, the second question?

587 Mr. {Pallone.} The other one is that it should meet an
588 unmet medical need.

589 Dr. {Woodcock.} By definition, we would want it to meet
590 an unmet medical need. People who are facing infections
591 where there is no current satisfactory treatment would meet
592 the definition of an unmet medical need.

593 Mr. {Pallone.} Okay. Let me get to the gases, and that
594 is the H.R. 2227. From what I understand, medical gases are
595 regulated by the FDA as drugs. However, because they differ

596 in some ways from most other drugs, FDA has tried to adjust
597 its requirements to fit them and has taken a risk-based
598 approach to enforcement. However, the Compressed Gas
599 Association believes that medical gases are different enough
600 from other drugs that they warrant a new set of regulations.
601 So my questions relate to that. Can you explain how FDA
602 regulates gases now, in particular, the commonalities and
603 differences between your regulation of gases and your
604 regulation of other drugs and the safety profile of gases?
605 And then, you know, as I said, this bill provides for a
606 streamlined process that would deem certain gases approved if
607 the applicant submits a certification that the gas is among
608 certain designated gases that are considered to be well
609 understood and safe. So what is your view on that? And then
610 last, what do you think about establishing a separate
611 regulatory system for gases that covers things like good
612 manufacturing practices, labeling, distribution? Do you
613 think we should have a separate system? I am throwing these
614 all in because we only have 2 minutes, so try to cover it if
615 you can.

616 Dr. {Woodcock.} Number one, for designation, certain
617 uses of medical gases have been used so long in medicine that
618 they actually didn't fall under the FDA review process that
619 was instituted when the Food, Drug and Cosmetic Act was

620 passed and so technically those uses are unapproved because
621 no applications have been submitted, and so we feel for those
622 traditional medical gases for traditional uses that a
623 designation process would be useful.

624 As far as a whole new regulatory regime for medical
625 gases on manufacturing, we believe that might not be
626 necessary. We believe we could work with the manufacturers
627 and actually I would commit to working with the manufacturers
628 to develop an appropriate and flexible interpretation of our
629 regulations and their application to medical gases for
630 traditional uses that I think would be mutually satisfactory.

631 Mr. {Pallone.} Obviously, one of the things that they
632 have said to me is if there was some way that you could meet
633 with the Compressed Gas Association to see if there is some
634 way to accommodate their needs and eliminate the need for
635 legislative action. You seem to be suggesting that. Is that
636 fine?

637 Dr. {Woodcock.} I would be happy to meet with them
638 personally.

639 Mr. {Pallone.} All right. Let me just ask one thing.
640 Did you respond to the question about the streamlined
641 approval process?

642 Dr. {Woodcock.} What I said was that some designation
643 process would probably be most satisfactory. These oxygen--

644 Mr. {Pallone.} These are streamlined for the ones that
645 have been around for a while?

646 Dr. {Woodcock.} Exactly. For all medical gases, we
647 could conceive of high-tech new uses that actually should be
648 studied, but traditionally, giving someone oxygen because
649 they have low blood oxygen, it is really not that
650 controversial.

651 Mr. {Pallone.} So the streamlined would be for the one
652 that have been around?

653 Dr. {Woodcock.} Yes.

654 Mr. {Pallone.} All right. Thank you very much.

655 Thank you, Mr. Chairman.

656 Mr. {Pitts.} The Chair thanks the gentleman and
657 recognizes the gentleman from Texas, Vice Chairman of the
658 Subcommittee, Dr. Burgess, for 5 minutes for questions.

659 Dr. {Burgess.} I thank the Chairman for the
660 recognition.

661 Dr. Woodcock, always good to see you. The last time we
662 were together, we talked a little bit about drug shortages,
663 and in fact, in October, the President put out an executive
664 order, and you were kind enough to receive myself and my
665 staff out at the FDA about a week or so later. We talked
666 about this. This was early November. Then you came to the
667 Committee a few weeks ago and we talked extensively about a

668 particular shortage called Doxil, or doxorubicin. I think
669 sterile methotrexate came up in the discussions as well, and
670 of course, I was very glad to see then shortly thereafter we
671 found a way to circumvent some of the problems with Doxil.
672 There was difficulty in establishing bioequivalency because
673 in order to do the studies to establish bioequivalency meant
674 that the drug had to be taken away from patients who were
675 dependent upon it for therapy, those patients suffering from
676 ovarian cancer who really couldn't afford a lapse in therapy
677 and the FDA didn't really provide a way out of that. So now
678 you have, and I am grateful for that, and that involved
679 actually I guess the use of some of the same compound or
680 similar compound that was available overseas. I am not quite
681 sure how the methotrexate got resolved but I am glad to see
682 that it did.

683 But you provided us with a really extensive list of
684 drugs that were in shortage, and of course, some of them were
685 sterile injectables, the cancer drugs which are clearly
686 pretty important stuff. So I guess my question to you is--
687 and you have also testified, if I remember correctly, that
688 this is a complex problem. It is not the same thing causing
689 the shortages across the board. So we look at it and say we
690 are going to draft legislation, we are going to fix this
691 problem, we are going to stop it, but it is difficult to do

692 because the problems are so complex and yet your agency had
693 the ability to reach out somewhere and solve these two very
694 serious problems for patients across the country. So I guess
695 my question to you is, what can you do as a regulatory agency
696 to go down that list? Do you have a task force that is
697 trying to identify the most critical needs, the most critical
698 shortages, get those things, whatever we need to do to get
699 them through the regulatory hoops in a safe and efficient
700 manner and get them delivered to patients of this country?

701 Dr. {Woodcock.} Yes. We certainly have a shortage team
702 who is really working overtime, and we have augmented that
703 team with additional people. We have looked at every one of
704 the drugs on the shortage list, and if we have had a generic
705 applicant that is pending, we jump the queue. We expedite
706 the review of that application and try to get that approved
707 as soon as possible so that additional sources could be on
708 the market.

709 In addition, even when a shortage is impending, we think
710 there is an impending shortage, we will start looking at
711 alternative supply? Can other manufacturers in the United
712 States ramp up their production? We contact them, we talk to
713 them. Are there X U.S. manufacturers with acceptable
714 facilities and product that could increase their production
715 and thus cover the U.S. drug supply as well? So we do all

716 this. Despite this, we are still experiencing shortages,
717 primarily because a lot of facilities in the United States
718 making sterile injectables have been experiencing
719 manufacturing problems.

720 Dr. {Burgess.} Yes, let me ask you about that because
721 some of the manufacturing problems actually relate to the
722 company's ability to get a return on investment or even break
723 even in the process, and they say look, it is not worth it to
724 us to revamp our manufacturing line for this product. Is
725 there anything you can do at the FDA as far as providing the
726 incentives so that company will stay in the business because
727 then they don't have to go through the whole reapplication
728 and all of the approval process again?

729 Dr. {Woodcock.} We have very little to do with the
730 economic side of drug production and reimbursement. We focus
731 on making sure that the facilities and processes are in place
732 to make a reliable drug product. I don't think that cutting
733 corners in manufacturing sterile drug products is the answer
734 because the problems that these facilities have experienced
735 are significant. They include endotoxin contamination,
736 bacterial contamination and particulates in injectables, and
737 these types of problems do not result in useable sterile
738 injectables.

739 Dr. {Burgess.} I need to interrupt you because time is

740 running short. I have some things I am going to submit in
741 writing about conflicts of interest, stuff we have covered
742 before to some degree and I have got some new questions. But
743 can you update us on--the New England Journal of Medicine had
744 an article probably back in 2010 or maybe 2009 on the curious
745 case of colchicine, and colchicine is a drug that has been
746 around for 3,000 years to treat gout and familial
747 Mediterranean fever, as I recall, and because of some things
748 that happened at the FDA, suddenly this drug spiked in price
749 and was becoming more difficult for patients to receive.

750 Dr. {Woodcock.} That situation still continues. The
751 FDA has something called an Unapproved Drugs Initiative, and
752 we are trying to get drugs that are not approved by--there is
753 no approved version by the FDA into the fold of proper drugs
754 in the United States, and sometimes these efforts do have
755 unintended consequences and I certainly I have heard--I am a
756 rheumatologist. I certainly have had from a large amount of
757 the community and patients about this particular issue of
758 affordability of this medicine. We are trying to make the
759 balance between availability and affordability and the
760 ability to assure a reliable supply of a drug. When drugs
761 are not FDA approved and they are simply on the market, there
762 are many opportunities for problems. So we try to walk this
763 path, but believe me, we are very aware of the problems that

764 have been created for patients.

765 Dr. {Burgess.} Thanks, Mr. Chairman. I will yield
766 back.

767 Mr. {Pitts.} The Chair thanks the gentleman and yields
768 to the Ranking Member of the Full Committee, Mr. Waxman, for
769 5 minutes for questions.

770 Mr. {Waxman.} Thank you very much, Mr. Chairman.

771 Dr. Woodcock, I want to ask you about Accelerated
772 Approval. There is a bill by Mr. Towns and Mr. Stearns, and
773 Dr. Maraganore will discuss this on our second panel. The
774 act would clarify and improve FDA's ability to use surrogate
775 and clinical markers for the Accelerated Approval pathway.
776 Dr. Allen, also on our second panel, describes in his
777 testimony another approach for breakthrough products. This
778 approach would ensure that the FDA works closely with
779 companies in helping them develop clinical trial designs that
780 would expedite approval of important drugs showing promise in
781 early trials. And then we also have the Infectious Disease
782 Society of America and they submitted testimony for the
783 records that discusses yet another approach, and this one is
784 focused on facilitating approval of drugs that would treat
785 serious diseases in limited populations.

786 My biggest concern in looking at these proposals is
787 whether they do or have the potential to change the approval

788 standard, which is something I hope we can all agree we don't
789 want to do. Can you briefly, because I have another set of
790 questions, describe for us what you see as any benefits of
791 these proposals as well as any concerns you have with any of
792 them?

793 Dr. {Woodcock.} On Accelerated Approval, as I said
794 earlier, I think the main point is a clarity of our ability
795 to approve drugs on an early clinical endpoint or a surrogate
796 endpoint that is reasonably likely to predict clinical
797 benefit. But I do not believe that changing the standards
798 for safety and effectiveness would be a benefit to patients.
799 So it is more about clarifying what approval mechanism we can
800 use but not changing the evidentiary standard.

801 As far as breakthrough therapies, I have had several
802 people who are involved in the AIDS epidemic and the
803 development of drugs to address that epidemic say to me if we
804 had treated that as business as usual, we would never have
805 solved this epidemic, we would have never gotten effective
806 drugs available, and HIV is not the only terrible life-
807 threatening people that people face, so breakthrough therapy
808 is not about the approval standard. It is about getting all
809 hands on deck when we find early in development a product is
810 found to potentially have a tremendous benefit, a life-
811 changing benefit in a serious disease. And we all should get

812 together at that point--this is my professional opinion--and
813 figure out the most effective and efficient way to evaluate
814 that therapy to see it really has the promise that it appears
815 to have, so if it does, patients will not have to wait years
816 to have that therapy.

817 Mr. {Waxman.} Do we need legislation to do that?

818 Dr. {Woodcock.} No. However, I believe that
819 designating that as a very important process that the agency
820 would have would provide benefit.

821 Mr. {Waxman.} I want to ask you about the integrity of
822 our drug supply chain and preventing safety crises. You have
823 already indicated you think that we ought to require drugs to
824 be tracked all the way down to the unit level, but only
825 require that supply chain entities track a lot number of the
826 product. I want to ask you about the question of the
827 pharmacies because in the coalition bill, the pharmacies are
828 essentially excluded from that proposal, and I am concerned
829 about preempting State laws that are strong California's. So
830 I would like to know FDA's views of the importance of the
831 differences between the two models. You have already talked
832 about the supply chain. You might just repeat it again, but
833 what do you think about excluding the pharmacies? And if we
834 have a single federal system, how important do you think it
835 is that pharmacies be included and that drugs are traced to

836 the unit level instead of the lot level?

837 Dr. {Woodcock.} If our goal is to prevent our patients
838 from receiving counterfeit drugs before they receive them
839 rather than going back and trying to reconstruct what happens
840 after they have received counterfeit drugs and we have
841 detected them, then we are going to have to have a system
842 that is a real-time system that tracks the drugs through the
843 system down to the pharmacy level. Why? Because diversion
844 and insertion of counterfeits can occur at any point during
845 the drug distribution chain and you leave a big gap there for
846 the criminals, and we know there are a lot of criminals out
847 there outside of our country who want to make profit by
848 putting counterfeit drugs into our distribution chain or by
849 stealing drugs, perhaps adulterating them and then
850 reinserting them back.

851 Mr. {Waxman.} You would include pharmacists and
852 pharmacies?

853 Dr. {Woodcock.} We have had some cases like that.

854 Mr. {Waxman.} This is going to be expensive, and I
855 suppose that the technology advances quickly and gets cheaper
856 over time, so we need to work a robust system as possible but
857 realize that we have to phase it in, I suppose.

858 Dr. {Woodcock.} Right. I think that there are costs,
859 significant costs, associated with it. You have to balance

860 the costs against the potential benefits, and I think we have
861 to ask ourselves, are we going to wait until we have a mass
862 sort of poisoning from insertion of counterfeit drugs or when
863 we assume those costs, is the benefit worth the costs. There
864 is no doubt that there will be costs to all members in the
865 supply chain to do this.

866 Mr. {Waxman.} Thank you, Mr. Chairman.

867 Mr. {Pitts.} The Chair thanks the gentleman and
868 recognize the gentleman from Illinois, Mr. Shimkus, 5 minutes
869 for questions.

870 Mr. {Shimkus.} Thank you, Mr. Chairman. Welcome, Dr.
871 Woodcock.

872 My first question is kind of really a response to an
873 answer you gave to Congressman Pallone on the discussion on
874 the GAIN Act. I am an original sponsor on Dr. Gingrey's bill
875 along with Dianna DeGette, Anna Eshoo, Gene Green and other
876 members, and we have been working a long time. The intent is
877 to list the biggest unmet needs, the pathogens, and then
878 allow you all to add new pathogens.

879 Dr. {Woodcock.} Yes.

880 Mr. {Shimkus.} I think in the question-and-answer
881 period, the concern was removal and flooding of the market
882 with ones that aren't needed. We have concerns about that,
883 and let me address the concerns. The intent is not obviously

884 to try to remove folks. First of all, there is really not a
885 market unless there is something that really happens bad. So
886 our concern is someone developing an antibiotic to meet a
887 specific pathogen that is on the list and then all of a
888 sudden they get pulled off the list. Now, what incentive
889 would that be for anyone, really, anyone, to go in and try to
890 take advantage of this process?

891 Dr. {Woodcock.} Well, I would say that the FDA has
892 various processes such as orphan drug designation and other
893 designation processes now that we operate, and generally the
894 simpler the rules, the easier these are to operate
895 administratively. We also have a process that was
896 established under the user fee--

897 Mr. {Shimkus.} Yes, and I was real involved with the
898 orphan drug provisions, but really, the question still is,
899 there will be a debate, it sounds like, on both sides on the
900 ability to remove. I think our basic analysis is, one, there
901 is no need to remove; two, it is really a disincentive. And
902 I would ask you to look at that provision from the folks who
903 want to innovate, those who may have already spent a lot of
904 money and then all of a sudden it is off the list.

905 Let me go to my other questions. As Dr. Frieden of the
906 CDC testified in 2010, antibiotic resistance is a public
907 health problem of increasing magnitude and finding effective

908 solutions to address this problem is a critical focus of the
909 CDC activities. Is it safe to say that you feel similarly
910 that finding solutions to addressing this problem is a
911 critical focus of your activities?

912 Dr. {Woodcock.} Yes.

913 Mr. {Shimkus.} And how important is new drug
914 development in the fight against this public health threat?

915 Dr. {Woodcock.} It is crucial.

916 Mr. {Shimkus.} Thank you. It kind into this whole
917 obviously the GAIN Act in which we are focused on today, part
918 of it we are focused on today.

919 One of the issues is on the ventilator-assisted
920 pneumonia example where our rules are that it can't be tested
921 if the population has already received antibiotics so a lot
922 of this testing occurs overseas, and then as I have stated
923 numerous times, there is a concern with that because you are
924 there, you are testing, you are spending money. You may
925 segue into the E.U. system and then we may lose that
926 population. How do we get around, or is that exclusion of
927 testing a population that has never received antibiotics, is
928 that really a hurdle that we can't overcome in our testing
929 aspects here in the United States?

930 Dr. {Woodcock.} We are currently in discussions both
931 with the industry and the Infectious Disease Society of

932 America and other interested parties about what the drug
933 development paradigm should be for multi-drug-resistant
934 organisms, and we actually feel that a much abbreviated
935 development program, a very small development program which
936 would be an incentive for developing these types of
937 antibiotics would be highly feasible if in fact it were
938 linked to the concept of good antibiotic stewardship post
939 market.

940 Mr. {Shimkus.} So there is hope?

941 Dr. {Woodcock.} Absolutely, but I think that is
942 something that we need to discuss more as far as the good
943 antibiotic stewardship aspect of this.

944 Mr. {Shimkus.} Great. Thank you, Mr. Chairman. I
945 yield back my time.

946 Mr. {Pitts.} The Chair thanks the gentleman and
947 recognizes the Ranking Member Emeritus, Mr. Dingell, for 5
948 minutes for questions.

949 Mr. {Dingell.} Mr. Chairman, I thank you for your
950 courtesy.

951 Dr. Woodcock, welcome.

952 Dr. {Woodcock.} Thank you.

953 Mr. {Dingell.} One way to address the threats in a
954 supply chain is to know who is responsible for the
955 pharmaceutical product at each point in the supply chain. I

956 am sure you agree with that. Yes or no?

957 Dr. {Woodcock.} Yes.

958 Mr. {Dingell.} As you know, the PDSA proposal would
959 provide for lot-level traceability. Would lot-level
960 traceability be helpful in identifying where in the supply
961 chain a violation occurred?

962 Dr. {Woodcock.} It might be difficult due to the size
963 of lots.

964 Mr. {Dingell.} But you would be better off than you are
965 now?

966 Dr. {Woodcock.} I think the benefits of doing that
967 would have to be balanced against the costs of even enacting
968 such a system.

969 Mr. {Dingell.} Now, some have advocated for unit-level
970 traceability over lot level so that you could track
971 individual products and identify threats before incidents
972 occur. Would unit-level traceability be helpful in the
973 instance of contamination or entry of a counterfeit product?
974 Yes or no.

975 Dr. {Woodcock.} Yes.

976 Mr. {Dingell.} Now, one concern I continue to have is
977 contamination or diversion of prescription drugs by persons
978 outside the supply chain. Would lot-level traceability help
979 the FDA to identify the path of a contaminated product as it

980 traveled through domestic distribution?

981 Dr. {Woodcock.} Only partially, and would have to be
982 reconstructed I think after the fact.

983 Mr. {Dingell.} What would be the obstacles or the
984 difficulties there?

985 Dr. {Woodcock.} Because large numbers of any given lot
986 are manufactured, then determining if some counterfeits of
987 that lot were added at some point would be difficult unless
988 you had real-time tracking and you kept account of the
989 volume.

990 Mr. {Dingell.} Now, in the instance of contamination or
991 diversion, would lot numbers be helpful if a particular lot
992 of drugs traveled through multiple distributors and reached
993 multiple pharmacies?

994 Dr. {Woodcock.} It would be helpful in retrospectively
995 determining perhaps the point of entry of the contaminated
996 version but it would not be helpful, I don't think, in real
997 time.

998 Mr. {Dingell.} Thank you. Now, I happen to believe
999 that manufacturers, distributors and dispensers should keep
1000 accurate and thorough records detailing who is buying and
1001 selling a drug throughout the distribution chain. I am sure
1002 you agree with that.

1003 Dr. {Woodcock.} I agree.

1004 Mr. {Dingell.} Would it be helpful to FDA to have each
1005 entity in the supply chain--manufacturers, wholesale
1006 distributors, dispensers--accountable for the authenticity of
1007 their product here?

1008 Dr. {Woodcock.} Yes.

1009 Mr. {Dingell.} Now, again, I want to commend the
1010 industry for their work on the Rx proposal. Traceability is
1011 a vitally important tool in securing our drug supply and one
1012 I believe would complement the drug safety proposal that I
1013 have been pushing. I look forward to working with industries
1014 and my friends on the Committee to ensure that traceability
1015 proposals move through this Committee in a way that will best
1016 achieve the mutual goal of preventing counterfeit and
1017 contaminated products from entering our drug supply.

1018 Doctor, thank you for your presence.

1019 Dr. {Woodcock.} Thank you.

1020 Mr. {Pitts.} The Chair thanks the gentleman and yields
1021 to Dr. Gingrey from Georgia for 5 minutes for questioning.

1022 Dr. {Gingrey.} Mr. Chairman, thank you.

1023 Dr. Woodcock, thank you. The GAIN Act is squarely
1024 focused on serious bacterial pathogens with equally serious
1025 unmet medical need including Gram-negative bacteria, a
1026 specific one that was dubbed Iraqibacter due to the
1027 propensity of infections among our wounded soldiers in Iraq.

1028 It is an increasing cause of hospital-acquired infections in
1029 intensive care units leading to tens of billions of dollars
1030 in expenses and it is increasingly resistant to numerous
1031 drugs, leading to a high number of fatalities. It can show
1032 up as pneumonias, complicated skin infections, tissue
1033 infections, and indeed even septicemia, which is better known
1034 in common parlance as bloodstream infections. Most
1035 worrisome, Doctor, the pipeline for novel therapies against
1036 something like Iraqibacter is slim to virtually nonexistence.
1037 Now, Dr. Fauci, the Director of the CDC, testified before
1038 this Committee in April of 2010 that our focus should be on
1039 infections derived from problematic pathogens like this Gram-
1040 negative bacteria Iraqibacter. Dr. Woodcock, do you agree
1041 with Dr. Fauci that encouraging drug development to combat
1042 infections that arise from Gram-negative pathogens like
1043 Iraqibacter is an appropriate role for Congress and the FDA?

1044 Dr. {Woodcock.} Absolutely.

1045 Dr. {Gingrey.} According to the website of the FDA, you
1046 have launched several initiatives to combat antibiotic
1047 resistance including encouragement of the development of new
1048 drugs, vaccines and improved tests for infectious diseases.
1049 Yet many public health organizations, patient groups and drug
1050 companies have stated that greater incentives are needed if
1051 we hope to increase new antibiotic drug development. Do you

1052 believe that current FDA actions are enough to encourage the
1053 numbers of new antibiotics we need to meet the growing public
1054 health threat that antibiotic resistance poses?

1055 Dr. {Woodcock.} No, clearly it is not enough.

1056 Dr. {Gingrey.} So the provisions in the GAIN Act, very
1057 specifically, Dr. Woodcock, like increasing the time of
1058 exclusivity from 10 to 15 years and to be very specific in
1059 regard to the pharmaceutical community that are developing
1060 these new drugs and biologics, do you agree that they need to
1061 know ahead of time that all of this cost and expense and
1062 innovation and research and development that literally the
1063 rug is not going to be pulled out from under them by some
1064 indiscriminate decision after the fact that the FDA might
1065 make in regard to a list of pathogens that we already know
1066 are causing serious medical illnesses no matter where they
1067 might strike, whether it is in the bloodstream or in the
1068 lungs causing pneumonia or in the skin causing things like
1069 necrotizing disease, which indeed can be deadly. So my
1070 question in regard to all of this is, don't you agree, or do
1071 you disagree that being very specific about the pathogens and
1072 things like MRSA, methicillin-resistant staph aureus, and a
1073 lot of these Gram-negative bacteria, enterococcus and things
1074 like that, these need to be designated on the front end, and
1075 of course, the Director of the FDA has the opportunity or the

1076 Secretary of HHS, you know, to add additional things to the
1077 list. So comment on that for us.

1078 Dr. {Woodcock.} Certainly. It is obvious, and we know
1079 from experience that industry needs, because of the cost and
1080 the risk, a very clear pathway to market, and that is a big
1081 incentive if that is very clear and laid out, so that is
1082 extremely important. I agree with that.

1083 As far as how to do this in this specific instance I
1084 think we are more administratively looking at how
1085 administratively you would set such an incentive up, and
1086 because antibiotic resistance evolves rapidly and this is a
1087 dynamic field and actually many organisms are implicated in
1088 this, it would seem that in general for Congress to set up
1089 some more general criteria and then have FDA designate that
1090 way. We then could make agreements with companies about the
1091 designation at the time they come and talk to us about their
1092 development program and what the pathway would be. So it
1093 just seems that stipulating in the statute certain things
1094 rather than what the criteria might be, maybe setting the
1095 criteria would be a better way to go.

1096 Dr. {Gingrey.} Mr. Chairman, I realize I am over time,
1097 but let me just conclude here.

1098 Dr. Woodcock, I think you answered my question or my
1099 premise in the affirmative, and this is sort of what I think

1100 Mr. Shimkus was getting at in regard to the ability to add
1101 to, and you have that in the GAIN Act. You have that ability
1102 as things develop to be able to add to the list but I think
1103 the list at the outset in the law should be very specific.

1104 So with that, Mr. Chairman, I yield back, and thank you
1105 for your patience.

1106 Mr. {Pitts.} The Chair thanks the gentleman and
1107 recognizes the gentlelady from Illinois, Ms. Schakowsky, for
1108 5 minutes for questions.

1109 Ms. {Schakowsky.} Thank you, Mr. Chairman.

1110 As I said in my opening statement, I am interested in
1111 the balance between hurrying the drugs that we need to market
1112 and making sure that we protect safety. It seems to me that
1113 most of the claims about FDA's poor performance have in fact
1114 been disproved, and you described quite powerfully how
1115 effective FDA has been at using its current Accelerated
1116 Approval authorities. So it is surprising to me that we are
1117 still talking about the need for yet another accelerated
1118 approval pathway, and I hope we can all agree that we have to
1119 be somewhat cautious in this area. At the very least, we
1120 need to ensure that we don't force FDA into a position where
1121 its approval standards are lowered and the agency ends up
1122 force to approve ineffective or unsafe drugs, which is in no
1123 one's interest.

1124 So let me just ask you this. Does the FDA have concerns
1125 about H.R. 4132, the FAST Act, for example, having the
1126 potential to lower the approval standards?

1127 Dr. {Woodcock.} Well, we would look forward to working
1128 with Congress and Committee on any given language and
1129 providing technical assistance. I think it is important to
1130 not lower the standards for safety and efficacy and to be
1131 clear in the language while we do support the idea of
1132 clarifying what can be used as the basis for Accelerated
1133 Approval.

1134 Ms. {Schakowsky.} And do you take into account the fact
1135 that people who are gravely ill are in fact willing to take
1136 more risks, and what is the mechanism for doing that, for
1137 separating out those individuals who in fact willing to take
1138 some more risks?

1139 Dr. {Woodcock.} Well, we always balance benefit and
1140 risk. Obviously, cancer drugs aren't as safe as headache
1141 drugs, and so we are taking that into account. The user fee
1142 program, the prescription drug user fee program that is
1143 before Congress now, will have as part of it a formal
1144 mechanism where we go out and solicit patient input into
1145 these tradeoffs, especially for diseases that aren't well
1146 understood and so that we can understand how much risk people
1147 are willing to take for a certain amount of benefit. And

1148 then after marketing, typically there is patient information
1149 and we are moving toward getting uniform patient information
1150 in the United States so that when people get a prescription
1151 drug, they understand the benefits and the risks and they can
1152 make that tradeoff for themselves because individual values
1153 differ.

1154 Ms. {Schakowsky.} And do we distinguish between people
1155 who are pretty desperate to try things as opposed to sort of
1156 for the general population? I mean, is there any flexibility
1157 in that way?

1158 Dr. {Woodcock.} Well, what we typically do is have--the
1159 drug is studied and so understand the magnitude of the
1160 benefit and then all the risks are described, and then it is
1161 determined between the patient and the physician when that
1162 treatment decision is being considered that they would
1163 discuss both the upsides and downsides of the therapy so the
1164 patient can make an informed choice.

1165 Ms. {Schakowsky.} So the obligation then of the FDA is
1166 to just make sure that there is complete disclosure of the--
1167 let me ask you this. Do you need more authorities to speed
1168 new therapies to market?

1169 Dr. {Woodcock.} No, we don't think that new authorities
1170 are needed. Perhaps some clarification might be useful but,
1171 no, we feel that we can get safe and effective drugs, that

1172 more risk is tolerated for cancer, for life-threatening
1173 diseases and so forth. We can get these therapies to the
1174 patients with an appropriate balance of benefit and risk.

1175 Ms. {Schakowsky.} Thank you. Unless someone wants my
1176 time, I yield back.

1177 Mr. {Pitts.} The Chair thanks the gentlelady and
1178 recognizes the gentleman from Pennsylvania, Dr. Murphy, for 5
1179 minutes for questions.

1180 Mr. {Murphy.} Thank you for being here, Dr. Woodcock.
1181 I always appreciate your testimony and find you to be a very
1182 trustworthy source, and thank you for your leadership.

1183 I want to ask you about drug shortages in particular.
1184 From what I understand, many of these are cancer drugs. Can
1185 you explain why we are facing shortages in cancer drugs?

1186 Dr. {Woodcock.} I think the HHS Assistant Secretary for
1187 Planning and Evaluation report has the best explanation of
1188 what happened. Most of these cancer drugs are off-patent
1189 sterile injectable drugs and they were very few manufacturers
1190 in the United States making them, sometimes only one
1191 manufacturer. They were making a large list of sterile
1192 injectables also. And they developed some manufacturing
1193 problems. Multiple manufacturers developed problems making
1194 the drugs and had to shut down their lines or interrupt
1195 production, and this, as I said last time, is a perfect storm

1196 where this all sort of came together. Multiple manufacturers
1197 of the few that existed in the United States for sterile
1198 injectables all developed problems. As the report shows,
1199 many manufacturers had added newer injectable drugs that
1200 probably had increased profit margins as they came off
1201 patent, added them to their list and so they were producing a
1202 very extensive list of products, and when they ceased
1203 production or had to restrict their production, then there
1204 were other places to turn in the United States.

1205 Mr. {Murphy.} Is the FDA taking any steps to change
1206 some of these things to address the shortage issue?

1207 Dr. {Woodcock.} Yes. The steps we take, number one, we
1208 work with the manufacturers. We do everything we can to keep
1209 these particular shortage drugs in production. We have even
1210 gone to the lengths of testing the drugs, see if the
1211 particles could be filtered out and allowing them to be
1212 shipped to the patients, to the doctors if they would filter
1213 them at the time of use. Okay. That isn't what you would
1214 want of a drug supply but it is better than not having those
1215 drugs available. We also expedite any applications for
1216 making additional sites or additional manufacturers who want
1217 to make these drugs, we expect their generic drug
1218 applications. If we have to, we work with foreign suppliers
1219 who may be making these drugs and see if they can ramp up

1220 their production and import temporarily into the United
1221 States to cover the shortage situation, and we have some of
1222 that happening right now.

1223 Mr. {Murphy.} Let me ask about another area. I am a
1224 psychologist by training and worked in pediatrics also. I
1225 served in the Navy and worked with PTSD and TBI veterans.
1226 And one of my concerns is also the abuse of drugs. It is a
1227 sad story that we have to address, and of course, the abuse
1228 of drugs also is associated with some shortages. Some of the
1229 stimulant medications used for attention disorder, for
1230 example, have shortages. That hurts those who really need
1231 them but there is also people using that shouldn't be having
1232 them and other class II and III drugs that are being used
1233 too, and I wonder about addressing these as other issues of
1234 taking care of the shortages by doing such things on a
1235 federal level, an issue I am working on legislation much like
1236 a couple of States have done, and that is, requiring a photo
1237 ID when people pick up some of these drugs. It is not
1238 difficult and it is not a secret that someone could take a
1239 Medicare patient's prescription, take it to the drugstore,
1240 fill it for Vicodin or something else, and next you see
1241 Grandpa can't find his prescription, the doctor writes
1242 another one, and these things go on. It is similar for abuse
1243 of some of the drugs used by children which they may sell or

1244 they may redistribute, and I get particularly concerned when
1245 we have so many veterans who end up self-medicating
1246 themselves out of their pain. So I wondered if this is
1247 something that in terms of States, I think Maine and North
1248 Carolina have put in some laws in effect requiring a photo ID
1249 or a designated person to pick up the drug when that person
1250 can't do it. If you know of any research in terms of, is
1251 this addressing some of the issues with regard to reduction
1252 of abuse or at least helping a situation where drugstores are
1253 not put in the middle of basically becoming suppliers to drug
1254 abuse networks?

1255 Dr. {Woodcock.} Thank you. We are doing quite a bit in
1256 this area. The Administration last year announced an
1257 initiative to try to combat the epidemic of prescription drug
1258 abuse in the United States, and we have multiple efforts that
1259 we are working on. I am not familiar with the results of the
1260 research on photo ID and what impact that might have on
1261 decreasing diversion to people who are not supposed to get
1262 the prescriptions, but it is clear that we need to take
1263 additional measures to control this epidemic. It is ravaging
1264 some communities.

1265 Mr. {Murphy.} I appreciate that. I am aware of one
1266 chain, CVS, requires on their own a photo ID, contacting the
1267 physician, asking for the diagnosis to verify a number of

1268 these steps in that process, and that helps, and I certainly
1269 know when I have talked to some pharmacists and they languish
1270 with this idea that say someone shows up with a prescription,
1271 we are filling it but worried that it is actually being
1272 abused, so I would love to be able to with you more in
1273 addressing this, and I do appreciate your dedication to this.
1274 Thank you so much.

1275 I yield back.

1276 Mr. {Pitts.} The Chair thanks the gentleman and
1277 recognizes the gentleman from Louisiana, Dr. Cassidy, for 5
1278 minutes for questions.

1279 Dr. {Cassidy.} Hi, Dr. Woodcock. How are you?

1280 Dr. {Woodcock.} I am fine. Thanks.

1281 Dr. {Cassidy.} I have concerns about online pharmacies.
1282 As I gather, they are unregulated. It is kind of a Wild West
1283 out there and lots of issues associated with them. The
1284 latest article in the Wall Street Journal of course is on
1285 online pharmacies. Now, we have heard testimony recently
1286 about abuse potential drugs and the problems of prescription
1287 drug abuse. So both adulterated and abuse potential. Can
1288 you comment on the role of online pharmacies in these two
1289 issues?

1290 Dr. {Woodcock.} It is clear that online pharmacies can
1291 be--

1292 Dr. {Cassidy.} By the way, just to be clear, there are
1293 legitimate and illegitimate pharmacies, so I am sorry,
1294 continue.

1295 Dr. {Woodcock.} No, I agree with that. There are
1296 obviously sites around the world that can pose as pharmacies
1297 and are distributors and may introduce improper drugs or
1298 provide drugs without a prescription or sometimes provide
1299 drugs that are counterfeit to people. The VIPPS program,
1300 which certifies certain Internet pharmacies as appropriate
1301 and has criteria, is one guide to consumers. We have
1302 educational material that we have tried to put out and tried
1303 to educate patients and consumers on what proper procedures
1304 might be for ordering drugs over the Internet because
1305 unguided they may well run into harm.

1306 Dr. {Cassidy.} Now, is it fair to say, though, that--
1307 now, first, I am a physician who happens to be a Congressman
1308 who is married to a doctor, and I had never heard of the
1309 VIPPS program until today, which is not a criticism of FDA.
1310 Frankly, it is a criticism of my wife. Just kidding. But
1311 that said, is it fair to say that the current mechanism has
1312 some inadequacy if even someone who theoretically would be
1313 educated such as I does not know?

1314 Dr. {Woodcock.} I think it is a very difficult problem.
1315 The whole system was set up for brick-and-mortar pharmacies.

1316 Our whole control system was set up that way. Now we have
1317 the Internet. As you said, it is the Wild West, and
1318 definitely it is putting American patients and consumers in
1319 harm's way.

1320 Dr. {Cassidy.} I am struck that as we speak about unit-
1321 level tracking, really, that doesn't mean anything if I am
1322 buying online from something which I think is legitimate but
1323 which is illegitimate and I am getting an adulterated drug
1324 from another country. Is that a fair statement too?

1325 Dr. {Woodcock.} Absolutely.

1326 Dr. {Cassidy.} So until we can actually do something
1327 about the online pharmacies, we are going to continue to have
1328 a leaky bucket allowing things to come in which should not?

1329 Dr. {Woodcock.} That is correct.

1330 Dr. {Cassidy.} Any sense of how much of the drugs that
1331 are abuse potential being used here would come in through
1332 online pharmacies? Do we have a sense of the scope of the
1333 issue?

1334 Dr. {Woodcock.} We do not.

1335 Dr. {Cassidy.} And do we have a sense of how many of
1336 the online pharmacies are legitimate versus illegitimate?

1337 Dr. {Woodcock.} Again, the Internet is a very rapidly
1338 changing and evolving--

1339 Dr. {Cassidy.} Fair answer. Now, let me ask you again,

1340 I am aware of the issue of valid prescriptions versus invalid
1341 and would just like your comments upon that.

1342 Dr. {Woodcock.} Well, I think the definition of a valid
1343 prescription is an important keystone of any efforts and we
1344 have to do that in light of, you know, now the electronic
1345 prescribing and phone prescribing and so forth, but I think
1346 that is a very important component.

1347 Dr. {Cassidy.} So the valid prescription, just for
1348 those who may not be familiar with it, currently pertains to
1349 a controlled substance but not to an uncontrolled substance.
1350 So I can get an antihypertensive, which doesn't require a
1351 valid prescription, but the Vicodin, I would, but the absence
1352 of the requirement of a valid prescription for the
1353 antihypertensive may mean I get an adulterated drug. Fair
1354 statement?

1355 Dr. {Woodcock.} Yes, if you happen to order from an
1356 inappropriate pharmacy on the Internet.

1357 Dr. {Cassidy.} So ideally, we would come up with--we
1358 apply the definition of valid prescription--I am just saying
1359 this to see if you would agree--the definition of a valid
1360 prescription which would apply both to controlled and non-
1361 controlled substances?

1362 Dr. {Woodcock.} Yes.

1363 Dr. {Cassidy.} I know we are about to vote and so I

1364 yield back to other members. Thank you.

1365 Mr. {Pitts.} The Chair thanks the gentleman and
1366 recognizes the gentleman from New Jersey, Mr. Lance, for 5
1367 minutes for questions.

1368 Mr. {Lance.} Thank you very much, Mr. Chairman, and I
1369 respectfully request my opening statement be placed into the
1370 record.

1371 Mr. {Pitts.} Without objection, so ordered.

1372 [The prepared statement of Mr. Lance follows:]

1373 ***** COMMITTEE INSERT *****

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1374 Mr. {Lance.} Thank you, Mr. Chairman.

1375 I want to follow up on questioning from Congressman
1376 Pallone regarding medical gases, and I know that you are
1377 working on this issue. As I understand it, the six medical
1378 gases that make up 99 percent of the prescriptions in the
1379 United States--oxygen, nitrogen, nitrous oxide, carbon
1380 dioxide, helium and medical air--are mostly derived from the
1381 air that we breathe. The FDA has a long history of using its
1382 enforcement discretion in exempting medical gases from its
1383 New Drug Application process but recent changes to federal
1384 policy, I believe, have left both manufacturers and patients
1385 uncertain of the future of FDA-approved medical gases.

1386 The legislation that Congressman Pallone referenced,
1387 legislation I have introduced, the Medical Gas Safety Act,
1388 which is bipartisan in nature--I have introduced it with my
1389 colleague, Congressman Murphy, Chris Murphy--tries to address
1390 this situation in a bipartisan capacity. I want to work with
1391 you in this regard. Can you comment on where you might be
1392 going regarding this issue?

1393 Dr. {Woodcock.} Certainly. We feel also that there are
1394 long-recognized and medically acceptable uses of these
1395 traditional medical gases and that some designation would be
1396 very useful rather than having an application process,

1397 approve something we already know, all right?

1398 Mr. {Lance.} Yes.

1399 Dr. {Woodcock.} But as far as some of the other issues
1400 relating to the manufacturing process and so forth, we
1401 believe that our regulations are sufficiently flexible that
1402 we can work out an approach without additional legislation
1403 that would be mutually satisfactory to the industry and to
1404 the FDA.

1405 Mr. {Lance.} Thank you, Doctor. I know that your staff
1406 has some reservations about developing separate, current good
1407 manufacturing practice regulations for the medical gases.
1408 Codifying current regulatory experience with medical gases
1409 is, in my judgment, the best way to resolve some of the
1410 confusion, and the Compressed Gas Association, which is the
1411 safety-standard-setting organization for the industry, has
1412 offered its full resources to assist in the rulemaking
1413 process. I want to thank you for your willingness to meet
1414 and work with the association, with the staff here on this
1415 Committee, with my staff on this issue.

1416 I do not necessarily think that guidance can remove the
1417 requirements from existing regulations, so I do think that
1418 some changes in the regulations are necessary, and I
1419 respectfully request that we continue to work together on
1420 this issue as PDUFA is reauthorized.

1421 Dr. {Woodcock.} We will be happy to work with you.

1422 Mr. {Lance.} Thank you very much, Mr. Chairman, and I
1423 yield back the balance of my time.

1424 Mr. {Pitts.} The Chair thanks the gentleman and
1425 recognizes the gentleman from Ohio, Mr. Latta, for 5 minutes
1426 for questions.

1427 Mr. {Latta.} Well, thank you, Mr. Chairman, and Dr.
1428 Woodcock, thanks for being with us today. If I could just
1429 kind of go back to a question that was asked by Dr. Burgess
1430 and one also that was asked by Dr. Murphy. One of the
1431 questions that Dr. Burgess asked, and I want to make sure
1432 that I wrote it down correctly when you said that, that he
1433 asked what can the FDA do to help incentivize businesses to
1434 stay in business in the manufacturing process, and your
1435 answer was at the time that, you know, your focus is really
1436 on that reliability. And Dr. Murphy then had asked a
1437 question in the same vein because there is a lot of questions
1438 about there on the drug shortages, that the question as to
1439 manufacturing problems and that you had stated that in trying
1440 to address that problem you would work with the manufacturer.
1441 Is there a difference between trying to keep people in
1442 business and those companies out there that are manufacturing
1443 right now?

1444 Dr. {Woodcock.} Can you rephrase the question?

1445 Mr. {Latta.} Well, the first part of the question is
1446 that you had said that as Dr. Burgess had asked the question,
1447 he asked what can the FDA do to help incentivize businesses
1448 sustain manufacturing processes of producing the product, and
1449 you had said in response to his question that your only focus
1450 is really on the reliability end and not on trying to keep
1451 them in business. So that would be a company out there that,
1452 you know, might be trying to incentivize somebody to stay in
1453 that type of a process in manufacturing but Dr. Murphy had
1454 asked the question as to if there are manufacturing problems
1455 and keeping pills out there or other drugs in the
1456 manufacturing stream to get to the patients and that you
1457 would say that you would work with those manufacturers. I am
1458 just trying to figure out what the difference between the two
1459 is on the reliability and working with them.

1460 Dr. {Woodcock.} My understanding of Dr. Burgess's
1461 question was, did we help with the economic incentives, and
1462 we don't have really any role in the economic aspects of drug
1463 production and marketing and so forth. We do work with
1464 manufacturers to try to keep them manufacturing shortage
1465 drugs or any other drugs and we try to work with
1466 manufacturers to keep them manufacturing a reliable supply of
1467 the medicines that they produce. I do believe that the
1468 generic drug proposal that is before Congress right now will

1469 help with this because it will help us clear out our backlog
1470 of generic drug applications that have decreased the
1471 predictability of a generic drug review process and hopefully
1472 we may encourage more entrants into that process. So we do
1473 work with them but we are not involved in the marketing and
1474 reimbursement or any of those aspects.

1475 Mr. {Latta.} And also in answer to some of Dr. Murphy's
1476 questions, could you define when you say you would help
1477 filter?

1478 Dr. {Woodcock.} Yes. Manufacturers of sterile
1479 products--that would be that go into your vein--we are
1480 finding they had particles in their products. That is bad.
1481 That is very bad but they can go into your lungs and get
1482 stuck and so forth, so it is not acceptable. So when those
1483 were in shortage, rather than say you can't send them out, we
1484 tested to make sure that a filter would take out the
1485 particles and not take out the drug, and then we let the
1486 drugs be shipped with a filter so that at the point of
1487 delivery, they could be filtered and get the particles out
1488 and the patient would still get that drug rather than have it
1489 be in shortage. So I think that is an illustration that we
1490 try to work with the manufacturers to keep these drugs out
1491 there.

1492 Mr. {Latta.} And also, other countries that are out

1493 there that have experienced drug shortages, how have they met
1494 the shortages like say in Europe?

1495 Dr. {Woodcock.} They work much the same way that we do,
1496 and we work with the European regulatory authorities to try
1497 to make sure the international drug supply remains robust.
1498 So they take the same sorts of actions we do.

1499 Mr. {Latta.} Again, just one last question, if I may.
1500 With the 1981 flu pandemic that might have killed between 25
1501 to 75 million individuals, it is being pretty much attributed
1502 now not to the flu but to tuberculosis, and in January of
1503 this year, a completely 100 percent drug-resistant form of TB
1504 was identified in India that would not be treatable with any
1505 known antibiotic. What is the FDA doing right now to try to
1506 prevent that from getting to these shores?

1507 Dr. {Woodcock.} Yes. Well, we certainly are working
1508 with the coalition that is working on developing new drugs
1509 for multi-drug-resistant tuberculosis. This is a serious
1510 threat. We recognize it and we are doing everything we can.
1511 Our combination investigational drug guidance, which is
1512 realize is very technical, that we put out that showed how
1513 you could develop several investigational drugs together to
1514 deal with a threat such as this I think is helpful in this
1515 effort. And as I said earlier, we believe that if provisions
1516 for good antibiotic stewardship were able to be instituted

1517 and we were sure that such a drug would only be used only for
1518 drug-resistant tuberculosis, we could have a very small
1519 development program that would allow that drug to get on the
1520 market. That would provide, I think, a tremendous incentive
1521 to manufacturers to get into this space and develop drugs for
1522 multi-drug-resistant TB.

1523 Mr. {Latta.} Thank you, Dr. Woodcock.

1524 Mr. Chairman, I yield back.

1525 Mr. {Pitts.} The Chair thanks the gentleman. That
1526 concludes the questions. Go ahead, Dr. Cassidy, for one
1527 follow-up.

1528 Dr. {Cassidy.} Mr. Lance brought up H.R. 2227, medical
1529 gas. Just to confirm that this would not apply to already
1530 approved substances, correct?

1531 Dr. {Woodcock.} Correct.

1532 Dr. {Cassidy.} They would continue to be regulated as
1533 they currently are?

1534 Dr. {Woodcock.} That is my understanding.

1535 Dr. {Cassidy.} Thank you. I yield back.

1536 Mr. {Pitts.} Thank you, Dr. Woodcock, for appearing
1537 before the Subcommittee this morning. We really appreciate
1538 your testimony and answering all of your questions. That
1539 concludes panel one.

1540 Dr. {Woodcock.} Thank you.

1541 Mr. {Pitts.} We will now call panel two to the witness
1542 table, and I would like to thank all of these witnesses for
1543 agreeing to testify before the Subcommittee today. I would
1544 like to quickly introduce our expert panel. First of all,
1545 Dr. John Maraganore is CEO of Alnylam Pharmaceuticals. Dr.
1546 Jeff Allen is the Executive Director of Friends of Cancer
1547 Research. Dr. Barry Eisenstein is Senior Vice President of
1548 Science Affairs at Cubist Pharmaceuticals. Dr. John Powers
1549 is the Assistant Clinical Professor of Medicine at George
1550 Washington School of Medicine. And Mr. Michael Walsh is the
1551 President of LifeGas. Mr. Walsh is appearing on behalf of
1552 the Compressed Gas Association.

1553 Again, we thank all of you for coming this morning. We
1554 have your prepared statements. Dr. Maraganore, we will begin
1555 with you. You are recognized for 5 minutes to summarize your
1556 testimony.

|
1557 ^STATEMENTS OF JOHN MARAGANORE, PH.D., CHIEF EXECUTIVE
1558 OFFICER, ALNYLAM PHARMACEUTICALS; JEFF ALLEN, PH.D.,
1559 EXECUTIVE DIRECTOR, FRIENDS OF CANCER RESEARCH; BARRY
1560 EISENSTEIN, M.D., F.A.C.P., F.I.D.S.A., F.A.A.M., SENIOR VICE
1561 PRESIDENT, SCIENTIFIC AFFAIRS, CUBIST PHARMACEUTICALS; JOHN
1562 H. POWERS, M.D., F.A.C.P., F.I.D.S.A., ASSISTANT CLINICAL
1563 PROFESSOR OF MEDICINE, GEORGE WASHINGTON UNIVERSITY SCHOOL OF
1564 MEDICINE; AND MICHAEL WALSH, PRESIDENT, LIFEGAS, ON BEHALF OF
1565 COMPRESSED GAS ASSOCIATION

|
1566 ^STATEMENT OF JOHN MARAGANORE

1567 } Mr. {Maraganore.} Thank you, Chairmen Upton and Pitts
1568 and Ranking Members Waxman and Pallone. It is my privilege
1569 to provide testimony before the Subcommittee today. My name
1570 is John Maraganore and I am the Chief Executive Officer of
1571 Alnylam Pharmaceuticals.

1572 As a scientist and a businessman, I have over 25 years
1573 of experience in biopharmaceutical research and development.
1574 I serve on the board of several biotechnology companies and I
1575 am also an advisor to Third Rock Ventures and a member of the
1576 Biotech Industry Organization Governing Board.

1577 Founded in 2002, Alnylam is a small, non-profitable

1578 biotechnology company located in Cambridge, Massachusetts.
1579 We are developing new medicines based on the science of RNA
1580 interference, or RNAi, which is a major breakthrough in
1581 biology that was recognized by the award of the 2006 Nobel
1582 Prize for Medicine or Physiology.

1583 Today our company has 120 employees who are working on a
1584 pipeline of innovative medicines that could truly be
1585 transformative in the lives of patients afflicted with a
1586 number of genetic diseases including diseases such as
1587 systemic amyloidosis, hemophilia, sickle cell anemia, severe
1588 hypercholesterolemia, Huntingdon's disease, liver cancer and
1589 also respiratory syncytial virus. If we are successful in
1590 our efforts, we can create a whole new class of medicines and
1591 treat disease in a fundamentally different way.

1592 I am here today to discuss the importance and the
1593 benefits of Congressman Stearns's and Towns's Faster Access
1594 to Specialized Therapies, or the FAST bill, which would
1595 modernize the Accelerated Approval pathway at the Food and
1596 Drug Administration. The Accelerated Approval pathway,
1597 implemented in 1992 by the FDA and codified by the Congress
1598 in 1997, has indeed been a great success story but only in
1599 part. While its applicability has been largely limited to
1600 certain disease areas, mainly cancer and HIV/AIDS and certain
1601 situations, the pathway has stimulated an explosion of

1602 investment and innovation in those diseases and has brought
1603 immense benefit to patients suffering from those diseases.
1604 There are several reasons why the Accelerated Approval
1605 pathway should be expanded and in fact modernized.

1606 First, as I just mentioned, the Accelerated Approval
1607 pathway has worked but only in part. That is, it has been
1608 largely limited in practice to drugs that treat cancer and
1609 HIV/AIDS along with a handful of other situations. While
1610 this is great news for patients afflicted with cancer and
1611 HIV/AIDS, it is not good news for patients suffering from
1612 other serious and life-threatening diseases. Nothing in the
1613 words of the current statute limits the Accelerated Approval
1614 pathway to just oncology and HIV/AIDS. In fact, the statute
1615 is worded broadly but the current FDA practice leaves many
1616 other treatments for rare and serious conditions effectively
1617 excluded from the pathway. We need certainty about how the
1618 FDA can apply Accelerated Approval in the future by ensuring
1619 that the pathway is available for all therapies which treat
1620 serious or life-threatening conditions by enacting the FAST
1621 Act.

1622 Second, it is important that the ability to utilize the
1623 Accelerated Approval pathway is both better understood by
1624 sponsors and more consistently applied by the FDA. This is
1625 especially true when it comes to FDA-accepted clinical

1626 endpoints including those that could be measured earlier than
1627 irreversible morbidity or mortality to demonstrate a
1628 reasonable likelihood of overall clinical benefit. While the
1629 pathway allows for approval based upon effects on clinical
1630 endpoints that are reasonably likely to predict clinical
1631 benefit, in practice, the lack of clarity surrounding such
1632 approval options has led to a very limited use of Accelerated
1633 Approval by sponsors and the FDA.

1634 Third, it is time to have an expanded and modernized
1635 Accelerated Approval pathway that incorporates the remarkable
1636 advances in the life sciences that have and will provide an
1637 unprecedented understanding of the underlying biological
1638 mechanisms and disease pathogenesis. These advances can
1639 enable novel drug development strategies that employ leading-
1640 edge methodologies and tools such as biomarkers and novel
1641 clinical trial designs that can overall improve how we
1642 implement Accelerated Approval. The FAST bill would achieve
1643 all of these objectives described above by expressing the
1644 sense of Congress that the FDA should utilize the Accelerated
1645 Approval pathway as fully and as frequently as possible while
1646 maintaining very importantly FDA's safety and effectiveness
1647 standards and by codifying, modernizing and expanding FDA's
1648 Accelerated Approval pathway with four targeted revisions.

1649 I thank you very much for your time and attention and I

1650 urge Congress to consider the FAST Act.

1651 [The prepared statement of Mr. Maraganore follows:]

1652 ***** INSERT 2 *****

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1653 Mr. {Pitts.} The Chair thanks the gentleman.

1654 We are presently voting on the Floor. We are going to
1655 try to get through a couple more of you. Dr. Allen, you are
1656 recognized for 5 minutes.

|
1657 ^STATEMENT OF JEFF ALLEN

1658 } Mr. {Allen.} Thank you. Good morning, Chairman Pitts,
1659 Ranking Member Pallone and members of the Subcommittee. I am
1660 Jeff Allen, Executive Director of Friends of Cancer Research,
1661 a think tank and advocacy organization based here in
1662 Washington. I would like to thank the staff of the Committee
1663 who have worked very hard in putting together this important
1664 hearing. It is an honor to be here today.

1665 While compelling progress continues to be made within
1666 the field of oncology, there is much more to be done. This
1667 year, cancer will claim the lives of over 570,000 Americans.
1668 This, Mr. Chairman, is roughly equivalent to every citizen in
1669 your home county of Lancaster, Pennsylvania.

1670 With such a profound toll, improved ways to combat
1671 cancer and other diseases are desperately needed. While
1672 there are many factors that make development of new drugs
1673 complex, assessments of the process often focus on the FDA.
1674 Critics have frequently portrayed the FDA as slow and
1675 inefficient compared to other countries. However, our
1676 research reveals that FDA is approving anticancer drugs in a
1677 more timely fashion than the European counterpart. In fact,
1678 since 2003, FDA has approved 42 new cancer medicines versus

1679 just 32 by the EMA. Of the 28 common approvals, all were
1680 available to U.S. patients first.

1681 A cornerstone of the FDA's standard for approvals was
1682 established in 1962 by Congress requiring that all new drugs
1683 demonstrate not only their safety but also efficacy. Without
1684 this requirement, American patients would have continued to
1685 have been given medicines that actually provided no
1686 improvement to their health. As this Committee seeks to
1687 optimize and improve FDA practices and maintain its standing
1688 as the global leader, the requirement that new drugs
1689 demonstrate both safety and efficacy must be upheld. While
1690 the need for new treatments is immense and the challenge is
1691 significant, the solution is not to arbitrarily lower this
1692 important standard that has been in place for 50 years.

1693 In 1992, as science progressed, and in acknowledgement
1694 of an increased public health need, regulations were
1695 developed to establish the Accelerated Approval mechanism.
1696 This is shown to be an important tool used by the FDA to
1697 uphold the rigorous scientific standards while facilitating
1698 timely access to lifesaving treatments. For example, in
1699 oncology, Accelerated Approval has been used for over a third
1700 of new cancer drug approvals since 1999. However, since
1701 2007, the number of oncology drugs approved through this
1702 mechanism has decreased.

1703 In order to optimize the use of this tool, Congress
1704 should take action to enhance Accelerated Approval to ensure
1705 that it is applied consistently, efficiently and effectively.
1706 This is not to suggest in any way that the standards of
1707 safety of efficacy should be altered but rather to examine
1708 additional opportunities in which Accelerated Approval is the
1709 optimal approach.

1710 Today, much like at important times throughout recent
1711 history, the FDA needs an updated mechanism to respond to the
1712 rapid advancement of science. With the expansion of
1713 knowledge about the biological basis of complex disease, new
1714 targeted therapies are being developed. For these new
1715 treatments that show remarkable benefit early in development,
1716 the traditional approach may not be appropriate. Currently,
1717 there are no clear guidelines to expedite subsequent studies
1718 that would generate the needed evidence and minimize the
1719 number of patients who would need to be assigned to the
1720 current standard of care.

1721 In order to address this, Congress should establish a
1722 mechanism that would allow the FDA to designate a new
1723 compound that shows substantial clinical activity in early-
1724 phase trials as a breakthrough product. Upon designation,
1725 the sponsor, working closely with FDA, would develop trial
1726 designs to abbreviate or combine traditional phases of

1727 development. This would avoid giving larger numbers of
1728 patients a potentially harmful or ineffective drug as part of
1729 a control arm while maintaining current safety and efficacy
1730 standards. This establishment of this new designation would
1731 help FDA respond to highly innovative new medicines quickly
1732 and consistently across the agency as well as to communicate
1733 and encourage drug developers to pursue trial designs that
1734 are able to show potential benefit earlier in development.

1735 I conclude my remarks today by reiterating that rigorous
1736 FDA standards cannot be compromised. The FDA should be given
1737 the ability to respond to cutting-edge science and the most
1738 promising therapies through an enhanced Accelerated Approval
1739 mechanism and a breakthrough product designation.

1740 I thank you for your time and I am happy to answer any
1741 questions you may have.

1742 [The prepared statement of Mr. Allen follows:]

1743 ***** INSERT 3 *****

|
1744 Mr. {Pitts.} The Chair thanks the gentleman.

1745 The Ranking Member and I have consulted. The last time
1746 we did, we missed a vote, so we had better break at this
1747 point. We will recess and come back to the panel as soon as
1748 the last vote of the series is over. The Subcommittee stands
1749 in recess.

1750 [Recess.]

1751 Mr. {Pitts.} Time of recess having expired, we will
1752 reconvene, and the Chair recognizes Dr. Eisenstein for 5
1753 minutes for an opening statement.

|
1754 ^STATEMENT OF BARRY EISENSTEIN

1755 } Dr. {Eisenstein.} Chairman Pitts, Ranking Member
1756 Pallone and members of the Subcommittee, thank you for the
1757 opportunity to testify today on the urgent need to spur
1758 greater innovation and accelerate the development of new
1759 antibiotics to combat the threat of drug-resistant pathogens.
1760 I am Dr. Barry Eisenstein, Senior Vice President of
1761 Scientific Affairs, Cubist Pharmaceuticals, a company focused
1762 on the research and commercialization of antibiotics.
1763 Headquartered in Lexington, Massachusetts, we currently
1764 market Cubicin, a first-line intravenous antibiotic for the
1765 treatment of methicillin-resistant staphylococcus aureus,
1766 better known as MRSA.

1767 Mr. Chairman, on behalf of patients and health care
1768 experts alike, I wish to commend the Subcommittee for holding
1769 this hearing and for the leadership of Congressmen Gingrey
1770 and Green and others for the introduction of the Generating
1771 Antibiotic Incentives Now, or GAIN Act of 2011. The
1772 bipartisan GAIN Act would directly promote the research and
1773 commercialization of new drugs and diagnostics against
1774 resistant pathogens. It offers our best hope to stimulate
1775 American innovation, particularly within small and mid-market

1776 companies, and strengthen the hand of clinicians and
1777 scientists in the fight against drug-resistant pathogens both
1778 here and abroad.

1779 Annually, at least 1.7 million Americans acquire a
1780 bacterial infection in the hospital and nearly 100,000 of
1781 them die, and we have heard the heartbreaking stories. A
1782 young high school football player loses his life to a bathe
1783 with MRSA, the woman who just had mastectomy surgery acquires
1784 a resistant post-op infection and goes into kidney failure.
1785 ICU patients in American hospitals and our troops in the
1786 Middle East alike are suffering untreatable Acinetobacter
1787 infections at alarming rates, referred to earlier as
1788 Iraqibacter. Two years ago, the U.S. Air Force testified on
1789 the challenging epidemic of multi-drug-resistant infections
1790 that has resulted in a shortage of safe and effective
1791 antibiotics.

1792 Just as antimicrobial resistance is rising, we are faced
1793 with a disturbing and dangerous lack of new antibiotic drugs,
1794 particularly against Gram-negative bacteria. The Pew
1795 Charitable Trust warns us that the antibiotic pipeline is
1796 dwindling and a global crisis looms. This threatens much of
1797 modern medicine because antibiotics are crucial from surgical
1798 recovery to cancer treatment. As Dr. William Evans, the CEO
1799 of St. Jude's Children's Research Hospital noted, ``We don't

1800 want to find ourselves in a situation in which we have been
1801 able to save a child's life after cancer diagnosis only to
1802 lose them to an untreatable multi-drug-resistant infection.

1803 The antibiotic pipeline is running dry because
1804 antibiotics uniquely are wasting assets. Bacteria evolve so
1805 quickly that the development of resistance is inevitable.
1806 Thus, each new antibiotic has only a finite lifespan.
1807 Appropriate stewardship is an important component of
1808 antibiotic use. That said by itself doesn't increase the
1809 supply of new compounds. Because antibiotics are used for
1810 acute conditions and for a short period, much of the
1811 biopharmaceutical industry does not invest in antimicrobial
1812 development and has instead turned its efforts to products
1813 aimed at more chronic diseases.

1814 The GAIN Act is targeted at precisely this problem. By
1815 building on current law and extending the new drug
1816 exclusivities created by the 1984 Hatch-Waxman Amendments
1817 only for urgently needed antibiotics, it would dramatically
1818 improve the prospects for tracking new investments for the
1819 development and approval of new antibiotics so needed by our
1820 patients. The act would send a powerful signal to scientists
1821 and investors exploring new molecules and forming new
1822 companies as well as to large established biopharmaceutical
1823 companies that Congress recognizes the unique challenge in

1824 this area and is opening the door to new innovation, new
1825 investigations and greater investor interest. The enhanced
1826 exclusivity for antibiotics as well as the straightforward
1827 designation of qualified infectious disease products is based
1828 on what Dr. Janet Woodcock of the FDA recently described as
1829 the wildly successful Orphan Drug Act.

1830 Mr. Chairman, this Committee has a unique opportunity to
1831 take timely action against a serious public health threat.
1832 The market failure that has strained our pipeline of
1833 important new antibiotics remains. I urge the members of the
1834 Subcommittee to move the GAIN Act through Committee and enact
1835 it into law during this 112th Congress.

1836 Thank you for the opportunity to testify today. I look
1837 forward to your questions.

1838 [The prepared statement of Dr. Eisenstein follows:]

1839 ***** INSERT 4 *****

|

1840 Mr. {Pitts.} Thank you, Dr. Eisenstein.

1841 Dr. Powers, you are recognized for 5 minutes for an

1842 opening statement.

|
1843 ^STATEMENT OF JOHN H. POWERS

1844 } Dr. {Powers.} Good afternoon. Thank you for inviting
1845 me to testify today. My name is John Powers, and I am a
1846 practicing infectious disease and internal medicine physician
1847 and a medical researcher who actively cares for patients. I
1848 was a scientist at FDA for almost a decade, and while there,
1849 I was one of the co-chairs of the Interagency Task Force on
1850 Antimicrobial Resistance.

1851 I would like to share with you today my perspectives as
1852 a clinician, researcher, and having been a patient myself on
1853 appropriately developing incentives for antibiotics where
1854 there is the greatest need. My remarks are my own views, and
1855 I am not representing any agency or organization, but I am
1856 here speaking on behalf of the patients for whom I care.
1857 Several patients and consumer and public health groups have
1858 expressed the same views as I will present here today.

1859 Government intervention is needed to spur antibiotic
1860 development because antibiotics are less profitable for drug
1861 companies than other therapeutic areas resulting in decreased
1862 investment. The Generating Antibiotic Incentives Now, or
1863 GAIN bill, provides those incentives to develop new
1864 antibiotics.

1865 In any policymaking, as in science, one must first
1866 outline the problem, then come up with potential solutions
1867 while minimizing unintended consequences, implement that
1868 policy, and then measure whether it has its intended effects.
1869 The problem of serious diseases for which there are no
1870 effective therapies has been well outlined. The question now
1871 is, how best can GAIN address these problems. If the public
1872 to make an investment on new antibiotics, the public should
1873 get something of measurable value in return while not
1874 worsening the problem of antibiotic resistance. Several
1875 changes to GAIN might help it focus to best address public
1876 health needs while limiting potential adverse consequences.

1877 First, GAIN should focus on patients and their diseases
1878 rather than organisms. I have never had a patient tell me
1879 their E. coli hurts or that their Klebsiella is killing them.
1880 Patients present with disease syndromes like pneumonia, and I
1881 have certainly heard enough people in this room coughing
1882 today to show that symptoms are a problem.

1883 The human body contains more bacterial than human DNA,
1884 and organisms do not cause problems for patients until they
1885 cause disease. In fact, the word ``pathogen'' implies
1886 pathology and disease. Any list of organisms in the bill
1887 would be quickly outdated and hard for FDA to implement. In
1888 addition, FDA regulations appropriately point out that drugs

1889 are approved for recognized diseases or conditions, and
1890 organisms are neither. Use of antibiotics to eliminate
1891 organisms in the absence of disease would paradoxically
1892 increase antibiotic resistance.

1893 Second, GAIN should focus on the treatment of serious
1894 and life-threatening diseases where lack of safe and
1895 effective therapies results in death or serious disability.
1896 Antibiotic resistance in the test tube has little effect on
1897 patients who would recover without antibiotics but it is
1898 inappropriate use in these settings that has worsened
1899 antibiotic resistance. Despite efforts by CDC, FDA and
1900 others, a substantial portion of antibiotic prescriptions are
1901 still not warranted, provide no benefits to patients and
1902 cause the problem of antibiotic resistance we are trying to
1903 control.

1904 Third, there should be valid scientific evidence based
1905 on FDA's standard of substantial evidence from adequate and
1906 well-controlled trials that these drugs actually unmet
1907 medical needs. In 1979 landmark Supreme Court case, Thurgood
1908 Marshall pointed out that people with terminal diseases
1909 should not receive less protection under the law from unsafe
1910 and ineffective drugs than persons with curable diseases.
1911 Test tube and animal studies are helpful in choosing drugs to
1912 study in people, but people are not rodents. The complexity

1913 of the human body is totally humbling. Three-fourths of
1914 antibiotics submitted to FDA for review with promising test
1915 tube and animal studies ultimately fail to show safety and
1916 efficacy in human disease. Approving antibiotics today
1917 hoping for some future promise makes no sense as resistance
1918 is inevitable with all antibiotics, sometimes occurring
1919 before the drug is even marketed. There is no guarantee that
1920 a drug approved today will address resistance tomorrow. In a
1921 study from Boston, almost half of antibiotics approved since
1922 1980 have disappeared from the market, either because of
1923 safety and efficacy issues or because of poor sales because
1924 they did not address public health needs. Therefore, numbers
1925 of drugs approved is not a measure of public health benefits.

1926 Fourth, we need new tools to evaluate antibiotics that
1927 will make trials more efficient and less expensive for
1928 companies to perform. Determining who needs and who does not
1929 need antibiotics and developing better outcome measures to
1930 evaluate directly how patients feel and function are urgently
1931 needed so we can get the valid evidence we need to know if
1932 the drugs actually meet unmet medical needs.

1933 Fifth and finally, any incentives should go hand and
1934 hand with programs for appropriate stewardship of
1935 antibiotics. For any scarce resource, conservation should
1936 accompany increased production. Unfortunately, we as

1937 physicians have been only moderately successful at policing
1938 ourselves to appropriately use antibiotics but greater
1939 efforts are underway. FDA should be given the authority to
1940 develop strategies to evaluate and ensure appropriate
1941 antibiotics where they are most needed and to minimize
1942 antibiotic resistance. An HHS-level internal group to
1943 address issues related to antibiotic resistance would help
1944 strengthen ongoing efforts of the interagency task force.

1945 Focusing the GAIN bill on the five ways I have just
1946 outlined will result in addressing the goals it sets out to
1947 achieve: developing new and safe antibiotics with an
1948 appropriate evidence base to positively affect patients'
1949 lives while simultaneously limiting antibiotic resistance.

1950 Thank you very much.

1951 [The prepared statement of Dr. Powers follows:]

1952 ***** INSERT 5 *****

|
1953 Mr. {Pitts.} Thank you, Dr. Powers.

1954 Mr. Walsh, you are recognized for 5 minutes.

|
1955 ^STATEMENT OF MICHAEL WALSH

1956 } Mr. {Walsh.} Thank you. Mr. Chairman, Mr. Ranking
1957 Member, thank you for inviting me to testify today. My name
1958 is Mike Walsh. I am President of LifeGas. This is part of
1959 Linde North America. We are headquartered in New Jersey. We
1960 have about 4,500 employees in the United States.

1961 I am here today to testify on behalf of the Compressed
1962 Gas Association, of which we are a member. CGA represents
1963 companies engaged in the manufacture and distribution of
1964 compressed gases including medical gases.

1965 The Compressed Gas Association was founded in 1913 and
1966 currently has more than 120 member companies. CGA serves as
1967 a safety standard-setting organization for the medical gas
1968 industry. The medical gas companies in our coalition employ
1969 about 21,000 employees and have around 4,500 locations, half
1970 of which are small businesses. I personally entered into
1971 this industry, the medical gas industry, as a small business
1972 owner.

1973 Linde and other members of the Compressed Gas
1974 Association provide medical gases that are used by doctors,
1975 primarily for respiratory care. You can find our products in
1976 hospitals, clinics, doctors' offices and in homes across the

1977 country.

1978 On behalf of the CGA, I want to offer my thanks to
1979 Congressman Leonard Lance and Chris Murphy for introducing
1980 the Medical Gas Safety Act. Your leadership role in this
1981 issue has been pivotal. I also want to thank Chairman Pitts
1982 and Ranking Member Pallone for your willingness to address
1983 these issues in the very important bill you are working now.
1984 Naturally, I also want to thank Chairman Upton and Ranking
1985 Member Waxman of the Full Committee as well.

1986 Medical gases like oxygen are used by medical
1987 practitioners as prescription drugs every day. We have over
1988 a million patients using it in a variety of conditions.
1989 Medical oxygen has been used for more than a century.
1990 Medical gases were in use for decades before the FDA was
1991 created and a New Drug Application process was initiated.
1992 And here is the really key point. Medical gases have a long,
1993 long history of safe and effective use. The most common ones
1994 are derived today, things we are breathing today. These
1995 common medical gases are a unique class of drug products that
1996 are different from traditional pharmaceuticals in a lot of
1997 ways. We have different properties than pharmaceutical
1998 drugs. We have a different delivery method. We have a
1999 different manufacturing process. We have a different type of
2000 container that holds the product. Medical gas manufacturers

2001 make no medical claims for medical gases, which is very
2002 different for traditional prescription drugs.

2003 However, the FDA currently regulates medical gases with
2004 the same regulatory system as traditional pharmaceuticals.
2005 This has created significant and growing regulatory issues.
2006 These practical issues create uncertainty and drive up
2007 compliance costs for our industry. Medical gases need a
2008 separate regulatory system that takes into account these
2009 unique characteristics.

2010 The Medical Gas Safety Act addresses a number of
2011 critical regulatory issues facing the medical gas industry.
2012 It establishes an appropriate approval process for medical
2013 gases. It requires the creation of separate regulations for
2014 medical gases. It ensures that FDA fees do not
2015 disproportionately impact medical gas manufacturers, many of
2016 whom are small businesses. This legislation will create
2017 regulatory certainty for our industry. It will ensure that
2018 patients in the medical community have access to these
2019 lifesaving products. It will remove current uncertainty
2020 regarding the federal regulations of medical gases for
2021 federal and State inspectors.

2022 The FDA has recognized the unique nature of medical
2023 gases for a very long time. Until now, the FDA has generally
2024 used its enforcement discretion not to require medical gases

2025 to go through the New Drug Application process. Recently,
2026 the FDA began the Unapproved Drugs Initiative, which is
2027 intended to eliminate all unapproved drugs from the
2028 marketplace including medical gases. If the Unapproved Drugs
2029 Initiative is applied to medical gases, this would remove
2030 access for patients to gases as simple as oxygen.

2031 Recent changes in enforcement policies related to the
2032 export of unapproved drugs have also created serious
2033 challenges for our industry. Also, the regulatory system in
2034 place for medical gases does not take into account the unique
2035 characteristics of medical gases. In response to concerns
2036 raised by the Compressed Gas Association, the FDA stated in
2037 1976 in the preamble to the original Current Good
2038 Manufacturing Practices rulemaking that they intend to
2039 develop separate regulations for medical gases. No such
2040 regulations have been developed.

2041 This legislation will provide a clear, targeted
2042 regulatory structure for medical gases, creating a process
2043 for medical gases to become approved drugs and establishing
2044 specific regulations for medical gases which will reduce
2045 uncertainty, improve compliance and improve safety in what is
2046 already a very safe industry.

2047 I applaud all of you again for your willingness to
2048 address these important and longstanding regulatory issues.

2049 Thanks again on behalf of the CGA for the opportunity to
2050 testify.

2051 [The prepared statement of Mr. Walsh follows:]

2052 ***** INSERT 6 *****

|
2053 Mr. {Pitts.} Thank you. Thank you for your testimony.
2054 The Chair thanks the panel for being patient waiting while
2055 the members voted. We will now begin questioning, and I will
2056 recognize myself for 5 minutes for that purpose.

2057 Dr. Maraganore, in your testimony, you cite the success
2058 of FDA's Accelerated Approval pathway for HIV and AIDS and
2059 cancer treatments but indicate the Accelerated Approval
2060 framework has done little to help expedite treatments for
2061 rare diseases. Can you elaborate on why the accelerated
2062 pathway has not led to gains in the rare-disease space that
2063 you would all like to see?

2064 Mr. {Maraganore.} Yes. I think it really speaks back
2065 to the comments that Dr. Woodcock in terms of the clarity
2066 around the utility and the usefulness of the Accelerated
2067 Approval process for diseases outside of cancer and HIV/AIDS,
2068 and clearly what I think is being proposed in Congressmen
2069 Stearns's and Towns's proposal is a way of significantly
2070 enhancing and modernizing our understanding of Accelerated
2071 Approval to the point where it will be used more frequently,
2072 I would expect, for the purposes of rare or orphan diseases
2073 where there significant unmet medical need and certainly an
2074 important desire I think for patients and physicians to have
2075 access to medicines faster.

2076 Mr. {Pitts.} Now, some experts believe that FDA is
2077 seeking to limit the use of Accelerated Approval for cancer
2078 drugs. Is this the case? Rather than narrowing the use of
2079 Accelerated Approval in cancer, shouldn't we be looking for
2080 ways to expand it, and what should Congress to prevent FDA
2081 from limiting its use?

2082 Mr. {Maraganore.} I think there has been some concern
2083 around potential changes within the FDA's views on how
2084 Accelerated Approval would be used in cancer based on some
2085 hearings that were held about this time last year. You know,
2086 clearly, the FDA has used this approach for cancer-based
2087 medicines. We believe that the FDA will continue to do so.
2088 I think our desire is really to see it expanded and clarified
2089 as a system while very importantly maintaining the safety and
2090 efficacy standards that exist today for the approval of
2091 medicines.

2092 Mr. {Pitts.} And how would the FAST Act incentivize
2093 research and development of innovative therapies and
2094 treatments for serious diseases?

2095 Mr. {Maraganore.} Well, clearly, the ability of having
2096 a clear and established framework whereby medicines in the
2097 context of very serious unmet medical needs can be approved
2098 through an Accelerated Approval pathway would certainly
2099 encourage the investment that is needed to ultimately bring

2100 these types of products to the marketplace. Clearly,
2101 innovative medicines are increasingly being discovered by,
2102 you know, young companies like ours, of which there are many
2103 in this country, in a very vibrant industry but this industry
2104 as been challenged by the increasing time it takes to get
2105 drugs to the marketplace and the increasing costs, and
2106 Accelerated Approval in the context of very serious unmet
2107 medical needs would provide a framework for getting drugs to
2108 patients faster in a way that would be more acceptable to the
2109 investors that have to put capital at risk to ultimately
2110 bring these products to market.

2111 Mr. {Pitts.} Thank you.

2112 Dr. Eisenstein, while the threat of antibiotic drug
2113 resistance is a looming public health crisis, the drug
2114 development pipeline has not kept pace with this threat.
2115 What can we do to turn this around?

2116 Dr. {Eisenstein.} Thank you for your question, Mr.
2117 Chairman. I believe that the GAIN Act as presently
2118 formulated provides us with precisely the right tools to
2119 provide the incentives needed. To cite Dr. Woodcock's
2120 earlier testimony: ``We need economic incentives beyond the
2121 regulatory ones for these bad bugs.'' Industry needs a clear
2122 pathway to the market. I could not have said that better
2123 myself, and when one looks at the enormous success of the

2124 Orphan Drug Act that was enacted in 1983, the Office of the
2125 Inspector General in reviewing that in 2001 declared, A, that
2126 it was extraordinarily successful in enabling at the time
2127 over 200 new drugs. We are now over 350 new drugs through
2128 the Orphan Drug Act. But I would say equally importantly,
2129 they pointed out that the increased market exclusivity was
2130 the most important determinant of the success of that
2131 program. So I believe we have everything we need in the GAIN
2132 Act as it presently written.

2133 Mr. {Pitts.} Thank you.

2134 Mr. Walsh, I understand that FDA regulation has caused
2135 problems for many in the medical gas business. Many of these
2136 are small businesses. Can you explain how and why FDA
2137 regulation has caused these problems?

2138 Mr. {Walsh.} Yes. Thank you. I was one of those small
2139 business owners, and when I had started this business, we
2140 were under the guidelines of a grandfathered product, and if
2141 I would have known today what I had known back then, I would
2142 not have started this business. We went on and created
2143 through our employees a great organization with nearly 1,000
2144 employees but we are marketing, distributing and selling an
2145 unapproved drug, and so you are asking to invest in that and
2146 then the regulations if we were forced to go under a strict
2147 pharmaceutical standard would be too expensive for the small

2148 companies to follow.

2149 Mr. {Pitts.} My time is expired. The Chair recognizes
2150 the Ranking Member for 5 minutes for questions.

2151 Mr. {Pallone.} Thank you, Mr. Chairman.

2152 I wanted to ask Dr. Allen a question and then I wanted
2153 to ask Dr. Powers a question. Let me start with Dr. Allen.
2154 I think we all agree that FDA needs to be able to be flexible
2155 in determining approval requirements and we have heard from
2156 Dr. Woodcock and your testimony, there is ample evidence that
2157 FDA does in fact use its authority in a flexible manner, and
2158 that has enabled FDA to get important drugs through the
2159 regulatory process in a timely manner and some circumstances
2160 based on quite limited data. That being said, I recognize
2161 there can be advantages to clarifying and improving some of
2162 FDA's authorities to facilitate its use of Accelerated
2163 Approval pathways, and I think the pathway you propose for
2164 breakthrough therapies deserves serious consideration as does
2165 the pathway put forward in the FAST Act by Representatives
2166 Stearns and Towns and the Special Population Limited Use
2167 pathway proposed by IDSA in its submitted testimony.

2168 My main concern, Dr. Allen, is about any proposal to
2169 help speed new therapies to market is that it doesn't lower
2170 the safety or effectiveness standards by which FDA approves
2171 new medicines. Now, I know you mentioned that you don't want

2172 to--I think you actually said in your testimony ``I don't
2173 want to lower the safety or effectiveness standards.'' But I
2174 just wanted you to basically expand on that a little. Do you
2175 agree that whatever improvements we make--well, you said that
2176 you don't think they should lower the safety and
2177 effectiveness standards but if you would spend a little time
2178 just giving me some more information on that.

2179 Mr. {Allen.} Well, thank you for the question. First
2180 of all, I absolutely agree that the current standards of
2181 safety and efficacy that have been in place for decades need
2182 to continue to be upheld, first and foremost. I think the
2183 difference in what we are proposing here through the idea of
2184 a breakthrough designation, it is important to distinguish
2185 that Accelerated Approval is an approval mechanism where the
2186 breakthrough is a designation or a process-oriented question,
2187 and what we are seeing, and I am most familiar with oncology,
2188 of course, is that there are new drugs being developed that
2189 are highly targeted and being used in select populations
2190 where they achieve the greatest benefit and the lowest amount
2191 of toxicity, and in those cases, the traditional development
2192 plan of a phase I followed by a phase II followed by a phase
2193 III trial may not always be appropriate, and there may be
2194 ways to expedite that, and we have worked with several expert
2195 groups including the National Cancer Institute, the FDA, the

2196 Brookings Institute and others to look at those strategies,
2197 and while it was mentioned that there may not need to be new
2198 law, I think that the 1.5 million Americans that will hear
2199 the words ``you have cancer'' this year would appreciate
2200 looking at all policies that will help expedite promising new
2201 therapies to them quickly.

2202 Mr. {Pallone.} Well, thank you.

2203 Now, Dr. Powers, one of the things you alluded to is the
2204 issue of making sure the use of antibiotics is targeted to
2205 infections for which they are actually useful and making sure
2206 that the patients actually have those infections. One
2207 feature currently included in the GAIN Act is the
2208 availability of 6 months of additional exclusivity for an
2209 antibiotic if its manufacturer develops a companion
2210 diagnostic test to use with a new antibiotic. I understand
2211 that in order to really accomplish the goal of directing new
2212 antibiotics to the right patients, a test would have to help
2213 identify where in the body an infection is, what kind of
2214 bacteria is causing it, and should suggest or ensure that the
2215 antibiotic in question is an appropriate treatment for the
2216 infection. Did I get that right? Can you tell me more about
2217 whether you think it is possible to develop tests that
2218 accomplish this and how to make sure that we are not giving
2219 additional incentives for tests that may not help us conserve

2220 precious antibiotics?

2221 Dr. {Powers.} That is correct, and I think it gets back
2222 to the issue of disease versus just harboring an organism in
2223 your body. So if we were to develop diagnostics that merely
2224 tell you that you have an organism on your nose, that
2225 wouldn't help us if we then treat all those people when that
2226 treatment wouldn't help. On the other hand, if we
2227 specifically develop diagnostics to show that people have a
2228 disease, that would be more helpful, and through the current
2229 510(k) process that FDA utilizes for medical devices, you
2230 don't necessarily need to show anything other than you can
2231 detect an organism. So we would need to go beyond that and
2232 actually have helpful information, not only for clinical
2233 trials so we can enroll the right people but also those could
2234 be useful in practice as to who to direct antibiotics to and
2235 who not to treat.

2236 Mr. {Pallone.} But you think it is possible to develop
2237 tests that accomplish this, right?

2238 Dr. {Powers.} I think the technology is there, and I
2239 think that is why it is helpful to develop incentives that
2240 would help people to do this.

2241 Mr. {Pallone.} Thank you.

2242 Mr. Chairman, if I could ask--I know we gave this to you
2243 a little while ago, ask unanimous consent to include in the

2244 record the statement of the Infectious Diseases Society of
2245 America?

2246 Mr. {Pitts.} Without objection, so ordered.

2247 Mr. {Pallone.} Thank you.

2248 [The information follows:]

2249 ***** COMMITTEE INSERT *****

|
2250 Mr. {Pitts.} I thank the gentleman and recognize the
2251 gentleman from Georgia, Dr. Gingrey, for 5 minutes for
2252 questions.

2253 Dr. {Gingrey.} Mr. Chairman, thank you. I am going to
2254 start out with Dr. Eisenstein. I almost said Dr. Einstein
2255 after reading his résumé and I am most impressed with that.

2256 Dr. Powers testified that almost half of antibiotics
2257 approved since 1980 have disappeared from the market, either
2258 because of safety and efficacy issues or because of poor
2259 sales because the drug did not address public health needs.
2260 This is a question. Do you agree with Dr. Powers that
2261 current FDA oversight of antibiotics and the reality that
2262 market forces such as poor sales will help ensure generally
2263 that only those drugs that provide an unmet need will
2264 ultimately find their way to the market, or most importantly,
2265 be financial wins for the drug companies? Is that enough?

2266 Dr. {Eisenstein.} Well, I agree that for a drug to be
2267 successful needs to demonstrate utility with patients. What
2268 the FDA process does is provide evidence of efficacy and
2269 safety. It doesn't translate necessarily to effectiveness,
2270 which is what happens in the broad population. That said,
2271 with the enormity of medical need that we presently have with
2272 the enumerated organisms plus others that I can talk about if

2273 you like, there is clearly a medical need and there is
2274 clearly a market failure in terms of being able to provide
2275 the appropriate incentives for companies to be able to make
2276 the investments in antimicrobials, and it appears that all of
2277 my colleagues on this Committee are in complete agreement
2278 with that notion. That is again why I feel the GAIN Act as
2279 presently designated does provide exactly that sort of
2280 assistance.

2281 Dr. {Gingrey.} Well, I thank you for that, and there
2282 was one part of Dr. Powers' testimony, and maybe he will have
2283 time, Mr. Chairman, to respond to this as well, but I want to
2284 stay with Dr. Eisenstein for just a second. In regard to
2285 your comments in your testimony about the GAIN Act, the fact
2286 that we have been working on it for a number of years, it has
2287 wide bipartisan support, especially here on the Health
2288 Subcommittee of Energy and Commerce and listing these
2289 pathogens, these known pathogens, and I reference that in my
2290 opening remarks, whether it is MRSA or whether it is some
2291 Gram-negative--we talked about the Iraqibacter problem with
2292 the troops returning from Operation Iraqi Freedom and other
2293 conflicts. It is important, I think, and I think you pointed
2294 it out, that these are known pathogens.

2295 Now, Dr. Powers is suggesting that nobody comes in and
2296 says oh, this Klebsiella is killing me or I can't stand this

2297 Iraqibacter--you know, they say well, I am coughing and I
2298 think I may have pneumonia or I have got this horrible skin
2299 infection and my skin is sloughing off--to make a case for I
2300 guess some change to this carefully worked on piece of
2301 legislation, the GAIN Act, and to me, if I could make an
2302 analogy in the criminal justice system to say that if you
2303 have got a known thief out there that you don't make every
2304 effort to apprehend him or her, but rather you take all your
2305 law enforcement and your security measure and you pick two or
2306 three banks in the local neighborhood to protect because
2307 those are the areas where he might strike next. I don't know
2308 if that is a great analogy but I hope everybody understands
2309 the point I am trying to make. What say you about that? And
2310 then I will go to Dr. Powers and let him comment on that.

2311 Dr. {Eisenstein.} It is absolutely true what Dr. Powers
2312 says, that bugs by themselves don't mean that one has
2313 disease. If I were to look around the room here, that may
2314 be, what, 50 or 80 folks in the room, probably 20 of us have
2315 staph aureus and maybe 30 of us have staph aureus in our
2316 noses right now, and that about a third of the people that
2317 walk in this room have staph in their noses all the time, and
2318 the two-thirds left, about half of those have staph that come
2319 and go at various times, and we are seeing increasing numbers
2320 of those staph being MRSA staph. So perhaps 10 of us are

2321 walking around with MRSA staph in our noses right now, and
2322 yet, as an infectious disease physician, I wouldn't think
2323 about treating any of us for any of that. One has to have a
2324 condition, a disease, that says I am an infection causing a
2325 problem for this patient that goes along with certain
2326 manifestations. If it is pneumonia, the patient will have
2327 cough, will have shortness of breath, will have chest pain,
2328 will have fever. There are a constellation of methods that
2329 one can detect that. You are a physician as well. You
2330 understand that one makes the diagnosis based on what the
2331 patient shows, what the patient is saying, what your own
2332 examination of the patient shows.

2333 That said, if the patient appears to have a pneumonia
2334 and you are able to recover a pure culture of staph aureus
2335 from the expectorated sputum, you know that the patient is
2336 suffering from staphylococcal pneumonia, and every hour that
2337 goes by that you don't treat that patient, the likelihood of
2338 the patient dying goes up significantly, and if we don't get
2339 drugs on board fast enough, we may lose 25 to 30 percent of
2340 even relatively healthy individuals.

2341 Dr. {Gingrey.} To put it in really simple terms, and I
2342 know I am beyond my time, Mr. Chairman, I appreciate it, I
2343 will yield back, but it is like closing the barn door after
2344 the horse is long gone, so I thank you very much for that

2345 response.

2346 Dr. Powers, I apologize. I didn't have time to go you.

2347 Mr. {Pitts.} Dr. Powers, if you would like to respond?

2348 Dr. {Powers.} Sure, I would. I mean, I understand what
2349 you are saying. To use your thief analogy would be sort of
2350 like saying--and first I want to say, I think everyone is
2351 very appreciative about GAIN because we absolutely need to do
2352 something about this, and I think the question that I tried
2353 to bring up in my testimony is, can we focus the bill so we
2354 make sure that we do what we think we want to do without
2355 causing more harm. So I guess the concern is that, you know,
2356 if you see a bank robber and he is wearing a blue coat and
2357 the police say we are going to go out and arrest everybody
2358 who is wearing a blue coat, and so the thing that Dr.
2359 Eisenstein brought up is, these same organisms can cause
2360 less-serious disease and they can also cause more-serious
2361 disease.

2362 And Dr. Gingrey, all the diseases listed when you spoke
2363 earlier to Dr. Woodcock, they are all serious ones, but FDA
2364 actually has approved 64 new drug applications for these same
2365 kinds of organisms for non-serious, non-life-threatening
2366 diseases since 1980. So that is why I think the history
2367 shows, and also those are the more profitable areas to go
2368 because those less-severe infections are more common in

2369 patients. So I think that is the issue of trying to focus it
2370 to--we are all talking about serious and life-threatening
2371 diseases here. The question is if that is what we are
2372 talking about, could we actually focus the bill to that.

2373 Mr. {Pitts.} The Chair thanks the gentleman and
2374 recognizes the Ranking Member of the Full Committee, Mr.
2375 Waxman for 5 minutes for questions.

2376 Mr. {Waxman.} Thank you very much, Mr. Chairman.

2377 Dr. Powers, let me pursue that issue with you. The GAIN
2378 Act seeks to create incentives that would prompt drug
2379 companies to develop and market new antibiotics.
2380 Specifically, it would give 5 years additional exclusivity if
2381 a company gets a new antibiotic approved. If we are talking
2382 about giving such a generous reward to companies, I think we
2383 need to ensure that two things are in place at a minimum.
2384 First, we need to make sure that we are only providing
2385 exclusivity for the kinds of drugs that will truly benefit
2386 the public health. Only antibiotics to treat dangerous
2387 infections for which we do not already have effective
2388 treatment should be covered in my opinion.

2389 As currently written, the bill would provide exclusivity
2390 for drugs if they are targeted to treat specified bacteria.
2391 Some including you have expressed concern that this kind of
2392 model is both inappropriate and unusual for the FDA, and have

2393 instead suggested that we look at targeting drugs that treat
2394 specific infections instead of just bacterial species. More
2395 significantly, some believe that GAIN should be limited to
2396 new antibiotics for treating serious infections for which
2397 there is an unmet medical need. Can you explain a bit more
2398 about why focusing on specific infections is appropriate and
2399 why we should reserve incentives for drugs that treat serious
2400 infections with unmet medical need?

2401 Dr. {Powers.} Again, I think the issue is that
2402 antibiotics can be used to treat a wide array of infections
2403 caused by the same exact organism, and I can give an example
2404 of when I worked at FDA, several companies came in asking for
2405 indications for pneumonia that was caused by multi-drug-
2406 resistant organisms. Now, that was completely appropriate.
2407 At the same time, they asked for approval for multi-drug-
2408 resistant organisms for sinus infections and ear infections
2409 in kids and other things that predominantly get better on
2410 their own, sometimes even without antibiotics. So the
2411 history of what has happened before shows that--and in a
2412 sense, you can't blame a company for asking. FDA didn't
2413 grant those, though, because they applied the same exact
2414 standard that we are talking about today. It is not clear
2415 whether resistance in the test tube has much of an impact on
2416 patient outcomes in a disease where people will get better

2417 anyway. So it seems to make sense to focus on the areas of
2418 where when you have a resistant disease, that is what is
2419 going to kill you.

2420 The other thing is that this sort of comports with
2421 everything that FDA has ever done in the past related to
2422 providing incentives. Priority Review, Accelerated Approval
2423 that we are talking about today, and Fast Track designation
2424 as well as subpart E approvals all are based on serious and
2425 life-threatening diseases, unmet medical needs and added
2426 benefit above available therapies. So it fits in with the
2427 regulatory paradigm already, which of course would make it
2428 easier to implement as well.

2429 Mr. {Waxman.} Well, the second thing I think needs to
2430 be in place is a robust stewardship program. We need to make
2431 sure that any antibiotics that are approved under this kind
2432 of new system are protected once they are on the market. We
2433 have seen far too many antibiotics lose their effectiveness
2434 because the bugs they seek to treat become resistant, and
2435 that is a problem caused in large part by overuse of these
2436 drugs. So we need to make sure that doesn't happen with
2437 these new antibiotics that we have all invested so much in,
2438 after all. When extended exclusivity is granted, we all pay
2439 higher drugs for a longer period of time. Do you agree with
2440 that concept?

2441 Dr. {Powers.} I think that is absolutely key, and they
2442 have to go hand in hand. To pass something about giving
2443 incentives to develop new drugs now hoping that we will
2444 approve something about stewardship later probably doesn't
2445 make a whole lot of sense. These really need to be linked to
2446 each other because developing new drugs without the ability
2447 to use them in the appropriate places they need to be used is
2448 really a dangerous thing. That is kind of how we got to
2449 where we are today.

2450 Mr. {Waxman.} Can you elaborate more on what ideas you
2451 have about stewardship?

2452 Dr. {Powers.} I think that there is--I put a couple in
2453 my testimony in terms of how I think that allowing FDA to
2454 have the authority to designate where drugs should be used
2455 appropriately is a big step. In the past, FDA has had the
2456 authority to restrict drugs where they weren't safe and
2457 effective. Here we would be saying well, maybe these drugs
2458 could be used in less life-threatening diseases but we really
2459 think they ought to be reserved for these specific serious
2460 diseases. That would be novel. So I think giving FDA the
2461 authority to do that would be really important.

2462 The other thing is, having been on the Interagency Task
2463 Force myself, I know somebody said to me once, you know, it
2464 is different when it is your 25th job at the bottom of your

2465 list of things to do versus you come into work and every day
2466 and that is exactly what you have to focus on. So I think
2467 developing an HHS-level internal group that consists of
2468 agencies that address this problem might highlight the issues
2469 associated with antibiotic resistance and allow people to
2470 spend their time focusing on it.

2471 Mr. {Waxman.} Thank you very much.

2472 Mr. {Pitts.} The Chair thanks the gentleman and
2473 recognize the gentleman from New Jersey, Mr. Lance, for 5
2474 minutes for questions.

2475 Mr. {Lance.} Thank you, Mr. Chairman.

2476 Mr. Chairman, I ask unanimous consent to place in the
2477 record letters of support for the Medical Gas Safety Act from
2478 the Compressed Gas Association and three manufacturers: Air
2479 Products, Air Gas and Tri-Gas.

2480 Mr. {Pitts.} Without objection, so ordered.

2481 [The information follows:]

2482 ***** COMMITTEE INSERT *****

|
2483 Mr. {Lance.} Thank you, Mr. Chairman.

2484 To Mr. Walsh, can you give the Committee a couple
2485 examples of why FDA's current regulations are not a good fit
2486 for medical gases?

2487 Mr. {Walsh.} Sure. I think first of all, I would like
2488 to--because I don't think I testified for it, we do feel very
2489 fortunate that we have the FDA.

2490 Mr. {Lance.} Absolutely, and we are working well with
2491 the FDA and it is an excellent agency.

2492 Mr. {Walsh.} We have existed before the FDA came along
2493 and then the two of us have been working down this precarious
2494 path of discretionary enforcement and we are fortunate that
2495 we share the same principles that we want to send our
2496 employees home safe at night and we want our patients to be
2497 safe, so I think that is critical to say to say that we have
2498 been keeping it together because we are fortunate that the
2499 CGA and the FDA work so closely together.

2500 Having said that, the medical gases fall under a
2501 pharmaceutical standard yet our manufacturing processes are
2502 different, our containers that hold the drugs are different,
2503 and the characteristics of our drugs are different. From a
2504 manufacturing standpoint, a typical pharmaceutical company
2505 may have one plant that distributes their product nationally

2506 or perhaps even globally. We have 4,500 plants in the United
2507 States producing and selling oxygen, which occurs in a very
2508 tight radius of about 100 miles. And in terms of our
2509 containers, many of you probably have loved ones that you
2510 have seen on oxygen. They pull around a cylinder, which is
2511 about 2,000 psig under pressure. After it is empty, we pick
2512 it up, bring it back to our location and refill it. If the
2513 label, if you can still see the label and it is still in good
2514 working condition, it stays on there, or in large cases, you
2515 might see it at a hospital, a large cryogenic container where
2516 as it gets low, we come to fill it. You compare that to a
2517 typical disposal pill box that gets thrown away. And then
2518 the characteristics, most of our medical gases are on the
2519 periodic table. They never expire, which is very different
2520 from pharmaceuticals.

2521 Mr. {Lance.} Thank you, and what would the effect, in
2522 your opinion, be on patients if the FDA were to require an
2523 NDA, a New Drug Application, for medical gases?

2524 Mr. {Walsh.} I think Dr. Woodcock said it very well
2525 today in her goals. It is having a safe, effective and
2526 available product, and what gets me particularly concerned is
2527 the available if we have to go through an NDA process. An
2528 NDA is a long process to go through. We have 2 million
2529 patients alone on oxygen in the homes, not to mention in

2530 hospitals and doctor offices. So it could really have an
2531 impact on supply to these existing patients that we are
2532 supplying. And to what safety benefit? Our products have
2533 been used--oxygen we used as an example has been used for
2534 over 100 years. You could Google it and find physicians
2535 talking about oxygen therapy in the 1850s.

2536 Mr. {Lance.} Thank you. Google it now, not 100 years
2537 ago.

2538 Mr. {Walsh.} Google it now. Do not Google 100 years.

2539 Mr. {Lance.} Do you see some problems in particular of
2540 the current system for small business medical gas
2541 manufacturers?

2542 Mr. {Walsh.} I do, and I said before, I started from a
2543 small business, and if would have known--I was very young
2544 when I started the business, but if I would have known then
2545 what I know now, I would not have started that business
2546 because you are investing in something that is not approved.
2547 It is not under the approved drug status. Plus, if the FDA
2548 chose to enforce us to a strict pharmaceutical standard, many
2549 of the small companies would get out of the medical gas
2550 business.

2551 Mr. {Lance.} Thank you. I look forward to working with
2552 Dr. Woodcock on this issue and with those on the panel, and
2553 with that, Mr. Chairman, I yield back the balance of my time.

2554 Mr. {Pitts.} Do you have a follow-up?

2555 Dr. {Gingrey.} Mr. Chairman, I do, and thank you for
2556 yielding. First I would like to ask unanimous consent to
2557 submit a letter, a statement from the California Health Care
2558 Institute in support of H.R. 2182, the GAIN Act. Do I have
2559 unanimous consent to submit that for the record, Mr.
2560 Chairman? Mr. Chairman, I thank you for that, and I know the
2561 ranking member would like to look at it, and that is
2562 appropriate. I did want to ask one follow-up question if you
2563 will allow.

2564 This issue of stewardship, and again, I will go back to
2565 Dr. Eisenstein. This issue of stewardship, the judicious use
2566 of antibiotics, and this has come up a few times in
2567 testimony, and for members of the panel today and from the
2568 Committee members, in fact, the Ranking Member of the
2569 Committee. So I want to ask you this, Dr. Eisenstein. Can
2570 we solve global resistance through a Congressionally mandated
2571 stewardship program? And I think Dr. Powers referred to this
2572 as well. Are other forms like maybe the World Health
2573 Organization better suited to tackle this issue of antibiotic
2574 resistance from overuse, over-prescribing, etc.?

2575 Dr. {Eisenstein.} That is an excellent point. The
2576 problem with drug-resistant organisms, Dr. Gingrey, as you
2577 know, is they know no boundary. So when the New Delhi beta

2578 beta-metallo proteinase was discovered in strains of
2579 Klebsiella and other Gram-negatives in India, within 6 to 12
2580 months we saw patients infected in the United States, in
2581 Canada, in the United Kingdom, etc. I was at a meeting
2582 recently where an individual went to an unnamed southeastern
2583 country in Asia and showed five different pharmacies one
2584 after another where any individual could go into any one of
2585 those stores and choose any antibiotic essentially that they
2586 wanted. This is a much broader problem, and clearly,
2587 stewardship must be part of the solution. I would submit,
2588 though, that that is not the place for the GAIN Act.

2589 Dr. {Gingrey.} Well, I thank you for that, and very
2590 quickly, Mr. Chairman, I will go to Dr. Powers now.

2591 Dr. Powers, you had sort of suggested just a few minutes
2592 ago that maybe there ought to be some federal mandate in
2593 regard to best practices and how infectious disease
2594 specialists such as yourself should prescribe antibiotics in
2595 the most judicious and efficacious manner. It would seem to
2596 me that maybe that should come from the American Academy of
2597 Infectious Disease Subspecialists and their best practices
2598 paradigm, but you seem to think, if I understand your
2599 testimony correctly, that maybe the federal government should
2600 do that. Would you suggest that that would be within the
2601 auspices of the FDA or maybe from some other government

2602 bureaucracy such as IPAB?

2603 Dr. {Powers.} I don't think they are mutually
2604 exclusive. To answer the question you asked to Dr.
2605 Eisenstein, resistance is both global and local, and that is
2606 that there have been countries where their antibiotic usage
2607 has decreased, where they have been able to decrease local
2608 resistance. That doesn't mean that we shouldn't have a
2609 global approach. I think what I was trying to suggest was
2610 that FDA should have the authority to be able to designate
2611 drugs for special uses. That doesn't mean they are
2612 regulating the practice of medicine or telling doctors how to
2613 use it, but having worked at FDA, I certainly understand the
2614 importance of giving doctors the information they need to be
2615 able to practice appropriately. That is more of what I was
2616 suggesting, not that FDA should designate who can use what.
2617 And I think that means working with those other outside
2618 organizations and developing stewardship programs at
2619 hospitals.

2620 Dr. {Gingrey.} Thank you, Dr. Powers.

2621 And Dr. Eisenstein wanted to make another comment. Is
2622 that okay, Mr. Chairman?

2623 Mr. {Pitts.} Yes.

2624 Dr. {Eisenstein.} Yes, just to continue on two points
2625 that I would like to make, or actually three points. One of

2626 them, in terms of the FDA being able to approve ad rug
2627 because it happens to get a very bad organism, you still have
2628 to--the manufacturer still has to go through normal
2629 procedures to demonstrate efficacy, which means that the drug
2630 is better than placebo and that the agency has got to
2631 designate it, therefore approved on that basis. That is
2632 point number one.

2633 Point number two, the practice of medicine, as you know
2634 as a former practicing physician, has changed dramatically
2635 over 40 years. I graduated from medical school 40 years ago,
2636 and antibiotics were used essentially willy-nilly at that
2637 time. In the last 10, 15 years, the stewardship that we see
2638 already in place in hospitals is so exact, we could not get
2639 our own antibiotic on formularies anywhere in this country
2640 without it being severely restricted so that only infectious
2641 disease experts were able to give the approval for the use of
2642 that drug, and in part, because of that, we believe Cubicin,
2643 the drug that we now have had approved for 8-1/2 years, still
2644 has a 99.9 percent susceptibility rate against MRSA despite
2645 8-1/1 years on the market. So we can use drugs appropriately
2646 and they have been used appropriately.

2647 And lastly, I would just like to wholeheartedly agree
2648 with the Society of Infectious Disease Pharmacists who noted
2649 that inclusion of stewardship language in the GAIN Act may

2650 broaden the scope of the act and take the focus away from the
2651 appropriate incentives that we are talking about. If you try
2652 to put too much in the way of disincentives back in this
2653 bill, you are actually creating the same problem that we are
2654 trying to solve.

2655 Mr. {Pitts.} The Chair thanks the gentleman.

2656 The unanimous consent request of Dr. Gingrey with the
2657 letters is approved.

2658 [The information follows:]

2659 ***** COMMITTEE INSERT *****

|
2660 Mr. {Pitts.} The Chair recognizes the ranking member
2661 for 5 minutes for questions.

2662 Mr. {Pallone.} Thank you, Mr. Chairman. I just wanted
2663 to ask Mr. Walsh, you heard Dr. Woodcock, who is still here,
2664 on the first panel say that FDA is concerned with the concept
2665 of creating an entirely new regulatory structure for medical
2666 gases, and she said she would be willing to meet with you
2667 personally to discuss whether there are other ways to
2668 address the Compressed Gas Association's concern short of
2669 legislation. So I am trying to get you together here, you
2670 see? Would you be willing to meet with Dr. Woodcock to see
2671 if there is a different solution here?

2672 Mr. {Walsh.} We definitely have an interest of working
2673 directly with Dr. Woodcock and her staff to come up with the
2674 actual legislation that can give us the guidelines and
2675 regulations specific for medical gases.

2676 Mr. {Pallone.} Okay. Because I think it sounds like
2677 you have some valid concerns but I just hope the FDA can be
2678 responsive and find a way to resolve these issues without
2679 actually having to pass legislation. That is my hope, so we
2680 will see if you can get together. It would be helpful.

2681 Mr. {Walsh.} I do think legislation is important. We
2682 have been operating under the guidelines for many, many

2683 years, and so I think it is important that we have something
2684 very strict and by law that we can operate off of.

2685 Mr. {Pallone.} All right. Well, let us see what
2686 develops out of the meeting in any case. Thank you.

2687 Mr. {Pitts.} The Chair thanks the gentleman, and I
2688 would like unanimous consent to enter into the record
2689 statements from the National Association of Chain Drugstores,
2690 and Pharmaceutical Research and Manufacturers of America. I
2691 think you have seen this. Without objection, so ordered.

2692 [The information follows:]

2693 ***** COMMITTEE INSERT *****

|
2694 Mr. {Pitts.} That concludes panel two. Thank you very
2695 much for your testimony, and we appreciate your patience.

2696 We will now go to panel three, and I would like to call
2697 them to the witness table, and I would like to thank all of
2698 you for agreeing to testifying before the Subcommittee today,
2699 and I will quickly introduce our final panel.

2700 First of all, Mr. Shawn Brown is the Vice President of
2701 State Government Affairs at the Generic Pharmaceutical
2702 Association. Then we have Ms. Elizabeth Gallenagh, who is
2703 the Vice President of Government Affairs and General Counsel
2704 for the Healthcare Distribution Management Association. And
2705 Mr. Tim Davis, who is the Owner of the Beaver Health Mart
2706 Pharmacy and representing the National Community Pharmacists
2707 Association. And Mr. Allan Coukell, the Director of Medical
2708 Programs at the Pew Health Group.

2709 Again, we thank all of you for coming. We have your
2710 prepared statements. Mr. Brown, we will begin with you. You
2711 are recognized for 5 minutes to summarize your testimony.

|
2712 ^STATEMENTS OF SHAWN BROWN, VICE PRESIDENT, STATE GOVERNMENT
2713 AFFAIRS, GENERIC PHARMACEUTICAL ASSOCIATION; ELIZABETH A.
2714 GALLENAGH, J.D., VICE PRESIDENT, GOVERNMENT AFFAIRS, AND
2715 GENERAL COUNSEL, HEALTHCARE DISTRIBUTION MANAGEMENT
2716 ASSOCIATION; TIM DAVIS, PHARM.D., OWNER, BEAVER HEALTH
2717 PHARMACY, ON BEHALF OF NATIONAL COMMUNITY PHARMACISTS
2718 ASSOCIATION; AND ALLAN COUKELL, DIRECTOR, MEDICAL PROGRAMS,
2719 PEW HEALTH GROUP, THE PEW CHARITABLE TRUSTS

|
2720 ^STATEMENT OF SHAWN BROWN

2721 } Mr. {Brown.} Good morning, Chairman Pitts, Ranking
2722 Member Pallone and members of the House Energy and Commerce
2723 Subcommittee on Health. Thank you for inviting me to testify
2724 before the Subcommittee on the important topic of securing
2725 our Nation's pharmaceutical supply chain.

2726 I am Shawn Brown, Vice President of State Affairs at the
2727 Generic Pharmaceutical Association. GPhA represents the
2728 manufacturers and distributors of finished does generic
2729 pharmaceuticals and suppliers of other goods and services to
2730 the generic industry. We appreciate the efforts of members
2731 of this Committee particularly Congressmen Matheson and
2732 Bilbray, to address this important issue and we share their

2733 goal of ensuring the security of our supply chain.

2734 For many years, GPhA had worked closely with multiple
2735 stakeholders across the supply chain to ensure U.S. consumers
2736 benefit from the safest and most secure prescription drug
2737 supply in the world. Both industry and FDA are exceptionally
2738 vigilant against the distribution and sale of counterfeit and
2739 adulterated medicines.

2740 GPhA believes the problem of counterfeit medicines
2741 raises a significant public health concern that must be
2742 addressed on a range of levels from local to global and
2743 throughout the drug supply chain. Our commitment to this
2744 issue is further evidence by the Generic Drug User Fee Act,
2745 which recognizes that while providing earlier access to
2746 effective medicines is critical, FDA's central mission is
2747 ensuring drug safety. It is worth noting that generic drugs
2748 are rarely, if ever, targeted by counterfeiters. The primary
2749 focus of counterfeiters is on more profitable and expensive
2750 brand name products. GPhA is not aware of a single instance
2751 of a counterfeit generic product occurring within the normal
2752 chain of distribution in the United States.

2753 Nevertheless, the generic industry has been a leader in
2754 supporting numerous anti-counterfeiting efforts and
2755 developing methods to further protect the integrity of the
2756 pharmaceutical supply chain. As these efforts move forward,

2757 however, it is vital to ensure that any system is practical,
2758 focused and uniform across the country. The uniform system,
2759 founded on reliable technology and business practices, would
2760 avoid creating cost barriers to the distribution of safe and
2761 effective medicines.

2762 For example, some anti-counterfeiting efforts such as
2763 the California model taking effect in 2015 would require
2764 implementation of full unit-level track and trace
2765 capabilities where theoretically the entire distribution
2766 history and location of every unit in the supply chain can be
2767 determined at any time. GPhA believes that adoption of the
2768 California model or a similar one would raise the cost of
2769 medicine by billions of dollars over time, would be prone to
2770 error, and would have at best similar results to the less
2771 expensive, more efficient model that we support.

2772 With billions of units moving quickly and efficiently
2773 through the supply chain to fill more than 4 billion
2774 prescriptions per year, the magnitude and complexity of such
2775 a system is not technically feasible. The California law
2776 does include language providing for preemption of its
2777 requirements in the event that federal legislation is
2778 enacted. With California's initial effectiveness date fast
2779 approaching, GPhA has helped lead an effort to develop a more
2780 efficient model.

2781 In partnership with stakeholders from every area of the
2782 pharmaceutical supply chain, the Pharmaceutical Distribution
2783 Security Alliance, or PDSA, has developed a consensus
2784 technological model that we believe will deliver greater
2785 patient safety and help to achieve FDA's stated goals for a
2786 supply chain security system.

2787 The PDSA is a multi-stakeholder initiative whose
2788 membership spans the U.S. pharmaceutical distribution system
2789 including manufacturers, wholesale distributors, third-party
2790 logistics providers, and pharmacies. As a member of the
2791 PDSA, GPhA strongly supports the alliance's proposed
2792 electronic traceability system, known as the Pharmaceutical
2793 Traceability Enhancement code, or RxTEC. This system would
2794 increase patient access to safe medicines while improving the
2795 security of our country's drug distribution system. In
2796 addition, the RxTEC system would aid State and federal
2797 agencies in tracing the distribution history of suspect
2798 products, replace the inconsistent and inefficient patchwork
2799 of State laws, increased efficiency throughout the drug
2800 distribution system, and establish foundational technology
2801 for future enhancements.

2802 The PDSA model is based on technological solutions that
2803 are achievable and scaleable, and unlike a full track and
2804 trace system, which is not technically feasible in the near

2805 term, the RxTEC system would provide immediate measures to
2806 increase supply chain security. The legislation would
2807 provide regulators with new authorities to establish new
2808 penalties to address counterfeit products, cargo theft and
2809 illegal online drug sellers and create new rules regarding e-
2810 labeling that will increase patient safety. It would also
2811 improve the efficiency and effectiveness of drug recalls and
2812 returns, and enable health care providers to leverage
2813 technology for recordkeeping purposes. We urge the inclusion
2814 of the proposal in the user fee package to accomplish these
2815 goals.

2816 In conclusion, Mr. Chairman, GPhA and the industry share
2817 the concerns of the Committee with regard to maintaining the
2818 security of our drug supply and preventing the entry of
2819 counterfeit, diverted, stolen or other substandard medicines.
2820 The development of a uniform national system is needed to
2821 give regulatory authorities another tool for enforcement,
2822 make it more difficult for criminals to breach the supply
2823 chain, and enhance the ability of the supply chain to respond
2824 quickly when a breach has occurred. We believe the RxTEC
2825 model proposed by the PDSA achieves all of these goals

2826 Thank you, and I would be happy to answer any questions.

2827 [The prepared statement of Mr. Brown follows:]

2828 ***** INSERT 7 *****

|

2829 Mr. {Pitts.} The Chair thanks the gentleman.

2830 Ms. Gallenagh, you are recognized for 5 minutes.

|
2831 ^STATEMENT OF ELIZABETH GALLENAGH

2832 } Ms. {Gallenagh.} Good afternoon, Chairman Pitts,
2833 Ranking Member Pallone and members of the Subcommittee on
2834 Health, I am Liz Gallenagh, Vice President of Government
2835 Affairs and General Counsel at HDMA. Thank you for the
2836 opportunity to inform the Subcommittee today regarding this
2837 critically important issue of prescription drug pedigree,
2838 traceability and pharmaceutical supply chain safety. I would
2839 also like to thank Congressmen Bilbray and Matheson for their
2840 bipartisan leadership in this area.

2841 The pharmaceutical distribution industry's primary
2842 mission is to operate the safest, most secure and efficient
2843 supply chain in the world. As part of this mission, HDMA's
2844 members work to eliminate counterfeit and diverted medicines
2845 by capitalizing on the technological innovation and constant
2846 improvements in efficiency that are the foundation of our
2847 industry.

2848 Today, I am here to express HDMA's strong support for a
2849 national uniform approach to pedigree and the traceability of
2850 medicines throughout the supply chain. HDMA believes that
2851 reform should have tighter wholesaler licensing standards and
2852 a new federal ceiling for pedigree requirements to improve

2853 safety and uniformity across the country while establishing
2854 targets and parameters for longer-term electronic
2855 traceability solutions.

2856 In addition to fundamentally addressing counterfeit and
2857 diverted medicines, we also believe that federal pedigree may
2858 have some potential as a useful tool in discouraging gray-
2859 market activity associated with drug products in short
2860 supply. After many years of debate, 2012 is the best window
2861 of opportunity to enact national pedigree legislation. This
2862 is in large part due to broad consensus among supply chain
2863 partners as well as the possibility of attaching national
2864 pedigree and traceability provisions to PDUFA
2865 reauthorization.

2866 Basic guidelines for pedigree were set forth nearly 25
2867 years ago with the enactment of the federal PDMA. Since that
2868 time, activity at the State level has varied with some
2869 enacting complex electronic pedigree laws and other never
2870 going further than the original 1988 guidelines. Based on
2871 our experience, the complexities of dealing with multiple
2872 approaches in the States will only get worse if we fail to
2873 solve this problem now at the national level.

2874 Since Florida's first foray in raising pedigree and
2875 licensure requirements in 2003, we have seen dramatic
2876 variation across the country in both legislation activity and

2877 regulatory interpretation. This has occurred despite our
2878 attempts to work in every State along with our fellow
2879 stakeholders and interested legislators to achieve more
2880 uniformity. Today, for example, 29 States have acted beyond
2881 the federal PDMA standards. For instance, the States of
2882 California and Florida are thought to be the most stringent
2883 and leaders in this area. However, they take completely
2884 different viewpoints with Florida considered to the most
2885 stringent today and California thought to be the most complex
2886 in the future in 2015 when their law is implemented.

2887 This patchwork not only creates operational challenges
2888 but also creates openings for bad actors to shop for more
2889 lenient States rules, openings that could mean the difference
2890 between a fake or diverted medicine being dispensed or
2891 administered to an innocent patient in need of treatment.
2892 Because of this State-by-State variation, we believe that
2893 pedigree and traceability should be under the purview of
2894 Congress and the FDA.

2895 HDMA is currently a part of an industry alliance, a
2896 consortium of other industry partners called the PDSA.
2897 PDSA's consensus model calls for the following: national
2898 requirements for wholesaler licensing standards and for
2899 direct purchase and standard pedigree upon the effective date
2900 of the legislation; manufacturer serialization at the unit

2901 and case levels, enabling unique identification of
2902 prescription drug products for the first time; the
2903 development of electronic systems to facilitate traceability
2904 and transaction data exchange to provide additional
2905 efficiency and safety benefits within the supply chain;
2906 appropriate transition time and development phases for the
2907 migration to traceability for each segment of the supply
2908 chain. Further, federal legislation must also preserve the
2909 critically important role of the States, for instance, in the
2910 area of wholesaler licensure and enforcement. There is no
2911 single element that will protect the supply chain from every
2912 threat but rather a comprehensive solution should incorporate
2913 each of these elements.

2914 We urge the Subcommittee to consider this important
2915 issue for inclusion in PDUFA legislation. Now is the time
2916 for Congress to act to bring cohesion and consistency to our
2917 national drug supply chain. Thank you.

2918 [The prepared statement of Ms. Gallenagh follows:]

2919 ***** INSERT 8 *****

|

2920 Mr. {Pitts.} The Chair thanks the gentlelady.

2921 Dr. Davis, you are recognized for 5 minutes.

|
2922 ^STATEMENT OF TIM DAVIS

2923 } Mr. {Davis.} Chairman Pitts, Ranking Member Pallone and
2924 members of the Subcommittee, thank you for conducting this
2925 hearing and providing me an opportunity to share my views and
2926 my perspective as an independent pharmacist on the issue of
2927 securing the pharmaceutical supply chain.

2928 My name is Tim Davis of Beaver County, Pennsylvania, and
2929 I own the Beaver Health Mart Pharmacy in that town and
2930 county. I have been a practicing pharmacist for 12 years,
2931 and I am here today representing the National Community
2932 Pharmacists Association. It is an association of over 23,000
2933 independent pharmacists, and we are the pharmacists that
2934 represent over 40 percent of the prescriptions dispensed in
2935 this country.

2936 It is my belief that the pharmaceutical supply chain in
2937 the United States is largely safe and secure. I believe that
2938 today most practicing pharmacists have a heightened awareness
2939 of the possibility of counterfeit or diverted drugs and
2940 therefore recognize the critical importance of purchasing
2941 medications only from trusted wholesalers or trading
2942 partners. In addition, most pharmacists today make a
2943 concerted effort to carefully examine and make note of drug

2944 packaging and the appearance of the drug itself to make sure
2945 that there are no suspicious anomalies.

2946 It has been my observation that certain types of
2947 prescription medications tend to be the target of
2948 counterfeiters. High-dollar medications that can be easily
2949 produced and readily sold generally enable counterfeiters to
2950 create an attractive profit margin. Presently, generics are
2951 not typically a target for this type of activity. Some drugs
2952 that I have seen are particularly susceptible and are
2953 lifestyle drugs such as Viagra as well as a number of very
2954 expensive injectable medications, and most recently, Avastin.
2955 These are typically not carried in community pharmacies but
2956 rather dispensed through consolidated specialty pharmacies or
2957 directly through physicians.

2958 In my career, I have seen an example of counterfeiting
2959 at the local level. We received manufacturer information
2960 that a particular drug had entered the drug supply chain in
2961 counterfeit form, and the manufacturer instructed us on how
2962 to recognize the genuine product versus the fake. Upon
2963 receipt of a daily shipment in the morning from our wholesale
2964 distributor, we checked and found that the item we received
2965 was indeed one of the counterfeit products. We immediately
2966 contacted and discussed the situation with the wholesaler.
2967 Our answer was to stop doing business with them due to lack

2968 of believable responses.

2969 That being said, NCPA does believe that there are a
2970 number of different approaches or tactics that could be
2971 employed to provide further confirmation of integrity. These
2972 strategies could include national uniform federal licensure
2973 standards for wholesale distributors, increased oversight or
2974 security measures to deter pharmaceutical cargo theft and
2975 illegitimate online drug sellers, and lot-level form of
2976 tracking for prescription drugs to assist the FDA or State
2977 authorities in the event of recall or to investigate suspect
2978 product.

2979 Raising the standards for wholesaler licensure in a
2980 uniform fashion would provide the community pharmacist at any
2981 location in the United States with an additional layer of
2982 confidence in the integrity of the medications purchased from
2983 such companies. Therefore, NCPA recommends that the U.S.
2984 government set national uniform and federal licensure
2985 standards for wholesale distributors. At the present time,
2986 these distributors are licensed at the individual State
2987 level, which has resulted in a patchwork of requirements of
2988 varying rigor.

2989 There are a number of other approaches that could also
2990 further secure the pharmaceutical supply chain. S. 1002, the
2991 SAFE DOSES Act, would expand the penalties for pharmaceutical

2992 cargo theft, and in addition, H.R. 4095, the Online Pharmacy
2993 Safety Act, would create a publicly available white list of
2994 legitimate Internet pharmacies. This list would help to
2995 eliminate rogue Internet pharmacies that exist and often prey
2996 on consumers looking for bargain-priced medications.

2997 NCPA is a member of the Pharmaceutical Distribution
2998 Security Alliance, a working group comprised of
2999 representatives from all sectors of the pharmaceutical supply
3000 chain. It has been collaborating on a comprehensive proposal
3001 to address supply chain security issues. The RxTEC Act is
3002 currently in draft form. However, it includes language that
3003 would create the registry of legitimate online pharmacy
3004 websites, increase the penalties for counterfeiters as well
3005 as provide for tracking of prescription medications at the
3006 lot level.

3007 The actual tracking of prescription drugs through the
3008 supply chain is a topic that has been discussed for a number
3009 of years, and independent community pharmacists have had
3010 significant concerns in the past about the cost of the
3011 hardware, software and employment burdens placed upon the
3012 association. This is a complex issue both in terms of the
3013 technologies necessary to implement it as well as the fact
3014 that each of the sectors involved in the supply chain operate
3015 under very different business models and very greatly in

3016 terms of financial resources and technological
3017 sophistication. Community pharmacies are largely small
3018 businesses. Any system that would require a pharmacist to
3019 electronically scan each item would create a burdensome and
3020 time-consuming exercise that would further limit the amount
3021 of time that we have to provide patient care and counseling
3022 or any other activities necessary to keep that small business
3023 running.

3024 The tracking system proposed under RxTEC Act is one that
3025 is lot-based tracking, would require that the encoded
3026 information on each unit be both machine and human readable,
3027 and would allow for collaboration between all members of the
3028 supply chain. The proposed system is one that could be built
3029 upon in the future if it was determined that this course of
3030 action was advisable but is one that would not impose an
3031 undue burden either financially or as it relates to work flow
3032 upon independent community pharmacists.

3033 I have a greater degree of confidence in the United
3034 States drug supply than I did just a few years ago, largely
3035 due to heightened awareness of those in the supply chain and
3036 the possibility of counterfeit or diverted medications being
3037 discovered. That being said, community pharmacies take very
3038 seriously our role in ensuring the safety of medications that
3039 we personally dispense to our patients and we remain

3040 committed to working with our colleagues in the supply chain,
3041 other pharmacy organizations, wholesalers and manufacturers
3042 as well as with State and federal authorities to make any
3043 needed improvements. Moving forward, it is essential that
3044 all stakeholders make a concerted effort to keep the lines of
3045 communication open so that consumers can continue to
3046 implicitly trust the integrity of the medications that they
3047 depend on.

3048 I thank you, and welcome any questions.

3049 [The prepared statement of Mr. Davis follows:]

3050 ***** INSERT 9 *****

|
3051 Mr. {Pitts.} The Chair thanks the gentleman and
3052 recognizes Mr. Coukell for 5 minutes for a statement.

|
3053 ^STATEMENT OF ALLAN COUKELL

3054 } Mr. {Coukell.} Chairman Pitts, Ranking Member Pallone,
3055 Subcommittee members, thank you for the opportunity to
3056 present testimony. Thank you for your work on this issue and
3057 especially to Representatives Bilbray and Matheson for
3058 introducing a bipartisan bill that would help protect
3059 Americans from counterfeit and diverted drugs.

3060 My name is Allan Coukell. I am a pharmacist and
3061 Director of Medical Programs for the Pew Health Group of the
3062 Pew Charitable Trusts.

3063 The safety of the drug supply has been a long-term focus
3064 for Pew. Last year we issued a major report, and one of the
3065 key findings was that we currently have no national system to
3066 detect or prevent counterfeits, and with close to 2,000
3067 individual wholesalers and many more individual pharmacies
3068 and actors, it provides multiple points of entry to our
3069 system.

3070 Let me illustrate the risks with just a few examples of
3071 diversion, theft and counterfeiting. First, the black market
3072 for diversion and resale of drugs that have already been
3073 dispensed to patients and paid for, often by Medicaid. Two
3074 years ago, federal officials in Florida brought down a ring

3075 that illegally purchased \$13 million worth of prescription
3076 drugs, buying them from patients and then selling them to
3077 pharmacies through a licensed wholesaler in Texas. Similar
3078 schemes have been documented in other States.

3079 Drug theft is another threat. In 2009, thieves stole a
3080 tractor-trailer containing 129,000 vials of insulin. After
3081 disappearing for several months, some of this temperature-
3082 sensitive drug was later found on the shelves of chain
3083 pharmacies in Texas, Georgia and Kentucky. In another case,
3084 thieves cut through the roof of an Eli Lilly warehouse in
3085 Connecticut using forklifts to load a truck with \$75 million
3086 worth of prescription drugs. The fate of those drugs isn't
3087 known, but some experts believe that the thieves may be
3088 letting the alarm die down before selling them back into the
3089 system.

3090 And then finally, we have incidents of outright
3091 counterfeits. In recent weeks, a counterfeit cancer drug,
3092 Avastin, made its way reportedly from Egypt through multiple
3093 European countries to a licensed U.S. pharmaceutical
3094 wholesaler that had been supplying numerous clinics. In
3095 2001, counterfeit Serostim, a high-cost injectable for AIDS
3096 patients, was found in at least seven States and passed
3097 through multiple wholesalers. The manufacturer of that drug
3098 has since put in place a secure distribution program with a

3099 unique serial number assigned to each vial that must be
3100 verified by the dispensing pharmacy.

3101 Unlike for that drug, for most drugs there is no
3102 currently no way to check whether they are authentic or
3103 counterfeit. Some State laws exist. California is
3104 implementing a comprehensive system under which manufacturers
3105 will put a unique serial number on each unit, and wholesalers
3106 and pharmacies will check to ensure that the drugs they buy
3107 and sell are authentic.

3108 A strong national standard would be preferable to a
3109 patchwork of State laws, but a national system has been under
3110 discussion for years and won't happen without legislation.
3111 Congress is now considering a compromise proposal developed
3112 between various industry sectors, and Pew supports a number
3113 of the elements of this proposal including strengthened
3114 standards for wholesaler licensure, but the proposal falls
3115 short in a couple of crucial aspects.

3116 First, the key to improved security of drug distribution
3117 is knowing who handles the drugs as they move from
3118 manufacturer through a succession of wholesalers to the
3119 pharmacy or the hospital and ultimately to the patient. The
3120 industry proposal calls for tracking drugs at the lot level,
3121 but a lot, as we heard already this morning, can contain
3122 numerous cases and many thousands of individual bottles and

3123 each case or individual unit can be sold separately, and
3124 tracking by lot doesn't allow industry or regulators to ever
3125 know who bought and sold a given drug.

3126 Maintaining data about lots may provide an incremental
3127 benefit over the status quo, but it would fail to catch
3128 unsafe drugs in many scenarios. If part of a lot was stolen
3129 and illicitly reintroduced into commerce, a pharmacist or a
3130 patient would have no way to tell if the product on their
3131 shelf was compromised. That same lot will be sitting on the
3132 shelves of dozens or hundreds of pharmacies, but if
3133 individual units are tracked, specific stolen bottles could
3134 be identified.

3135 While the PDSA proposal would result in a unique serial
3136 number being placed on each unit of sale, keeping track of
3137 the drugs would be impossible unless the serial numbers can
3138 be associated with the case in which they are shipped. Even
3139 if we decide that we don't need unit-level tracing now, the
3140 PDSA system proposed would make it difficult or impossible to
3141 track drugs at the unit level in the future.

3142 Next, under the proposed system, neither the pharmacy
3143 nor any other party in the system would ever be required to
3144 verify the authenticity of drugs. A criminal could sell a
3145 vial of counterfeit drug with a fake serial number, and no
3146 one would detect it because no one would be required to check

3147 it. Pew supports required authentication of drug products by
3148 the companies involved in distribution as outlined in H.R.
3149 3026, the Bilbray-Matheson bill.

3150 Let me conclude by noting again that the impending
3151 California law creates momentum for a single national
3152 standard. Such a standard should protect Americans today and
3153 provide the flexibility of future refinements.

3154 Thank you, and I welcome your questions.

3155 [The prepared statement of Mr. Coukell follows:]

3156 ***** INSERT 10 *****

|
3157 Mr. {Pitts.} The Chair thanks the gentleman and thanks
3158 all the witnesses, and we will begin questioning. I will
3159 recognize myself for 5 minutes for that purpose.

3160 Let me ask a question to all of you first. You can each
3161 respond. We are all concerned about the safety of our drug
3162 supply, and we want to ensure that diverted drugs and
3163 counterfeit drugs do not reach our Nation's patients.
3164 However, as we look at policies to help, we also have to
3165 think about the cost to our Nation's small businesses. They
3166 are struggling right now. We need to take them into account
3167 as we analyze every policy idea.

3168 The first question, how do we ensure the safety of our
3169 prescription drugs in the most cost-effective way? And then
3170 two, why is a national standard necessary? Mr. Brown?

3171 Mr. {Brown.} I think I would say the PDSA model, we
3172 have got a consensus throughout industry from chain
3173 drugstores, independent pharmacies, secondary wholesalers,
3174 third-party logistics providers, brand and generic
3175 manufacturers. We believe this is a scaleable system and a
3176 feasible system that we are proposing, and I think that this
3177 will help to achieve all of FDA's stated goals, one of which
3178 being to prevent introduction and to help identification of
3179 counterfeit medicines. We are concerned about the cost as

3180 well, but the system that we are proposing is exponentially
3181 less than the system would be if we had to implement the
3182 California model, which we don't think is technically
3183 feasible.

3184 Mr. {Pitts.} Ms. Gallenagh?

3185 Ms. {Gallenagh.} I would agree with Mr. Brown. We
3186 believe that the best approach is something that is done at
3187 the national level, and our members have told us that it
3188 would be more cost-effective to operate the RxTEC proposal
3189 that PDSA has put forth and that we have worked on rather
3190 than work toward California and then deal with potentially
3191 New York or Illinois or whatever State is next in this arena.
3192 We are already--as wholesalers, we see firsthand the 50-State
3193 patchwork that you hear so much about, and that really is a
3194 reality for our members in terms of dealing with 50 different
3195 laws, and so automatically we think that we get greater
3196 efficiencies and cost benefits from going with the PDSA
3197 proposal.

3198 Mr. {Pitts.} Dr. Davis?

3199 Mr. {Davis.} The PDSA proposal also looks at the
3200 problem in a multifaceted approach. The only place that
3201 rogue pharmacies can get counterfeit or diverted medications
3202 is from rogue wholesalers, so we need to look upstream. I
3203 think the PDSA looks at creating national standards to help

3204 us feel that the drug supply above us is intact. I also feel
3205 that it takes a look at the rules and regulations set against
3206 counterfeiters to prevent that sort of activity long before
3207 it gets to a pharmacy level, and I think that the
3208 infrastructure built on the serialization and lot numbers
3209 included in the RxTEC Act prepare this for adaptation in the
3210 future. We need a system that is going to adapt to the
3211 health care needs of the near future, not necessarily the
3212 legislative needs that we foresee coming, and this market is
3213 going to continue to change and the products that we are
3214 going to experience are going to continue to change,
3215 positioning us very well to scale effectively.

3216 Mr. {Pitts.} Mr. Coukell?

3217 Mr. {Coukell.} Mr. Chairman, along with the compliance,
3218 or the costs of compliance that my colleagues raise, I think
3219 the other argument for a national system is that the
3220 companies involved in drug distribution work across State
3221 lines, so in the case of Avastin, it was a Tennessee-licensed
3222 wholesaler that sold the drugs but they ended up in Illinois,
3223 Texas and California, or at least those are the practices
3224 that have been mentioned. So that argues for a national
3225 standard, and clearly we have to do it in a way that has the
3226 least necessary cost impacts. So it is important to say what
3227 are the goals of the system, do we want to be able to

3228 identify counterfeit drugs when they come in, and if so, what
3229 is the most effective way to do that, and secondly, do we
3230 want to be able to track product as it moves through the
3231 system and what is the most cost-effective way to track the
3232 product at the level we want to be tracking it at.

3233 One of our concerns with the proposal is that companies
3234 are going to make a capital investment to be able to
3235 serialize their product, and we certainly recognize they are
3236 stepping forward to do that, and I think the question we have
3237 to ask is, if we think that eventually we want to get to a
3238 system where we are tracking individual units and we are
3239 putting into place an infrastructure now that is lot-level
3240 tracking, are we going to be back here in 5 or 8 years when
3241 we have a crisis because have counterfeit drugs on the
3242 shelves asking them to invest again in a new system to track
3243 at the unit level or should we get it right now.

3244 Mr. {Pitts.} Mr. Brown, can you speak what would the
3245 costs be to manufacturers if the California approach were
3246 adopted?

3247 Mr. {Brown.} Yes, I can give you an approximate
3248 estimate. If we think about the number of packaging lines
3249 that serve the consumers in the United States, it is about
3250 3,000. I have heard some estimates higher, some lower, and
3251 per packaging line, my manufacturers tell me that it ranges

3252 between \$500,000 and \$1 million per packaging line. So at
3253 the highest, I would say it is near \$3 billion just to
3254 implement the camera infrastructure. We are not talking
3255 about the data management costs or the costs of the barcodes,
3256 the ongoing costs. We are just talking about getting the
3257 infrastructure set up into the packaging lines.

3258 Mr. {Pitts.} My time is expired. The Chair recognizes
3259 the ranking member for 5 minutes for questions.

3260 Mr. {Pallone.} Thank you, Mr. Chairman.

3261 I was going to ask actually each of the panelists this
3262 question. In addition to the various provisions related to
3263 development of the RxTEC system, the proposal from the
3264 Pharmaceutical Distribution Security Alliance contains a
3265 number of provisions related to federal licensing of parties
3266 involved in the manufacture and distribution of
3267 pharmaceuticals. I understand these provisions are intended
3268 to create federal uniform for the regulation of these parties
3269 and could help prevent bad actors from engaging in the drug
3270 supply chain. But I would like to ask each of you if you
3271 support the provisions requiring federal licensure for
3272 manufacturers, distributors, repackagers and third-party
3273 logistics providers, and if not, what concerns they have.
3274 And I am just looking for a yes or no at this point.

3275 Mr. {Brown.} Yes.

3276 Mr. {Pallone.} Ms. Gallenagh?

3277 Ms. {Gallenagh.} We support the provisions that are
3278 contained in the proposal, but if I could clarify, on the
3279 wholesaler licensure piece, we support federal standards and
3280 still retain the issuances of licenses with the State.

3281 Mr. {Pallone.} Okay.

3282 Mr. {Pallone.} Dr. Davis, do you agree with that?

3283 Mr. {Davis.} We agree as well.

3284 Mr. {Pallone.} Mr. Coukell?

3285 Mr. {Coukell.} As do we.

3286 Mr. {Pallone.} Now, let me ask Mr. Coukell, I
3287 understand that from the patient safety perspective, the best
3288 system would be one in which the pedigree system goes to the
3289 unit level--you talk about this--in which the pharmacist
3290 verifies the pedigree of all the units he receives for
3291 dispensing. I also understand that the current industry
3292 proposal does not have serialization information down at the
3293 unit level but it enables tracing back only to the lot level.
3294 You stated that, or one of you did. Meanwhile, that proposal
3295 does not require a pharmacist to verify any pedigree
3296 information whatsoever before dispensing, although it would
3297 facilitate traceback once the problem has been identified.
3298 So it appears that the industry proposal does not go as far
3299 as some would like and certainly not as far as the California

3300 law appears to go. However, what many of us have heard is
3301 that the California law is proving much more difficult to
3302 implement than anticipated and that the industry plan can
3303 serve as a building block towards reaching the goal that
3304 California law sets out.

3305 So my question, I will ask you first, Mr. Coukell, is,
3306 do you agree with that, what I just said, or do you see the
3307 industry proposal as a step that while containing many useful
3308 items ultimately puts a roadblock in front of ever reaching
3309 unit-level tracing and verification, and I will ask Ms.
3310 Gallenagh if you would respond as well?

3311 Mr. {Coukell.} Thank you for that question. If I could
3312 begin with one point of clarification, under the industry
3313 proposal, there would be a unique serial number on each vial.
3314 It just wouldn't be tracked as it moved through the system.
3315 So potentially on a case-by-case basis, somebody could look
3316 that up and check it. But what you don't have is at the
3317 point where there is no suspicion that vial being checked
3318 and, you know, these counterfeits are pretty good. You can't
3319 by the naked eye in a lot of cases detect them and so there
3320 is no system here where a flag is automatically thrown up.

3321 So I think the key question in looking at how to move
3322 forward is, what are the basic elements that we want now and
3323 what are the basic elements that we are going to want within

3324 a reasonable time frame, and does this system give us enough
3325 to build on, and as I said already, we are a little concerned
3326 that if we go with this system, then we may not be able to
3327 get where we need to go in the future.

3328 Mr. {Pallone.} Okay. Ms. Gallenagh?

3329 Ms. {Gallenagh.} Sure. Thank you, Congressman. I
3330 think a couple of things in this area. One, I am to agree
3331 with Mr. Coukell's explanation. There is an SNI or serial
3332 number included in the RxTEC data, so the 2D barcode would
3333 include the SNI information as well as lot and expiration.
3334 What we think is that that would alone for the first time
3335 provide unique identification of medicines and would be a
3336 very big step for the industry. Today we don't have that at
3337 all, and we are dealing with paper and electronics sometimes,
3338 always lot level and no real standard in terms of what
3339 different States are doing across the country. I think we
3340 also would think that going with the PDSA proposal is not a
3341 roadblock but sticking with the 50-State patchwork may be a
3342 roadblock to actually ever getting to a true electronic
3343 system across the country. I think that, you know, we need
3344 to take a broader perspective of this issue and that patient
3345 safety really does belong in the purview of Congress right
3346 now. Right now is probably the best opportunity we have, and
3347 we do have industry consensus and that is something that we

3348 have never achieved before, and so I think that goes a long
3349 way, and I believe that my members, other industry partners,
3350 once those things are in place that are put forth in the PDSA
3351 proposal like unit-level serialization, I think that building
3352 on the innovation that we have built on in the past and the
3353 efficiencies can be achieved as we learn more about the
3354 technology, we may eventually find other uses for the
3355 technology and it may go further than what we have initially
3356 set out to do.

3357 Mr. {Pallone.} Thank you.

3358 Thank you, Mr. Chairman.

3359 Mr. {Pitts.} The Chair thanks the gentleman and
3360 recognizes the Vice Chairman of the Subcommittee, Dr.
3361 Burgess, for 5 minutes for questions.

3362 Dr. {Burgess.} Thank you, Mr. Chairman.

3363 Dr. Davis, you were probably in the room earlier when
3364 Dr. Woodcock was here and you heard our exchange about the
3365 drug shortages. She had been here 3 or 4 weeks ago, and this
3366 was a lot of follow-up to that. Can you tell me from a
3367 community pharmacist's perspective what you are encountering
3368 in the drug shortage arena?

3369 Mr. {Davis.} A single day doesn't go by where drug
3370 shortages don't affect patients in one manner or another. So
3371 of the hundreds of prescriptions that we fill daily in my

3372 pharmacies, we know we have to have a conversation every
3373 single day with a patient to alter therapy, to choose a
3374 different therapy or to come to a consensus with the
3375 prescribers and other caregivers as to how to change therapy
3376 to still get the best result for that patient without the
3377 agent available that we need.

3378 Dr. {Burgess.} Can you give us some examples of how
3379 that might come up in the course of your day? What are the
3380 ones you are seeing very frequently? You heard my exchange
3381 with Dr. Woodcock. We had the executive order in October,
3382 and as far as I can tell, not a darn thing happened. But
3383 then when we had a very intense discussion about Doxil 3 or 4
3384 weeks ago, suddenly you got some movement on that and people
3385 were able to find oh, yeah, there is some supply that we
3386 could free up. So help me here. Tell me what you are having
3387 the most trouble with. I will write a letter to Dr.
3388 Woodcock. We will see what we can do.

3389 Mr. {Davis.} The most trouble that is arising is mostly
3390 solid dosage forms. At the community pharmacy level, we
3391 dispense very few injectable medications or infusible
3392 medications so the cancer drugs that you are referencing are
3393 not necessarily a problem in the community, but what we do
3394 see are the ADHD medications, solid dosage forms of those,
3395 medications in some neurological disorders as well.

3396 Methotrexate has been recently a problem for us in the
3397 treatment of RA and a couple of other disease states. And in
3398 those cases, they are patients that were managed and well
3399 managed on these medications and now we have disruption of
3400 therapy. So we have to make a decision, can we still achieve
3401 the clinical outcomes with another agent, and it is proving
3402 to be burdensome. It is proving to burn time that we
3403 shouldn't necessarily have to burn because this patient has
3404 already been managed effectively and efficiently within the
3405 system.

3406 Dr. {Burgess.} How involved do you get with cost of
3407 prescriptions? I get to do a number of telephone town halls
3408 with other Members of Congress because they like for me to be
3409 there, and invariably a caller calls and they are on whatever
3410 and it is frightfully expensive, and then you kind of know in
3411 the back of your mind, there is a generic available for that
3412 that probably is much less. How do you handle that at the
3413 community pharmacy level when somebody is having difficulty
3414 paying for their medication and there might be a generic or
3415 there might be something that is just a little bit different
3416 but perhaps suitable? Do you communicate with the physician,
3417 the prescribing physician, in those instances?

3418 Mr. {Davis.} Absolutely. Something to keep in mind is,
3419 we are probably the only health care professional that

3420 actually gets to see the cost of care as it is rendered, so
3421 as someone is standing in front of us approaching the
3422 instance of therapy, we know what that is going to cost and
3423 how that is going to impact that patient. We are also the
3424 only professional that still has one-on-one time to render to
3425 those patients to help them understand and navigate the
3426 waters associated with the cost of those medications. So we
3427 do reach out to our prescribers in the community and offer
3428 recommendations based on what we understand to be the
3429 outcomes and efficacy of that drug while still maintaining
3430 the integrity of the intent of that prescriber but being able
3431 to do it at a lower cost.

3432 Pharmacists are doing it each and every day over and
3433 over again throughout their day. It is not necessarily a
3434 recognized function but we have transitioned from being the
3435 makers of salves and potions into clinically based social
3436 workers and helping people to navigate Medicare, helping
3437 people to navigate Medicaid, helping people to understand
3438 what is going on with the PBMs and the cost of their
3439 medications.

3440 Dr. {Burgess.} Let me ask you this because the issue of
3441 Avastin came up, and I have to admit, a couple weeks ago I
3442 was pretty taken by surprise. Now, I get why Viagra might be
3443 a counterfeit and why there might be a market, you know, the

3444 incredible markup that occurs on that, but Avastin is hardly
3445 something you would just buy on the Internet and use. What
3446 is going on there?

3447 Mr. {Davis.} So the concern that I have is, it is a
3448 high-dollar medication so clearly to be able to counterfeit
3449 and move that into the supply chain puts a lot of value not
3450 only on the people that are actually counterfeiting and
3451 entering it in the supply chain but the hands that may touch
3452 it during the supply chain itself. And that is why I said,
3453 the integrity of our trading partners is of utmost
3454 importance, especially being the end dispenser of that. So
3455 to understand the components of the supply chain that come
3456 before us, to understand who your wholesaler is, to
3457 understand the integrity associated with that wholesaler and
3458 how they conduct business is vital to what we do at the
3459 community and ground level.

3460 With the case of Avastin, I understand that that
3461 particular medication changed hands through multiple sources
3462 multiple times after entering this country and did not
3463 necessarily enter through the channels that we would normally
3464 consider as part of the trusted lines.

3465 Dr. {Burgess.} It wasn't in the legitimate stream of
3466 pharmaceutical commerce?

3467 Mr. {Davis.} Correct.

3468 Dr. {Burgess.} Thank you, Mr. Chairman. I will yield
3469 back.

3470 Mr. {Pitts.} The Chair thanks the gentleman.

3471 That concludes our third and final panel. It has been
3472 very informative. We thank all of you for your testimony.

3473 I will remind the members that they have 10 business
3474 days to submit questions for the record, and I would like to
3475 ask the Director and witnesses to respond to the questions
3476 promptly. Members should submit their questions by the close
3477 of business on Thursday, March 22nd.

3478 Without objection, the Subcommittee is adjourned.

3479 [Whereupon, at 2:35 p.m., the Subcommittee was
3480 adjourned.]