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4 ``FDA USER FEES 2012: HOW INNOVATION HELPS PATIENTS AND
5 JOBS''
6 WEDNESDAY, APRIL 18, 2012
7 House of Representatives,
8 Subcommittee on Health
9 Committee on Energy and Commerce
10 Washington, D.C.

11 The Subcommittee met, pursuant to call, at 10:15 a.m.,
12 in Room 2123 of the Rayburn House Office Building, Hon. Joe
13 Pitts [Chairman of the Subcommittee] presiding.

14 Members present: Representatives Pitts, Burgess,
15 Shimkus, Rogers, Myrick, Murphy, Blackburn, Gingrey, Latta,
16 Lance, Cassidy, Guthrie, Barton, Bilbray, Upton (ex officio),
17 Pallone, Dingell, Engel, Capps, Schakowsky, Matheson, Eshoo,
18 Markey and Waxman (ex officio).

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

|
31 Mr. {Pitts.} The subcommittee will come to order, and
32 the chair recognizes himself for 5 minutes for an opening
33 statement.

34 Today's hearing addresses the FDA user fee package
35 discussion draft. This draft is the product of over a year
36 of hard work by various parties. While the individual
37 industries--prescription drugs, medical devices, generic
38 drugs and biosimilar drugs--represented in this draft were
39 negotiating with FDA on their user fee agreements, this
40 subcommittee was holding at least 10 hearings on subjects
41 related to the draft. After intense negotiation between both
42 sides of the aisle, we have arrived at a discussion draft
43 that I hope all members of the subcommittee will be able to
44 support.

45 There are still some outstanding issues that staff
46 continues to work on, and I hope that they can be resolved
47 before next week's subcommittee markup.

48 This package is critical to patients. It will ensure
49 that FDA has the resources and reforms needed to speed new
50 drugs, devices and treatments to those who are ill. These
51 user fee agreements will make the approval process more
52 transparent, more consistent and more predictable, benefiting
53 patients, but also keeping the United States the preeminent

54 leader in drug and device development and manufacturing.

55 Good-paying jobs in the drug and device industries, like
56 those in my home State of Pennsylvania, will be critical to
57 our economic recovery, and we cannot afford to outsource
58 them.

59 I look forward to hearing from our witnesses today, to
60 get their thoughts and reactions on the discussion draft.

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

62 ***** COMMITTEE INSERT *****

|

63 [The information follows:]

64 ***** INSERT 9 *****

|
65 Mr. {Pitts.} I yield the remaining time to the chairman
66 emeritus of the committee, Mr. Barton.

67 Mr. {Barton.} Thank you, Mr. Chairman, and thank you
68 for holding this hearing today.

69 Put me down, as I said at the last hearing you had on
70 this, as undecided on this particular bill. I know that you
71 have worked very hard and your staff has worked very hard and
72 the minority staff and members have worked very hard on the
73 bill. My basic problem is that I am not sure the FDA
74 deserves a large increase in user fees given the amount of
75 money that they have been receiving in general fund
76 increases.

77 As you know, under the Patient Protection and Affordable
78 Care Act, there is a new 2.3 percent gross sales tax on the
79 sale of all medical devices in the United States beginning in
80 the year 2013. This tax is supposed to raise \$20 billion to
81 help offset the cost of President Obama's \$1 trillion new
82 health bill. A 2.3 percent tax is imposed on revenues, as
83 you know, and not profits, so that the tax applies to devise
84 regardless of they are sold at a loss. This is on top of the
85 current federal tax rate of 35 percent on corporate profits
86 and all State and local taxes in addition. It is obvious
87 that companies have less incentive to stay in the United

88 States than they did before these bills became law.

89 This Administration has indicated that the increased tax
90 will have little to no negative effect on medical innovation
91 in the United States. That just begs credulity, Mr.
92 Chairman. When you increase taxes across the board and then
93 throw these user fee increases on top of it, that has to have
94 a negative effect. It is simply a law of physics, so to
95 speak.

96 In any event, I do want to commend you and others for
97 trying to come together on a bipartisan bill. I think it is
98 obvious by my comments that I may be a no vote but I do want
99 to be a positive part of the process if at all possible.

100 I want to thank our witnesses for being here today, and
101 with that, Mr. Chairman, I can yield the remaining 1 minute
102 to someone else or yield it back to you.

103 [The prepared statement of Mr. Barton follows:]

104 ***** COMMITTEE INSERT *****

|
105 Mr. {Pitts.} All right. The gentleman yields back.

106 The chair recognizes the ranking member of the Subcommittee
107 on Health, Mr. Pallone, for 5 minutes.

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

109 Today, the subcommittee is meeting to hear testimony
110 about the released discussion draft concerning the
111 prescription drug, medical device, generic drug and
112 biosimilar drug user fee agreements as well as several other
113 FDA-related proposals including programs to foster the
114 development of prescription drugs for children,
115 administrative and regulatory reforms at the FDA, and drug
116 shortages.

117 I will note as a matter of process that each of these
118 issues has had its own hearing in the subcommittee over the
119 course of the 3 months, and I want to commend Chairmen Pitts
120 and Upton and the staffs on both sides. We have worked very
121 hard to cover a lot of ground, and I would also like to thank
122 all the subcommittee members for their participation in these
123 hearings and I welcome their comments and suggestions on the
124 discussion draft as we continue to move forward.

125 Let me state that we have not yet reached full agreement
126 on the discussion draft in time for today's hearing. As we
127 will be seeing, the bill contains language largely identical

128 to the March draft released by the Republicans except for the
129 brackets surrounding a majority of the text. These brackets
130 indicate that the bill is a work in process and we continue
131 to make headway.

132 There are many issues that have been worked out.
133 Specifically, we have been able to make substantive changes
134 to the FDA reforms in this draft would have led to many
135 unintended and unacceptable consequences to FDA's regulatory
136 scheme. We have also been working hard to include language
137 that would equip the FDA with the authority and the resources
138 it needs to address a growing global drug supply. That
139 language has come a long way, and I am optimistic that we can
140 strengthen it further.

141 It is important to note that there are still key
142 concerns remaining but the process has been a good one to
143 date and I am hopeful that we can come together to address
144 those outstanding issues and generate a consensus, a
145 bipartisan product that both sides can support.

146 I just wanted to quickly comment on the four user fee
147 proposals that are the impetus behind this legislation. The
148 discussion draft is largely based on the agreements between
149 the FDA and the industry. These programs represent a
150 critical opportunity to work alongside FDA, industry and
151 other stakeholders to build upon and improve these critical

152 programs. Together we can help give patients access to safe,
153 effective and breakthrough medical treatments while
154 supporting the advancement of science and promoting a
155 thriving life science industry in the United States.

156 A particular note of course is the new generic drug user
157 fee agreement, which will dramatically improve the median
158 approval times for generic applications. This program will
159 cause an influx of generic drug products onto the market and
160 into the hands of consumers, thereby significantly lowering
161 health care costs.

162 I just want to welcome back our witnesses here today.
163 You have been a great resource to our subcommittee throughout
164 this process. We are eager to hear your opinions and your
165 suggestions, and I look forward to working with you, Chairman
166 Pitts, leading up to next week's scheduled markup to improve
167 the discussion draft further. And again, thanks for the
168 continued bipartisanship.

169 I would like to yield my 2 minutes left to the chairman
170 emeritus, Mr. Dingell.

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

172 ***** COMMITTEE INSERT *****

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173 Mr. {Dingell.} Mr. Chairman, I thank you for holding
174 today's hearing and I thank my good friend, Mr. Pallone, for
175 yielding to me.

176 I am delighted that we are having this hearing and I am
177 happy to work together with my colleagues in a bipartisan
178 consensus effort to achieve a good piece of legislation on
179 food and appliance and other performance by the FDA.

180 FDA's authorities are not sufficient to protect our drug
181 supply chain. Investigations by this committee found the FDA
182 not only lacks knowledge of how many drug manufacturing
183 facilities are operating overseas, what entities are
184 importing drugs or when incidents like adulteration, theft,
185 counterfeiting, contamination or repeated manufacturing
186 failures are posing health risks. FDA has lacked the
187 authority to detain or destruct harmful drugs, to prevent
188 medical product from entering the country if the manufacturer
189 prohibits inspection or to require importers to provide
190 compliance information at the border.

191 Current law has unintentionally created an unlevel
192 playing field which hurts our domestic manufacturers. While
193 FDA inspects domestic manufacturers every 2 years, it may or
194 may not inspect foreign manufacturing facilities, although it
195 occasionally gets around to it about every 9 years. This

196 committee must address these critical gaps in FDA's authority
197 and the knowledge of our entire food chain from active
198 ingredients to the patient's medicine cabinet. FDA ought to
199 know the parties who are manufacturing, distributing or
200 importing drugs and should be able to take action against
201 those who are allowing harmful drugs into the United States
202 market.

203 We have before us today an opportunity to deal with the
204 shortage of money and personnel and see to it that we stop
205 making Americans sick or killing Americans by having a
206 failure to have Food and Drug have the ability to carry out
207 its responsibilities. I thank you, Mr. Chairman.

208 [The prepared statement of Mr. Dingell follows:]

209 ***** COMMITTEE INSERT *****

|
210 Mr. {Pitts.} The gentleman yields back, and I now
211 recognize the chairman of the full committee, Mr. Upton, for
212 5 minutes.

213 The {Chairman.} Thank you, Chairman Pitts, for today's
214 hearing on the reauthorization of the FDA user fees and the
215 impact of innovation on American patients and jobs.

216 Since the beginning of February, this subcommittee has
217 held six hearings on the FDA, and during these hearings, we
218 have heard from witnesses from around the country on how
219 Congress can help FDA become more predictable, consistent and
220 transparent and how that will foster innovation here in the
221 United States. I have heard this back home from my
222 constituents as well. I think we all agree that fostering
223 innovation does help American patients and aids in creating
224 American jobs. As part of our efforts to foster that
225 innovation, we need to fix the recent problems with the
226 investigational device exemption approval process and the
227 medical device modifications guidance document. Recent FDA
228 policy changes have created some problems, and we intend to
229 use the user fee legislative process to rectify them.

230 I really want to thank Mr. Waxman and Mr. Pallone and
231 Mr. Dingell and other members of this committee for their
232 constructive and bipartisan work to reauthorize these user

233 fees. During the past couple of months, we have had a number
234 of productive conversations on ways to improve the regulatory
235 process at FDA. As I said at the start of this process, we
236 need to reauthorize the user fees by the end of June to
237 assure continuity at the FDA and increase predictability for
238 America's medical innovators and job creators. We still have
239 work to do but because of the bipartisan commitment from
240 members on both sides of the aisle, I am convinced that we
241 are on track to do that, and I appreciate all the hard work,
242 particularly from the staff as they have spent countless
243 numbers of hours working to make sure that we can have a
244 productive bill, and I yield the balance of my time to the
245 vice chairman of the subcommittee, Dr. Burgess.

246 [The prepared statement of Mr. Upton follows:]

247 ***** COMMITTEE INSERT *****

|
248 Dr. {Burgess.} I thank the chairman for yielding. I
249 want to thank the chairmen of the full committee and
250 subcommittee as well as the ranking members of the full
251 committee and subcommittee for moving this legislation
252 forward. I think the manner that this has been approached is
253 one that has been constructive and certainly been respectful
254 of individual member concerns. We have been sensitive to
255 patient concerns and we are focused on finding an end product
256 that is workable for the agency and for the patients that it
257 serves.

258 The impact of these areas, the medical device, the
259 pharmaceutical, the biologic and generic industries of the
260 United States certain reaches farther than the patients that
261 benefit from them, and we will hear a lot about job creation
262 and help to the economy, but the patient concerns must remain
263 our primary focus. And these industries do affect commerce.
264 They affect technology. They do affect the economy and they
265 provide quality jobs to Americans, which range from the
266 scientific to the highly skilled and technical and those
267 involved in their manufacturing.

268 The Food and Drug Administration has one of the most
269 important missions of any federal agency to ensure that
270 medical products are safe and effective. They are also the

271 gateway to providing patients with products that help them
272 maintain their health, perhaps help them live with a chronic
273 condition. We have to be certain that that gateway does not
274 become a bottleneck. I think there are constructive updates
275 that can be made and I appreciate so much the discussion
276 draft now being out there for all of us to reflect and offer
277 our thoughts.

278 Again, I want to thank the chairman for his approach to
279 the process, thank our witnesses for their willingness to
280 come before this committee multiple times, for the
281 transparency that they have exhibited and the fact that this
282 has come through under regular order and that the chairman
283 has worked to a product which I think both sides of the dais
284 can justifiably be proud, and I--

285 [The prepared statement of Mr. Burgess follows:]

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

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287 Mr. {Shimkus.} Will the gentleman yield?

288 Dr. {Burgess.} Yes, I will be happy to yield.

289 Mr. {Shimkus.} Thank you. I want to just take a minute
290 and talk about this process and some of the reforms that are
291 proposed and just make the point, especially in two areas
292 that I have been interested in, the investigative device
293 exemption and the 510(k) modifications.

294 The attempt is really to remedy through public policy
295 changes in the operation that the FDA has done in the last
296 couple years. So it is an attempt to return back to a day
297 when these two areas were working and we weren't losing
298 innovation and jobs and folks moving overseas to get these
299 approvals. And so I hope that you all will when we get into
300 that part of the discussion receive it in the attempt that we
301 are trying to portray it. We really want to get back to
302 where we don't have this backlog and we are the innovators,
303 we are the producers and we lead the world again.

304 I yield back my time.

305 [The prepared statement of Mr. Shimkus follows:]

306 ***** COMMITTEE INSERT *****

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307 Mr. {Pitts.} The chair thanks the gentleman and now
308 recognizes the ranking member of the full committee, Mr.
309 Waxman, for 5 minutes for an opening statement.

310 Mr. {Waxman.} Chairman Pitts, thank you for holding
311 this hearing today.

312 Although we were not able to come to full agreement in
313 time for the discussion draft released yesterday, I am
314 pleased with the progress that we have made on this user fee
315 package thus far. I am optimistic that we will get to full
316 agreement soon. We all know how important it is to
317 reauthorize the underlying user fee programs in a timely way.
318 No one is served by adding controversial proposals to the
319 bill. That would only serve to slow the process.

320 So far, we have worked together to avoid weighing down
321 this critical legislation with extraneous policies about
322 which we cannot agree. This will ensure that we get the work
323 on these critically important bills done in time.

324 I am particularly hopeful about the progress we have
325 made in the area of drug safety as it relates to the
326 increasingly globalized supply chain. Mr. Dingell has a
327 strong bill that has served as a template in this area, and I
328 appreciate all the work that Mr. Upton and Mr. Pitts have
329 done to incorporate provisions modeled on that bill.

330 I want to note however that I continue to have strong
331 concerns with respect to devices. We have all heard the
332 increasing rhetoric that FDA is slowing innovation and
333 forcing jobs abroad, but that does not justify the troubling
334 provisions that could compromise patient safety that are
335 under consideration. There are numerous examples of unsafe
336 medical devices that have been permitted on the market and
337 have caused incalculable suffering for victims. And that
338 occurs under the current system with the powers FDA has
339 today. Now is not the time to go backwards and take away
340 important authorities from the FDA that it needs to help
341 ensure the safety and effectiveness of devices. I will
342 continue to oppose any addition of any provisions that would
343 prevent FDA from doing what it feels necessary to protect
344 patients from unsafe and ineffective devices.

345 Let me turn now to the area of antibiotics. The
346 discussion draft includes the GAIN Act, which is a good first
347 step toward creating incentives for the development of new
348 antibiotics, which we all agree we desperately need. I
349 remain concerned that the bill does not narrowly target
350 antibiotics that treat dangerous infections for which we
351 don't have adequate treatments. The bill should also include
352 provisions to ensure that the efficacy of these newly
353 developed antibiotics is preserved once they are on the

354 market. These are goals we should all share and I am
355 optimistic that we will fix the bill to achieve them.

356 I also look forward to learning more today about the
357 proposal put forward by the Infectious Disease Society of
358 America, the Limited Population Antibacterial Drug, or LPAD--
359 it sounds like a new technical device sold by Apple--approval
360 mechanism. This proposal would establish a more rapid
361 regulatory pathway for new antibiotics targeted at the most
362 serious infections.

363 The concept appears to have great promise at speeding
364 important new antibiotics to the market, but I think we need
365 to be assured that these drugs will not be inappropriately
366 used. If we cannot get that assurance, we should all be
367 concerned about moving forward with this kind of proposal.

368 Strengthening and improving FDA is in the interest of
369 all Americans. I look forward to continuing to work with all
370 of my colleagues on this committee to reach bipartisan
371 agreement on this critically important legislation, and I
372 yield back the balance of my time.

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

374 ***** COMMITTEE INSERT *****

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375 Mr. {Pitts.} The chair thanks the gentleman.

376 We will now to go to panel one. We have two panels
377 today. Our first panel will have two witnesses, Dr. Janet
378 Woodcock, Director of the Center for Drug Evaluation and
379 Research at the FDA, and Dr. Jeffrey Shuren, Director, Center
380 for Devices and Radiological Health. We are happy to have
381 both of you here today.

382 Dr. Woodcock, you are now recognized for 5 minutes for
383 your opening statement.

|
384 ^STATEMENTS OF JANET WOODCOCK, M.D., DIRECTOR, CENTER FOR
385 DRUG EVALUATION AND RESEARCH, U.S. FOOD AND DRUG
386 ADMINISTRATION; AND JEFFREY E. SHUREN, M.D., J.D., DIRECTOR,
387 CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

|
388 ^STATEMENT OF JANET WOODCOCK

389 } Dr. {Woodcock.} Thank you. Mr. Chairman, members of
390 the subcommittee, thank you for the opportunity to testify
391 about the three important drug user fee proposals that are
392 laid out in the discussion draft. Each of three drug user
393 fee programs is important for the public, and will, if
394 enacted, impact positively on patients, industry and on
395 biomedical innovation.

396 The fifth iteration of the prescription drug user fee
397 program contains important advances for regulatory science
398 and patient-centered drug development as well as maintaining
399 consistent and predictable review process for the innovator
400 industry. The biosimilars user fee program will support the
401 growth of a new industry and will help provide more
402 affordable biological drugs to the public. Both I think are
403 very important public goals.

404 The generic drug user fee program as proposed would

405 represent a historic agreement to maintain a high and uniform
406 level of drug quality no matter where the drug is sourced in
407 the world. It also will ensure a robust and predictable path
408 to market for generic drugs that should invigorate the
409 industry.

410 That said, implementation of these three new programs if
411 enacted will create a significant body of work for the
412 agency. We are eager to undertake this but we are wary of
413 additional provisions, unfunded provisions. The experience
414 after the FDA Amendments Act I think is illustrative. While
415 FDA implemented the many needed safety programs that were
416 stipulated in the Amendments Act, we had to miss a number of
417 user fee goals under the prescription drug user fee program
418 and slow down our review process, and while that was a worthy
419 tradeoff, we have to recognize that any additional provisions
420 will have tradeoffs on workload.

421 I understand that there are other policy issues and
422 development challenges that are unaddressed by the user fee
423 proposals, which are really about process and procedures, and
424 I am happy to answer questions about these issues and I
425 really look forward to the discussion. Thank you.

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

427 ***** INSERT 1 *****

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428 Mr. {Pitts.} The chair thanks the gentlelady.

429 Dr. Shuren, you are recognized for 5 minutes for your

430 opening statement.

|
431 ^STATEMENT OF JEFFREY SHUREN

432 } Dr. {Shuren.} Mr. Chairman and members of the
433 committee, thank you for the opportunity to testify today.

434 As you know, on February 15th, FDA and representatives
435 from the medical device industry reached an agreement on
436 proposed recommendations for the reauthorization of the
437 Medical Device User Fee Act, or MDUFA, the details of which
438 we provided to you on March 16th. As required by law, we
439 held a public meeting on March 28th and sought public comment
440 on the proposal package. We plan to send the final package
441 to you by the end of this week.

442 When I came to CDRH in 2009, in response to concerns
443 expressed by industry and others, we initiated a review of
444 our device premarket review programs. The following year, we
445 released two reports that concluded as I have testified
446 before that we had not done as good a job managing the review
447 programs as we should have. The number one problem we found
448 was insufficient predictability, which was leading to
449 inefficiencies, higher costs for industry and FDA, sometimes
450 delays in bringing safe and effective products to market.

451 In January 2011, we announced a plan with 25 specific
452 actions that we would take that year to improve the

453 predictability, consistency and transparency of our premarket
454 programs. We announced additional steps since then. As of
455 today, 30 actions have been completed or well underway. They
456 are intended to create a culture change toward greater
457 collaboration, interaction, transparency and the appropriate
458 balancing of benefits and risk. They focused on assuring
459 predictable and consistent decision making and application of
460 the least-burdensome principle and implementing more
461 efficient regulatory processes.

462 Preliminary data indicate that the actions we have taken
463 have started to bear fruit. For example, the backlog of
464 510(k) submissions that had been steadily increasing from
465 2005 to 2010 decreased for the first time last year and are
466 continuing to decline in 2012. The backlog of PMA
467 submissions that had been steadily increasing from 2007 to
468 2011 has decreased this year for the first time, and average
469 total time for review appears to be decreasing for the first
470 time as well.

471 However, we still have much work to do. Reauthorization
472 of MDUFA will provide the resources that CDRH needs to
473 continue improving the device review programs and help reduce
474 the high staff turnover that has adversely affected review
475 predictability and consistency. The proposed MDUFA
476 recommendations we have agreed upon with industry includes

477 several important process improvements. For example, if a
478 performance goal on a device application is missed, the MDUFA
479 proposal would require FDA and applicants to work out a plan
480 to complete the work on the submission, ensuring that no
481 submission would be left behind, and requiring a new
482 substantive interaction between FDA and an applicant would
483 help assure sufficient time for the applicant to properly
484 respond to appropriate questions. These and other proposed
485 enhancements are intended to achieve a shared outcome goal of
486 reduced average total time to decision, which both we and
487 industry believe is an important indicator of a successful
488 premarket review program.

489 The agreement we have reached with industry strikes a
490 careful balance between what industry agreed to pay and what
491 FDA can accomplish with the amount of funding proposed.
492 However, we have concern that even if device user fee
493 resources are increased under MDUFA III, additional new
494 legislative mandates imposed on CDRH could divert resources
495 and undermine FDA's ability to achieve the new performance
496 goals. We are very willing to work with Congress on
497 initiatives that complement the user fee agreement. However,
498 just as FDA and industry mutually agreed that some
499 initiatives would be part of the formal agreement, we also
500 agree that some initiatives would not be part of the

501 agreement. Additional legislation to codify initiatives the
502 agency and industry chose not to devote resources to risks
503 diverting resources from achieving MDUFA goals and could
504 undermine the user fee agreement entirely.

505 When PDUFA was last reauthorized in 2007, as you heard,
506 the addition of new policy-related requirements ultimately
507 resulted in FDA's drug review program having to temporarily
508 suspend meeting its PDUFA review goals in order to meet the
509 statutory mandates. We want to avoid such a situation so
510 that CDRH can focus on meeting the ambitious new proposed
511 MDUFA program goals and achieving timely patient access to
512 safe and effective devices, which is an objective that we
513 share with industry, health care practitioners, patients,
514 consumers and you.

515 Mr. Chairman, we share your goal of timely
516 reauthorization of MDUFA. We look forward to working with
517 you toward enactment of this critical legislation. I commend
518 the subcommittee's efforts and am pleased to answer any
519 questions the subcommittee may have. Thank you.

520 [The prepared statement of Dr. Shuren follows:]

521 ***** INSERT 2 *****

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522 Mr. {Pitts.} The chair thanks the gentleman.

523 I will begin the question period and recognize myself
524 for 5 minutes for that purpose. Dr. Woodcock, we will begin
525 with you. In your testimony, you say that FDA is expediting
526 manufacturing change submissions to help with drug shortages.
527 In the discussion draft, we include a section on expediting
528 manufacturing changes that will alleviate a drug shortage.
529 In talking with patients and manufacturers and providers,
530 they tell me it is one of the best parts of the discussion
531 draft and it will really help with shortages. Do you agree
532 with those patients, providers and manufacturers that
533 expediting manufacturing changes that will alleviate drug
534 shortages is a good idea? I would like your comments on that
535 section.

536 Dr. {Woodcock.} We are currently able to expedite
537 manufacturing changes and we do to alleviate shortages or to
538 prevent them if we hear about them in advance. So we do not
539 need authority authorities to expedite a review of
540 manufacturing changes or implementation by manufacturers.

541 Mr. {Pitts.} All right. What is the latest on medical
542 gases? We had a hearing on this issue. Will you have a
543 proposal to share with the committee by the end of the week
544 on this?

545 Dr. {Woodcock.} Well, both parties will have to. We
546 are in active discussions with the association. I have had
547 personal meeting with the association and my staff and there
548 have been multiple additional discussions. I think we are in
549 substantial agreement but we are continuing to go back and
550 forth and make sure we have all the details nailed down, so I
551 can't guarantee, because it is only my side of it, that it
552 will done by the end of the week but we certainly are working
553 very hard on bringing this to a conclusion.

554 Mr. {Pitts.} The user fee discussion draft includes
555 language to enhance FDA performance reporting in the drug
556 space by including division-level data. I believe there is
557 great value in regularly gathering and analyzing the best
558 possible data in order to understand where there are working
559 and where they need improving. Collecting more granular
560 information at the review division level will allow FDA
561 management, patients, industry and Congress to better
562 identify where things are working and where improvements are
563 needed. As an example, in November of 2011, the agency
564 issued a report citing the approval of 35 innovative drugs
565 that represented advances in treatment for many serious
566 disorders. If we had division-level data, we could better
567 understand what practices led to such an accomplishment and
568 how we could apply those lessons in other areas. Do you

569 agree that collecting, reporting this information is a good
570 idea given that it will help us understand how we can apply
571 these best practices in other parts of the drug center and
572 agency? Would you comment on that, please?

573 Dr. {Woodcock.} Certainly. We have calculated the
574 requirements for personnel and investment in generating
575 additional formal reports. We really do believe in
576 transparency of all our processes, and I believe I as a
577 manager am accountable to you and to the public to make sure
578 that we review particularly lifesaving or life-altering drugs
579 as rapidly as possible. It is one of my highest priorities.
580 However, setting up additional reporting systems, we
581 calculate would cost us \$4.7 million based on what is laid
582 out in the draft and would require 15 FTEs, or full-time
583 equivalents, of people to work on that. Those people would
584 be diverted from working on reviewing the applications.

585 Now, the division-by-division variability in how many
586 applications come out and how many of those are approved and
587 so forth is primarily a function of the input. So right now,
588 if you looked at it sort of naïvely, you would say our cancer
589 group is like the most productive group and they do the best
590 job. But they get--right now there is a renaissance of
591 cancer therapies based on the molecular knowledge of cancer
592 that has been generated and so they are able to approve--we

593 are seeing a lot of very good applications and we are able to
594 approve those rapidly.

595 So I don't think you can make a cause-and-effect link
596 between what comes out in a given disease area and their
597 particular productivity. For example, I think our neurology
598 division is wonderful and does a fantastic job but we haven't
599 been able to approve a lot of new drugs for Alzheimer's
600 because those drugs have failed in development.

601 Mr. {Pitts.} The chair thanks the gentlelady. My time
602 is expired.

603 I yield to the ranking member, Mr. Pallone, for 5
604 minutes for questions.

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

606 I am going to start with Dr. Woodcock and may able to
607 get to Dr. Shuren if there is time. Well, first, welcome
608 back, and I appreciate your being with us again today. I
609 wanted to focus on review times for Abbreviated New Drug
610 Applications, or ANDAs. Under current law, what is the
611 length of time in which the FDA is required to review generic
612 drug applications?

613 Dr. {Woodcock.} This is like a quiz. I think it might
614 be--

615 Mr. {Pallone.} At least it is not yes or no.

616 Dr. {Woodcock.} I think it is 180 days.

617 Mr. {Pallone.} Okay. And what is the median review
618 time for ANDAs today?

619 Dr. {Woodcock.} Currently, the average or median or
620 approximately average review time is 30 months.

621 Mr. {Pallone.} And how long do you think it will take
622 to significantly reduce the review times for generic drug
623 applications?

624 Dr. {Woodcock.} I believe if the proposed user fee
625 program that is put within the discussion draft is enacted,
626 within several years we will be seeing a greatly improved
627 performance.

628 Mr. {Pallone.} And then can we expect to see any
629 meaningful reduction in review times in year one or year two
630 of the generic user fee program?

631 Dr. {Woodcock.} We will certainly try. However, we
632 have a backlog that comprises almost--there are 2,600
633 applications in the queue that we have to clear out, and that
634 would be our first priority.

635 Mr. {Pallone.} Chairman Pitts just asked and referred
636 to the discussion draft on PDUFA, and I guess on pages 18 and
637 19 there is some bracketed language that will require FDA to
638 report to Congress on various statistics about the agency's
639 drug reviews, and I wanted to ask you about this language.
640 Was this part of the negotiated user fee agreement?

641 Dr. {Woodcock.} Could you repeat the question?

642 Mr. {Pallone.} Sure. I'm talking about PDUFA, and the
643 chairman asked and referred to the discussion draft. On
644 pages 18 and 19, there is some bracketed language that would
645 require the FDA to report to Congress on various statistics
646 about the agency's drug reviews. I don't think that was part
647 of the negotiated user fee agreement, correct?

648 Dr. {Woodcock.} Yes, that was not part of what we
649 negotiated with the public and with industry, and it was not
650 accounted for in the resource calculations for the user fee.

651 Mr. {Pallone.} So that was my question. I am concerned
652 about putting a burden on the agency that is not funded by
653 user fees and could result in an unwarranted reshuffling of
654 resources that Congress intended to be dedicated to other
655 activities, and I think we need to be careful when we start
656 opening up the PDUFA agreement. I don't know if you wanted
657 to comment on that a little more.

658 Dr. {Woodcock.} Yes. I believe, as I said, very highly
659 believe in transparency and accountability of the new drug
660 review program to the public, to Congress and to any of our
661 stakeholders. However, we feel these additional tracking
662 requirements when unfunded will divert us from actually
663 accomplishing the objectives that are laid out by Congress in
664 the user fee agreement.

665 Mr. {Pallone.} Now, let me go to Dr. Shuren for a
666 question. I have a couple minutes or less. I wanted to ask
667 you about one of the provisions in the discussion draft
668 related to devices, specifically Section 706 would change the
669 standard for when device manufacturers are required to submit
670 a new 510(k) application for changes to their already cleared
671 devices. It might seem like an arcane issue, but I know it
672 is an extremely important one. Permitting companies to make
673 changes to their devices without first obtaining FDA
674 clearance could result in devices on the market over which
675 the FDA had had very little oversight and knows very little
676 about. Industry of course would say that if they are just
677 making small changes to the device, there is no need to go
678 through the 510(k) process again. But I wanted to get a
679 better sense from you about what is going on here. Is there
680 a need for any change here? Can you speculate on why the
681 language of 706 is being included in the draft, and basically
682 does the FDA have concerns about the language in Section 706?

683 Dr. {Shuren.} We believe the existing standard that we
684 have for modifications is a good one. Most modifications
685 made to a device do not come to the FDA for review. The only
686 ones that come are those that could significantly affect
687 safety or effectiveness. The issue right now is about a
688 guidance we put out on modifications that we did not put out

689 with the intention of increasing in any significant way the
690 number of 510(k)s coming in but provide greater clarity in
691 places that have been gray zones and emerging technologies.
692 We recognize there are many concerns with the guidance. That
693 is why we have had lots of meetings with industry. We have
694 even had two all-day meetings with a group of companies,
695 trade associations coming in the door and raising their
696 issues and working it through. Our intent is to get that
697 guidance right, and we know because of the concerns, our plan
698 is, we would actually put out a new draft guidance and make
699 sure we work it out.

700 Our concern with what has been proposed in the
701 legislation is it would change the existing approach that we
702 had that had been working for many years, and instead changes
703 it to only submit if it does significantly affect safety and
704 effectiveness. If it does affect safety and effectiveness,
705 you don't submit a 510(k). The product wouldn't come on the
706 market. So essentially companies will be making changes to
707 their devices and none of those changes will be coming to the
708 FDA for review. That causes significant concern. You have
709 devices like linear accelerators that blast radiation at
710 patients to treat cancers. You can now make modifications
711 that can impact that technology, and we won't see it, and we
712 have plenty of cases where companies made changes, they did

713 some testing, and there were big problems that but for the
714 FDA review, those unsafe technologies would have gotten to
715 patients, and that is what we worry would happen with this
716 change in the law.

717 Mr. {Pallone.} All right. Thank you, Doctor.

718 Mr. {Pitts.} The chair thanks the gentleman and now
719 yields to the vice chairman of the committee, Dr. Burgess, 5
720 minutes for questions.

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

722 Dr. Shuren, we might come back to the issue of
723 modifications if I have time, but let us talk for a minute
724 about the 510(k) process. It is my understanding that when
725 the Food and Drug Administration clears a device through the
726 510(k) process, it tells the company that they have received
727 a substantial-equivalence determination and then the FDA
728 sends a letter to the company that expressly states, please
729 be advised that the FDA's issuance of a substantial-
730 equivalence determination does not mean that the FDA has made
731 a determination that your device complies with other
732 requirements of the act, that being the Food, Drug and
733 Cosmetic Act. Is that a correct statement?

734 Dr. {Shuren.} As a paraphrase, and then the company is
735 responsible for assuring they have met what we have called
736 general controls, things that pertain to reporting

737 requirements or labeling or meeting our quality systems or
738 Good Manufacturing Practices.

739 Dr. {Burgess.} If there is a device that is found to be
740 defective that has been approved under a 510(k) authority and
741 another device is found to be substantially equivalent,
742 because of the defect that you discovered in the predicate
743 device, you would do something to prevent that follow-on
744 device from going to the market. Is that not correct?

745 Dr. {Shuren.} What we do in those cases, and there are
746 limited cases, we try to--within our authority we might put
747 explanations in the labeling, try to address it as best we
748 can. The challenge is that those may be ineffective. Right
749 now, there is not a responsibility on the part of the
750 manufacturer to show that if they replicate a design flaw,
751 for example, that they have put in appropriate mitigations to
752 make sure that does not affect patient safety or
753 effectiveness. It has been proposed by some in industry what
754 we would do is, well, you would clear it. They could go to
755 market and then you would build a legal case to say it is
756 misbranded and then take an enforcement action against the
757 company, which kind of puts the cart before the horse. In
758 reality, what we do is clear a device, then maybe take an
759 enforcement action, and what they would have to do is
760 actually come back in the door with another 510(k). So we do

761 what we can with the authorities that we have but it is not a
762 perfect solution. There is a way of solving it that focuses
763 very narrowly--

764 Dr. {Burgess.} Please let me ask a question so I am
765 sure that I understand it. Right now you are compelled to
766 approve an unsafe device under the 510(k) program?

767 Dr. {Shuren.} Well, compelled to determine that there
768 is substantial equivalence between the predicate and the new
769 product.

770 Dr. {Burgess.} Right. So substantial equivalence, but
771 then that does not necessarily infer that there is approval
772 to market the device under the Food, Drug and Cosmetic Act.
773 Is that correct?

774 Dr. {Shuren.} The terminology, just so we have it
775 right, is clearance. The manufacturer is then responsible
776 for meeting the other requirements of the law to then put it
777 on the market but they do not wait for any other affirmative
778 determination by the agency to go to market.

779 Dr. {Burgess.} This is important, and I am not trying
780 to be argumentative, but has the FDA allowed products that
781 they know to be harmful to reach the market?

782 Dr. {Shuren.} We believe that we have tried to take the
783 best actions we can to assure that the devices that come to
784 market are safe.

785 Dr. {Burgess.} Well, why didn't you just immediately
786 say these are misbranded and must not be marketed?

787 Dr. {Shuren.} So in the few cases where this has
788 happened, we have tried to either address it with labeling
789 and it is our hope that that will be an adequate mitigation.
790 What we don't have in a normal case in premarket review is
791 the data to support that it would be an adequate mitigation.

792 Dr. {Burgess.} Can you provide this committee--you keep
793 saying there are a limited number of examples. We actually
794 need to see those cases. I have to tell you, that concerns
795 me greatly that the Food and Drug Administration for all of
796 the heft that you have has allowed devices to come to the
797 market that may be inherently unsafe that you knew were
798 unsafe before they were marketed. So can you please--how
799 many cases do we have like that? You say there are a few but
800 is it like three or five or nine?

801 Dr. {Shuren.} There are a handful. We will get you
802 some of them. We would be happy to do so.

803 Dr. {Burgess.} All of them, Dr. Shuren. We need all of
804 them because we have to make a determination about where the
805 process is not working because clearly this is--I don't
806 believe you want it and I certainly don't want it where the
807 FDA is approving, because of a finding of substantial
808 equivalence, allows a device to come to market that is

809 inherently unsafe. I don't understand, why would you not
810 issue a mandatory recall immediately?

811 Dr. {Shuren.} Well, first of all, a mandatory recall,
812 if there is a problem, first of all, that we find the problem
813 thereafter. We tend to work with the company for a voluntary
814 recall. A mandatory recall winds up taking--can actually
815 take several years because it involves a formal hearing, and
816 oftentimes we work with the company--

817 Dr. {Burgess.} All I know is, in a medical staff
818 situation, if you know you have a provider, a doctor, who
819 presents a clear danger to patients, I mean, there is an
820 immediate revocation of that person's privileges. I don't
821 see why the same should not apply within your agency in the
822 device world.

823 Dr. {Shuren.} No, I appreciate that, and if folks think
824 that we actually have the authority to do that right now and
825 immediately stop it from going to market, it would be helpful
826 to us then to provide that clarity in legislation.

827 Dr. {Burgess.} Well, and part of the clarity is
828 providing us the cases because that is--Mr. Chairman, I think
829 we may need to involve the Subcommittee on Oversight and
830 Investigations to look into this because this is a
831 fundamental issue of patient safety, and if the primary
832 federal agency charged with providing that drugs and devices

833 are safe and effective is not meeting that first goal, that
834 is a serious, serious problem, and I will yield back my time.

835 Mr. {Pitts.} The chair thanks the gentleman and now
836 recognize the ranking member of the full committee, Mr.
837 Waxman, 5 minutes for questions.

838 Mr. {Waxman.} Thank you very much, Mr. Chairman. The
839 point Mr. Burgess raised is an important one, and if you feel
840 you need stronger or clearer legislation in that area, let us
841 know because we are concerned about whatever, even a handful
842 of devices that may be harmful.

843 Dr. Woodcock, I would like to ask you about two
844 proposals designed to help get new important antibiotics to
845 market. One is GAIN and the other is LPAD. First of all, on
846 GAIN, we know the pipeline for new antibiotics is essentially
847 dry. It is a serious public health threat and it is clear
848 that we need to look at ways to incentivize the development
849 of these lifesaving drugs. One way to do that, of course, is
850 to provide additional exclusivity. I think whenever we talk
851 about adding new exclusivity, we need to ensure that it is
852 truly necessary, and in this case, I think a good case can be
853 made that it is, but then it should be narrowly targeted so
854 that only the drugs we need to have developed are rewarded
855 with this generous prize, and exclusivity is often very
856 generous and you never get it back even when it is no longer

857 valid or useful.

858 I am concerned that the language in the discussion draft
859 does not adequately target, and I want to get your views on
860 that subject. As I read it, the legislation would provide 5
861 years additional exclusivity to an antibiotic that received
862 FDA approval based only its ability to treat or prevent
863 essentially any antibiotic-resistant bacterial pathogen. I
864 think this legislation should be narrowly targeted and only
865 apply to antibiotics approved for serious or life-threatening
866 diseases for which there is an unmet medical need. I would
867 like to know whether you agree. If so, how would that work
868 in practice? Is that a standard FDA could easily apply?

869 Dr. {Woodcock.} We do apply a standard on approval on
870 review called the Priority Review, and we determine whether
871 or not a product would be an advance in its class or is
872 simply yet another option amongst multiple options, so we do
873 have some experience in applying some standard like that. I
874 think of course it is up to Congress how you weigh these
875 different tradeoffs as far as the affordability of drugs
876 versus their availability. You don't want to set up an
877 incentive program, in my opinion, that drives developers
878 toward the broadest market and thus to neglect potentially
879 those challenging areas of, say, drug-resistant organisms,
880 which is where we have the greatest need for new antibiotics.

881 But because that is a narrow market, if you do an incentive
882 program, often the desire is to apply that to the broadest
883 market possible to gain the most obviously profit from doing
884 that. So I think Congress needs to think about what
885 incentive you are offering and how is that incentive going to
886 operate, and will it operate to solve the problem that has
887 been identified. There are several problems. One problem
888 is, we don't have antibiotics--

889 Mr. {Waxman.} Let me--it is very helpful but then I
890 think about all the things I still want to ask. So you agree
891 that we ought to be sure to narrowly focus this incentive
892 because otherwise an incentive becomes just very beneficial
893 to those who get it but not really solving the main problem
894 that we have. Is that correct?

895 Dr. {Woodcock.} I believe that Congress ought to define
896 the problem that you are trying to address and make sure you
897 design an incentive that incentivizes drug development to
898 solve that problem.

899 Mr. {Waxman.} I want to ask you about the LPAD
900 approach. This has been discussed by the Infectious Disease
901 Society of America, and as I understand it, this approach is
902 intended to establish a more rapid regulatory pathway for new
903 antibiotics targeted at the most serious infections. The
904 risk-benefit ratio for such antibiotics will often support

905 more narrowly tailored clinical trials that are needed for
906 other antibiotics. A fundamental aspect of this proposal is
907 that it would require that any antibiotic approved under this
908 pathway bear a strong label statement describing the limited
909 population of patients with serious or life-threatening
910 infections for which the drug had been approved and noting
911 that its safety and effectiveness had not been established
912 beyond this limited population. Companies would have to
913 provide their promotional materials to FDA before
914 distributing them. It seems this kind of approach could
915 really get help critically important antibiotics on the
916 market more rapidly than otherwise possible. However, for it
917 to work as intended and for it not to lead to lowering of the
918 approval standard, it has to have effective mechanisms for
919 ensuring that antibiotics approved for small populations are
920 indeed used by those small populations. I would like to hear
921 your views on whether you think LPAD maintains that balance.
922 Specifically, do you think that it will facilitate the more
923 rapid approval of important new antibiotics for limited
924 populations, and do you think that there are adequate
925 controls to prevent widespread off-label use in a much
926 broader population than for which it was tested and approved?

927 Dr. {Woodcock.} Yes, and yes. I believe that probably
928 a narrow development program, and we could offer, we believe,

929 a radically smaller development program than for an
930 antibiotic intended for broad uses is a stronger incentive
931 than financial--than exclusivity, number one. And number
932 two, we believe that particularly if Congress were to make a
933 statement about the antibiotic stewardship of this class of
934 products, good stewardship in the market, that that would
935 have the effect of limiting the use.

936 Mr. {Waxman.} Thank you.

937 Thank you, Mr. Chairman.

938 Mr. {Pitts.} The chair thanks the gentleman and
939 recognizes the gentleman from Illinois, Mr. Shimkus, for 5
940 minutes for questions.

941 Mr. {Shimkus.} Thank you, Mr. Chairman. Thank you all
942 for coming.

943 Dr. Woodcock, I agree that Congress needs to define a
944 problem we want to address, and that is part of this process
945 of the hearing and also some of the bills that have been
946 introduced. So I couldn't agree more, and of course, I will
947 focus mine on the IDE and the 510(k) issue.

948 First of all, Dr. Shuren, you said that the number of
949 applicants is down. Is that what you said in your opening
950 statement?

951 Dr. {Shuren.} No, the backlog, so the number of 510(k)s
952 that are still under review at the end of the year has gone

953 down. It had been going up for 510(k)s since 2005 every
954 single year.

955 Mr. {Shimkus.} Okay. Let me follow up then. According
956 to companies who I have talked to, your draft guidance could
957 increase 510(k) submissions by 300 to 500 percent. Do you
958 agree with that? And do you have the capability to respond
959 to that if that is the case?

960 Dr. {Shuren.} So first of all, we don't know if that
961 number is correct.

962 Mr. {Shimkus.} Have you heard that number before?

963 Dr. {Shuren.} We have heard that number before. But
964 putting aside whether data support that or not, we agree
965 there are concerns with the policy we put out, which is why
966 we are working with industry to make adjustments and try to
967 get it right. Our intent is not to see--

968 Mr. {Shimkus.} And that is what we are trying to do
969 legislatively also in response to what Dr. Woodcock said that
970 we should define a problem we want to address and we are
971 trying to legislatively address that problem.

972 Let me go to the IDE real quick, and you have also--a
973 couple concerns. First of all, one is that we do have an
974 issue that we think disregards the Administrative Procedures
975 Act in that it acts as--the guidance contradicts regulation
976 so concern one on that. It also--we do think it also could

977 be not in compliance with the Federal Food, Drug and Cosmetic
978 Act and a former IDE administrator says, and I quote, ``It
979 does not look like the authority is there to disapprove an
980 IDE based upon the fact that FDA doesn't anticipate that it
981 would support a marketing approval or clearance.'' So the
982 question is, how have innovators reacted to your policy
983 change?

984 Dr. {Shuren.} There have been concerns raised of what
985 we would not consider truly a policy change. Our IDEs, we
986 will not approve if it doesn't provide sound science or if
987 the investigational plan is inadequate. Now, what we said in
988 the guidance is, if it is a pivotal clinical trial and a
989 pivotal clinical trial is intended to demonstrate safety and
990 effectiveness--

991 Mr. {Shimkus.} The question is, how have the innovators
992 reacted? What have the innovators told you? I can tell you
993 what they have told me.

994 Dr. {Shuren.} So their concern is whether or not this
995 will actually lead to our not approving more clinical studies
996 than before. We think the language may not have articulated
997 clearly what we are talking about. That is namely that if
998 you submit a study that is producing sound science for its
999 intended purpose, what it is intended to do. In case of a
1000 pivotal trial--

1001 Mr. {Shimkus.} Let me--I only have a minute and 40
1002 left. One innovator told me that in 2012, he will only have
1003 been in the United States for 5 weeks prior to the first 5
1004 months of the year because he had to do clinical trials
1005 overseas. That is what we are hearing from innovators based
1006 upon this policy, and I think if the policy is questionable
1007 that it is against the Administrative Procedures Act and
1008 legally may be against the Federal Food, Drug and Cosmetic
1009 Act, I think that would raise some concerns as to the policy
1010 which is new and implemented under the last couple of years.

1011 Let me go to funding. In the last hearing, you did talk
1012 about funding and the like. Is it true that even under the
1013 agreement which doubles the user fees that FDA gets from
1014 industry, you will still get about 70 percent of your CDRH
1015 budget from appropriations?

1016 Dr. {Shuren.} About 65 to 70 percent of funding will
1017 come from--

1018 Mr. {Shimkus.} So you will have other non-user fee
1019 funds that are appropriated by Congress?

1020 Dr. {Shuren.} That is correct.

1021 Mr. {Shimkus.} Shouldn't Congress be able to give
1022 direction on how these funds are spent?

1023 Dr. {Shuren.} Congress has broad authority to weigh in
1024 on how we should actually use our funds.

1025 Mr. {Shimkus.} Thank you. Isn't it true that the FDA
1026 undertook activities during the life of MDUFA II that were
1027 significant resource investments and outside the agreement?
1028 And you probably know what I am talking about, the Institute
1029 of Medicine report that was unfinished and not totally
1030 accurate?

1031 Dr. {Shuren.} First of all, the IOM report, we didn't
1032 pay out of any user fee dollars.

1033 Mr. {Shimkus.} Right, and \$1.3 million of taxpayer
1034 funds went to the IOM report.

1035 Dr. {Shuren.} Well, there were concerns raised on the
1036 510(k) program, how well it was operating to meet the--

1037 Mr. {Shimkus.} But there was obviously concern about
1038 the accuracy of the IOM report also.

1039 Dr. {Shuren.} Well, we did disagree with one of their
1040 recommendations regarding the 510(k) program. We actually
1041 agreed with most of their other recommendations.

1042 Mr. {Shimkus.} Thank you, Dr. Shuren. I appreciate
1043 your time.

1044 Dr. {Shuren.} But I do want to make the point on
1045 clinical trials, because it is an important one, and we don't
1046 want innovators going overseas, but quite frankly, if we are
1047 approving a clinical trial and we are putting our name on it
1048 saying that this study is good enough to show safety and

1049 effectiveness but it doesn't and it is not going to then
1050 support that product coming to market, then we have put
1051 patients at risk because they are--

1052 Mr. {Shimkus.} But they are going overseas.

1053 Dr. {Shuren.} And then the companies come in the door,
1054 and this is exactly what was happening, with studies that
1055 then they weren't getting their products approved, and that
1056 is the worst thing for the company and it is the worst thing
1057 for patients. So the policies we have put out have actually
1058 tried to address the real problem, which is reviewers who are
1059 coming back to ask for a study that quite frankly they
1060 believe is the better study but that is not the point. It is
1061 the least-burdensome principle. They need to put out the
1062 study that is least burdensome and approve it. And the
1063 second is that they were holding up approvals trying to
1064 address questions that were not relevant at that time for
1065 making a decision and so draft policy we put out in the fall
1066 was meant to readjust that so that we were freeing up and
1067 making decisions and approving products. In fact, we are now
1068 seeing that first cycle approvals for clinical trials are
1069 going up.

1070 Mr. {Shimkus.} And I would just end by saying what I
1071 think we have done is moved our innovators overseas, and I
1072 yield back my time.

1073 Mr. {Pitts.} The chair thanks the gentleman and now
1074 recognizes the ranking member emeritus, Mr. Dingell, for 5
1075 minutes for questions.

1076 Mr. {Dingell.} Mr. Chairman, thank you. I commend you
1077 for this meeting of the committee and for your fine
1078 cooperation in framing this legislation and working with the
1079 minority. I also want to express the same commendations to
1080 our distinguished chairman.

1081 These questions go to Dr. Woodcock. Please respond yes
1082 or no. The heparin incident made it clear that there needs
1083 to be robust communications between drug manufacturers and
1084 FDA regarding unsafe or compromised drugs. Currently, does
1085 the Food, Drug and Cosmetic Act require manufacturers to
1086 notify FDA if they have reason to believe that their products
1087 have been adulterated, contaminated or misbranded prior to
1088 distribution? Yes or no.

1089 Dr. {Woodcock.} No.

1090 Mr. {Dingell.} Are drug manufacturers currently
1091 required to notify FDA if their drug has been stolen,
1092 counterfeited, lost or there have been repeated manufacturing
1093 quality incidents? Yes or no.

1094 Dr. {Woodcock.} My understanding is that they do have
1095 to notify us for quality problems under field alert reports.
1096 The rest is no.

1097 Mr. {Dingell.} Okay. Now, would requiring drug
1098 manufacturers to report such information to FDA confer
1099 benefit on the public health?

1100 Dr. {Woodcock.} Yes.

1101 Mr. {Dingell.} As FDA continues to regulate an
1102 increasingly globalized market, the ability of FDA to work
1103 and share information with trusted foreign regulatory
1104 counterparts is critical. Do you believe that, and is that a
1105 correct statement?

1106 Dr. {Woodcock.} Yes.

1107 Mr. {Dingell.} Doctor, is it true that FDA only shares
1108 commercial confidential information with State, local or
1109 trusted foreign regulators when FDA has written assurance
1110 that the agency will not disclose? Yes or no.

1111 Dr. {Woodcock.} Yes.

1112 Mr. {Dingell.} Doctor, can FDA currently share trade
1113 secret information with State, local or trusted foreign
1114 regulators? Yes or no.

1115 Dr. {Woodcock.} No.

1116 Mr. {Dingell.} Now, would authority to share this
1117 information with other regulators help monitor FDA's efforts
1118 to protect the American public with regard to today's
1119 globalized drug supply? Yes or no.

1120 Dr. {Woodcock.} Yes.

1121 Mr. {Dingell.} Now, would this authority help FDA to
1122 have better information to assess risk and target oversight?
1123 Yes or no.

1124 Dr. {Woodcock.} Yes.

1125 Mr. {Dingell.} Doctor, if given this authority, FDA
1126 would commit to only sharing such information with trusted
1127 foreign regulators when they have proper and satisfactory
1128 assurances that the foreign agency will not disclose. Is
1129 that correct?

1130 Dr. {Woodcock.} Absolutely yes.

1131 Mr. {Dingell.} Is that necessary for us to do?

1132 Dr. {Woodcock.} Yes.

1133 Mr. {Dingell.} I happen to think so. Now, Doctor, so
1134 then the agency would not share proprietary commercial
1135 information like the formulation of Coca-Cola with China or
1136 any foreign country. Am I correct on that?

1137 Dr. {Woodcock.} Yes.

1138 Mr. {Dingell.} And FDA would protect that concern and
1139 that policy. Is that right?

1140 Dr. {Woodcock.} That is correct.

1141 Mr. {Dingell.} Now, Doctor, I have a concern. We have
1142 the ability to regulate to some degree the shipment into this
1143 country of food, drug, cosmetics and devices. How about the
1144 raw materials or the components of this? What is FDA's

1145 ability to regulate? Do you have a statutory ability to
1146 regulate or not?

1147 Dr. {Woodcock.} We have very limited ability to
1148 regulate the supply chain of components.

1149 Mr. {Dingell.} Now, I must assume that being able to
1150 regulate that kind of activity and that kind of product would
1151 be extremely important to assure the safety of American
1152 consumers. Is that right?

1153 Dr. {Woodcock.} Yes.

1154 Mr. {Dingell.} We found that out in the heparin case,
1155 did we not?

1156 Dr. {Woodcock.} We did.

1157 Mr. {Dingell.} Now, this committee looked at this
1158 problem over the years of safety and that sort of thing, and
1159 one of the things that we found is that nobody seems to be
1160 able to keep out the admission of illegal substances, unsafe,
1161 counterfeits and things of that kind including some
1162 controlled substances, and I sense that a part of that,
1163 although not all, is the inability of Food and Drug to have
1164 the money, the personnel and the necessary cooperative
1165 agreements with other regulatory bodies that deal with entry
1166 of commodities and people into this country. Am I correct in
1167 that?

1168 Dr. {Woodcock.} Yes.

1169 Mr. {Dingell.} Do you need additional authority there?

1170 Dr. {Woodcock.} Yes.

1171 Mr. {Dingell.} Mr. Chairman, I notice I have used all
1172 my time. I thank you for your courtesy.

1173 Mr. {Pitts.} The chair thanks the gentleman and now
1174 recognizes the gentleman from Michigan, Mr. Rogers, for 5
1175 minutes for questions.

1176 Mr. {Rogers.} Thank you, Mr. Chairman.

1177 Dr. Woodcock, I want to thank you and your staff for
1178 working with us on the permanent reauthorization of BPCA and
1179 PREA. Thank you very much for doing that. I think it has
1180 been productive. I introduced that legislation with my
1181 friend, Ms. Eshoo from California, and Mr. Markey, and I
1182 think it is representative of good bipartisan work, which is
1183 included in the committee's draft today, so I am hoping that
1184 other members will join us in supporting that effort. I
1185 think they will, and I am proud to say the bill has support
1186 of numerous stakeholders, as you know, including the American
1187 Academy of Pediatrics, BIO and PhRMA. So I think we are in a
1188 good place. We will do good things. And again, I want to
1189 thank you and your staff for that. While making these laws
1190 permanent, the bill also includes important reforms to
1191 encourage earlier submission of pediatric plans, give the FDA
1192 new enforcement tools to make sure sponsors meet their PREA

1193 commitments and improve FDA's ability to track pediatric
1194 studies. I believe our bill strikes that right balance and
1195 will improve pediatric drug research, and I hope all members
1196 on the committee can support it.

1197 Dr. Woodcock, as you know, there was some language
1198 actually authored in 2007 that began the process of
1199 developing a standard numerical identifier, or SNI, to help
1200 the tracking and tracking of prescription drugs. However,
1201 the FDA currently does not have the authority to require the
1202 use of SNIs throughout the supply chain. Is that correct?

1203 Dr. {Woodcock.} That is correct.

1204 Mr. {Rogers.} So you are familiar with the proposal put
1205 forward by a broad group of stakeholders in the drug supply
1206 chain on this particular issue?

1207 Dr. {Woodcock.} Yes.

1208 Mr. {Rogers.} Great. So if you agree that additional
1209 statutory authority is needed to protect the drug supply
1210 chain, and I assume you aren't comfortable waiting another 5
1211 years, at least I hope you are not, for the next UFA
1212 reauthorization, to create a system that protects patient
1213 safety, I would encourage you to roll up your sleeves and sit
1214 down with this coalition, and I hope you can do that soon. I
1215 think it would be highly productive, and I believe there is a
1216 solution here that provides FDA with more authority than it

1217 has today but does so in a reasonable, thoughtful way that
1218 balances costs and enhancements to patient safety and the
1219 supply chain, so I am hoping that we can get a commitment
1220 that you will sit down with that coalition and begin that
1221 process.

1222 Dr. {Woodcock.} I would be happy to do so, and we
1223 obviously need to make advancements in this area. We are
1224 seeing, as we saw recently with the counterfeit Avastin and
1225 others, we are seeing more incursions of actual drugs that
1226 are totally fake into the U.S. drug supply.

1227 Mr. {Rogers.} Which is highly concerning, and
1228 concerning for you as well. So I look forward to hearing
1229 reports on those coalition meetings. Hopefully they will
1230 happen soon.

1231 Dr. Shuren, I have some concerns about that new
1232 proposal, and I know Mr. Shimkus talked about it a little bit
1233 on the 510(k) submissions. It is my understanding that they
1234 would have to submit these submissions under your new rules
1235 for small manufacturing issues like changing suppliers. Is
1236 that correct?

1237 Dr. {Shuren.} In a number of cases, it depends. The
1238 supplier change may be something that actually doesn't get
1239 reported to us.

1240 Mr. {Rogers.} But apparently there has been some

1241 confusion, but in some cases it would and in some cases it
1242 would not. Is that correct?

1243 Dr. {Shuren.} Yes, and we can actually get back to you
1244 with more details.

1245 Mr. {Rogers.} So there are details, so if I read that
1246 in total, as a manufacturer I would understand when exactly I
1247 have to report or when I do not have to report. Because my
1248 understanding is, there is confusion in the way it is
1249 written, and if you are on the manufacturing side of that,
1250 you are going to have to err on the side of reporting.

1251 Dr. {Shuren.} So there are a number of parts in that
1252 guidance where confusion has arisen. We recognize that. Our
1253 intent in the guidance was to clarify circumstances for
1254 submitting a modification because we had guidance out there
1255 beforehand and manufacturers were then running into
1256 circumstances where we have never addressed the question.
1257 They didn't know what to do. Our intent was to actually
1258 clarify those circumstances. We recognize there still is a
1259 lot of confusion, which is why we have taken the effort to
1260 try to work with industry and we will continue to do so to
1261 provide clarity that will be most helpful to them, but our
1262 goal is not to suddenly raise up the bar and see many more
1263 510(k)s getting in the door.

1264 Mr. {Rogers.} But unfortunately, the reality is, that

1265 is what is happening and they are going through these
1266 processes now believing that they have to do it, so having
1267 future conversations aren't really all that helpful.

1268 Dr. {Shuren.} Well, it is a draft guidance, so nothing
1269 has changed, and that is the whole point of the guidance
1270 process. We go out there, we get public comments and we can
1271 work this through. That happens all the time. If you
1272 actually look at the guidances we put out last year, it is
1273 about 44. We heard concerns about maybe three of them in any
1274 big way, and that kind of shows the process ultimately works.

1275 Mr. {Rogers.} I hear you, but that is the difference
1276 between not having to meet a payroll, meeting a payroll,
1277 meeting the guidelines for the government that regulates you.
1278 They will start to make adjustments based on those
1279 guidelines. It will cost them money. They are doing it
1280 today, which is exactly why we are hearing from innovators,
1281 this isn't worth it anymore, it is easier for me to head
1282 overseas than it is to try to deal with what is an untenable
1283 regulatory environment. That is what concerns me, and this
1284 notion that it is all just fine and it is only guidance and
1285 nobody should worry about it is absolutely incongruent with
1286 the real world. That worries me greatly, and I hope you will
1287 take a hard look at this and come back, and if that is the
1288 case, then start making serious indications to the folks who

1289 are actually under the gun for this investment to save kids'
1290 lives or devices or fill in the blank that you will make that
1291 early. Otherwise they are going to have to make these
1292 adjustments, and I think that is what you are missing and
1293 that is where the frustration is coming from. And I see my
1294 time is done, and I thank you, Mr. Chairman. I look forward
1295 to hearing about your progress in the coalition's effort to
1296 bring manufacturing and clinical trials back to the United
1297 States.

1298 Dr. {Shuren.} We would be happy to do it. We would
1299 actually be happy to come and talk to you in more detail on
1300 what is going on with clinical trials. In fact, some of the
1301 policies, if you really want to get technology to this
1302 country and keep it here, you focus on the very first
1303 clinical studies because the innovators have said loud and
1304 clear, if there is a good opportunity to start clinical
1305 studies here, we bring the technology here, we keep it here,
1306 because we keep going back to the same doctors and we put out
1307 policy in November to actually make it easier to start those
1308 early studies and start it earlier in device development than
1309 ever before. The feedback was very positive. In fact,
1310 companies have wanted to act under a draft policy, and we
1311 have allowed them if they wanted to because they like that
1312 policy so much, and we have heard very good feedback from the

1313 innovators on that.

1314 For modifications, it is a draft policy, it is not in
1315 effect, and we will work with companies and we are happy to
1316 come back and give you updates on it to finally get it right,
1317 and as I said, this is one where we anticipate we would go
1318 out with another draft before even moving to final.

1319 Mr. {Rogers.} Thank you, Doctor.

1320 Mr. {Pitts.} The chair thanks the gentleman and now
1321 recognizes the gentlelady from California, Ms. Capps, for 5
1322 minutes for questions.

1323 Mrs. {Capps.} Thank you very much, Mr. Chairman, and to
1324 our guests, thank you very much for being here today. I
1325 appreciate your testimony, Dr. Shuren.

1326 A couple of months ago at our hearing on medical device
1327 user fees, I had asked you about the Sentinel system for
1328 postmarket surveillance. The PDUFA V agreement allows for
1329 postmarket surveillance of prescription drugs through the
1330 Sentinel system. However, the same progress has not been
1331 made on the device side and the bill draft before us does not
1332 address this issue, and that is why I am working on language
1333 that would start the process of adding devices to the
1334 Sentinel program. I believe this would be a win-win for
1335 patients and the industry because patients would gain the
1336 security that potential device issues would be found early

1337 and recalls targeted to only those devices at risk.
1338 Similarly, industry would have the knowledge that data, not
1339 newspaper articles, would drive safety decisions. So I am
1340 going to have a question for Dr. Woodcock as well, but I
1341 would like you to discuss, please, the opportunities for
1342 Sentinel in the device base as you see them.

1343 Dr. {Shuren.} We think greater engagement for devices
1344 in Sentinel could be of tremendous value for not only
1345 patients but also for companies as we can identify if there
1346 is a problem more quickly so we don't get those big newspaper
1347 articles, and even more robust systems that we might be able
1348 to leverage in terms of informing for premarket review and
1349 ease some of the burden there. The barriers right now, the
1350 biggest one is, we don't have there a unique device
1351 identifier as we have on the drug side and therefore it is
1352 hard to link an actual device with a patient's experience
1353 with the device, and we have developed proposed legislation
1354 that--regulation--we can't do legislation yet--a regulation
1355 that is currently under review by the Administration that
1356 will help, and it was helpful when Congress said that
1357 Sentinel should be there, should be for drugs, because it
1358 gave a push for people to engage. We don't have quite the
1359 same push on the device side.

1360 Mrs. {Capps.} Well, so if we could get some language in

1361 this bill that would give you that push, if you will, would
1362 that be a value to you and do you see that it is not a one-
1363 to-one corollary, I am sure, but there are ways to make it
1364 possible for a direct connection to be made, at least some
1365 kind of connection to be made from the device to the
1366 patient's experience?

1367 Dr. {Shuren.} Yes, we do think that could be helpful.

1368 Mrs. {Capps.} I appreciate that. Thank you very much.

1369 Dr. Woodcock, I appreciate your testimony as well. Back
1370 in February at our hearing where you testified on generic
1371 drug user fees, you and I had discussed the drug shortage
1372 problems this country is facing. It is still facing them.
1373 It is a very important issue that affected then and continues
1374 to affect a great number of people including many of my
1375 constituents, and I had shared one story at that hearing.
1376 Given the gravity of this situation, I am pleased to see that
1377 current legislation now before us includes measures to try to
1378 address this problem, but I am concerned that the way the
1379 draft is written, it could preclude some health care
1380 providers from being involved. Currently, in three separate
1381 sections of the FDA user fee discussion draft, the bill lists
1382 stakeholders to be consulted with in regards to drug
1383 shortages. However, it doesn't specify what kind of
1384 stakeholders and health providers like nurse practitioners

1385 and physician assistants are notably absent from these lists,
1386 despite the fact that the work they do have been affected by
1387 drug shortages, in some ways even more directly because they
1388 are so much on the front lines. This is evident, for
1389 example, in a nurse anesthetist's difficulty in finding
1390 anesthesia drugs or an oncology nurse practitioner who is the
1391 actual person who dispenses the medication under the doctor's
1392 direction and they see firsthand the cancer drug shortages,
1393 so would you share with us your thoughts on the kinds of
1394 stakeholder engagement with regard to drug shortages?

1395 Dr. {Woodcock.} Well, we believe that we need to hear
1396 from the whole prescribing community, which includes a wide
1397 range of individuals. Also, the entire pharmacy community is
1398 a very important resource for us. So the stakeholders are
1399 almost anyone who uses, dispenses, prescribes or manages drug
1400 supply in this country and so it is a very broad group of
1401 people.

1402 Mrs. {Capps.} And I thank you for that. I believe
1403 there is an easy fix here, which I am sort of saying to our
1404 committee members to ensure participation and then just
1405 including the phrase ``all relevant health professionals''
1406 not just doctors and hospitals, and that is something you
1407 would then agree with?

1408 Dr. {Woodcock.} Yes.

1409 Mrs. {Capps.} That would be useful language to include?

1410 Dr. {Woodcock.} Yes.

1411 Mrs. {Capps.} I appreciate that. Thank you, and I
1412 yield back the balance of my time.

1413 Mr. {Pitts.} The chair thanks the gentlelady and now
1414 recognizes the gentlelady from North Carolina, Ms. Myrick,
1415 for 5 minutes for questions.

1416 Mrs. {Myrick.} Thank you, Mr. Chairman, and I thank
1417 both of you for being here.

1418 Dr. Woodcock, as you know, the discussion draft at hand
1419 makes an effort to further address the drug shortage issue,
1420 and I know the FDA is playing close attention to shortage
1421 issues as well as working with DOJ on issues of price gouging
1422 and stockpiling, but it recently came to my attention that
1423 there appears to be a growing problem with drug shortages for
1424 trauma and critical-care patients so I have got two questions
1425 for you. Does the FDA have a sense of how widespread the
1426 shortage is for drugs often used in trauma and critical-care
1427 settings, and how do the FDA and DEA need to work together to
1428 prevent further shortages in controlled substances used in
1429 the critical-care field? For example, are there changes that
1430 need to be made to the DEA number assignment system for
1431 controlled substances that are being substituted in the event
1432 of a shortage or are there other interagency solutions that

1433 could alleviate the shortage problem for DEA-controlled
1434 drugs, you know, short of an act of Congress, something that
1435 you could do internally or with the other agencies?

1436 Dr. {Woodcock.} Well, on the first question, we are
1437 well aware that both critical-care settings and trauma
1438 settings are being impacted by drug shortages. The shortages
1439 are for sterile injectable products, products that are
1440 injected directly into, say, a vein or your IV line
1441 primarily, and these actually are used in a wide variety and
1442 unfortunately very important medical illnesses, very serious
1443 and life-threatening illnesses. They are used in ICUs and
1444 emergency rooms as well as in cancer treatment, and we are
1445 aware of these shortages. We have heard from the
1446 professional societies, I have heard personally, and we are
1447 doing everything we can. This year we have averted 22
1448 shortages already because we have heard early notification.
1449 However, shortages do remain and they are causing serious
1450 consequences for the public.

1451 As far as the DEA, we work closely with the DEA. They
1452 have a system of allocating materials to companies based on--
1453 we provide information to the DEA on projected use for each
1454 year as part of their process, and we work with them on
1455 shortages, informing them and so forth, but I believe that
1456 further discussion of this might require going into more

1457 detail, and we would be happy to work with you on that.

1458 Mrs. {Myrick.} I would appreciate it very much if you
1459 could get back to us because that is an issue I think that
1460 there may be some solutions as other people have said with
1461 other things.

1462 I have got a second question too. Your testimony goes
1463 into some detail about FDA's calculation of risk and benefit
1464 when it comes to approving treatments for fatal diseases, and
1465 you list a recently approved metastatic-melanoma drug as an
1466 example of this risk-benefit approval calculation. It is
1467 stated it poses severe and even fatal autoimmune reactions in
1468 12.9 percent of the patients treated yet the drug was
1469 approved. The drug is not a cure but, you know, patients
1470 successfully treated live much longer than with others. My
1471 question is, was this drug approved in tandem with a
1472 screening test to distinguish the patients who might respond
1473 well from those who might suffer serious autoimmune
1474 responses?

1475 Dr. {Woodcock.} No. I think scientifically we aren't
1476 there yet to be able to predict that. I am a rheumatologist,
1477 and I can tell you our understanding of rheumatic diseases
1478 and autoimmunity is still not as advanced as it should be.

1479 Mrs. {Myrick.} Well, would it not be helpful to do some
1480 screening test to try and figure out in addition to what you

1481 are doing on this issue?

1482 Dr. {Woodcock.} Absolutely, and we support at FDA the
1483 concept of personalized medicine. It is simply that
1484 scientifically we don't have the tools to develop such a
1485 test, and because the patients can develop a wide range of
1486 autoimmune symptoms, and to predict each one of those and
1487 whether people would develop autoimmunity against their
1488 thyroid or their brain or their vessels, we don't have the
1489 technology to do that right now. But in the future, that is
1490 the future of medicine.

1491 Mrs. {Myrick.} Thank you, Mr. Chairman.

1492 Mr. {Pitts.} The chair thanks the gentlelady and now
1493 recognizes the gentlelady from Illinois, Ms. Schakowsky, 5
1494 minutes for questions.

1495 Ms. {Schakowsky.} Thank you, Mr. Chairman, and I want
1496 to thank both of you for your testimony.

1497 Dr. Shuren, I want to revisit a topic we discussed at
1498 the February 15th MDUFA reauthorization hearing. There had
1499 been suggestions that FDA's mission statement should be
1500 changed to include things like job creation and innovation,
1501 and in fact, the draft House user fee bill does include those
1502 changes to the FDA mission statement. And when you testified
1503 in February, you spoke about the ``unintended consequences''
1504 that could lead to ``troublesome changes'' at the agency,

1505 changes that could actually slow down or complicate the
1506 review process, not to mention change the standard of
1507 evidence for product approvals. You also said that changing
1508 the mission statement could even force the FDA to expose
1509 confidential industry information, something industry was
1510 telling you please don't do, and could require the FDA to
1511 review commercial financial records. So I am asking if you
1512 could comment on the implications of revising the FDA mission
1513 statement to include things like promoting innovation,
1514 economic growth, competitiveness, and I am particularly
1515 interested in whether you think these should be a part of the
1516 core mission of a public health agency. I would also like to
1517 know whether these and other requirements in the mission
1518 statement might be the basis for lawsuits or other challenges
1519 against the agency.

1520 Dr. {Shuren.} Well, we do have concerns about some of
1521 the changes that would be made to our mission statement, and
1522 the highlighted economic growth or job creation is of
1523 concern. If this now becomes a part of what we take into
1524 account in making decisions, think about approval decisions.
1525 Whose jobs are we talking about, the job of the companies
1526 coming in with a product and they may get some more jobs or
1527 the competitors who may lose jobs? In fact, when there is
1528 disruptive technology, many of the competitors, there are

1529 shakeups in the market and some of the companies, their
1530 product lines go and people's jobs may go. Are we talking
1531 about foreign companies? Are we talking about U.S.
1532 companies? Are we now taking into account financial
1533 considerations in terms of those companies' anticipated
1534 market growth or not? Those are things our scientists
1535 shouldn't be dealing with. We should focus on science in
1536 assuring that the products that come on the market are safe
1537 and effective, and that is protecting public health and we
1538 are also promoting public health, which is already in our
1539 mission statement.

1540 Regarding lawsuits, just within the past few months we
1541 have had two lawsuits where the mission was cited as one of
1542 the bases for that lawsuit, and we do see that coming. So if
1543 there are changes to the mission statement, yes, people will
1544 use that as a basis for lawsuits.

1545 Ms. {Schakowsky.} Thank you. Those changes concern me
1546 very much as taking away from the core mission that you have,
1547 and I would also like to ask Dr. Woodcock, because the
1548 dramatic changes to the FDA mission statement would apply
1549 across all product areas including drugs, I wonder if you
1550 could also comment on those proposed changes.

1551 Dr. {Woodcock.} I agree with Dr. Shuren. We neither
1552 have the expertise to figure out the economic consequences

1553 and parse them finally nor--our primary public is the people
1554 who take medicines and the people prescribing give those
1555 medicines. To them we owe our central obligation of making
1556 sure those drugs are safe and effective and they reach them
1557 as rapidly as possible. So I see this could have negative
1558 consequences.

1559 Ms. {Schakowsky.} And you are suggesting that those
1560 negative consequences could be patients, industry, the
1561 agency. What are your main concerns? I mean, would you view
1562 this as a distraction from what you are currently doing?

1563 Dr. {Woodcock.} Yes, and it would be primarily that we
1564 would have challenges of our approval decisions based on
1565 factors that most people would consider extraneous to whether
1566 the product will really help people. That has to be our main
1567 consideration, is it effective in the population, is it safe,
1568 and if we are asked--that is what I believe we should be
1569 focused on: impact on patients.

1570 Ms. {Schakowsky.} Well, I agree. I think this would be
1571 a dramatic shift in focus and one that really the agency has
1572 no historical expertise nor in my view should it. So I thank
1573 you and yield back.

1574 Mr. {Pitts.} The chair thanks the gentlelady and
1575 recognizes the gentleman from Pennsylvania, Dr. Murphy, for 5
1576 minutes for questions.

1577 Mr. {Murphy.} Thank you very much.

1578 Dr. Woodcock, welcome back. I always appreciate your
1579 candor and information to us. I also want to thank my
1580 colleague, Mr. Dingell, for working with us on some of the
1581 issues involving GDUFA. And finally, in your testimony, I
1582 want to thank you for working on the accelerated approval of
1583 Kalydeco for cystic fibrosis. Many of the patients I know in
1584 my area are grateful for that. I know it is a small step but
1585 it is a significant step, and I think it is an example of why
1586 we need to be moving on some things with accelerated action
1587 here.

1588 At a recent Senate hearing, you stated--you were talking
1589 about the challenges in international factory inspections.
1590 Here is your answer. You said there are two issues here. One
1591 is the FDA's ability to inspect to inspect those foreign
1592 facilities and the generic drug user fee program squarely
1593 addresses that, and I will level the playing field and make
1594 sure that the intensity of inspection, domestic, foreign, no
1595 matter where, will be the same and will be able to use a
1596 risk-based approach to inspection. Now, under the GDUFA
1597 goals letter, the FDA says it wants to achieve biannual
1598 inspection of foreign plants within 5 years, so here is my
1599 two-part question. First, is your answer from the Senate
1600 hearing still true, and two, can the FDA achieve parity

1601 between foreign and domestic facility inspections within the
1602 5-year \$1.5 billion time zone outlined in GDUFA?

1603 Dr. {Woodcock.} Yes, we believe that the answer is
1604 true. I was at a meeting yesterday where we were discussing
1605 this with our field organization and the Center for Drugs how
1606 we would implement this inspectional program, and we would
1607 really look forward to having that global safety net in
1608 place.

1609 Mr. {Murphy.} Thank you. Now, I should disclose an
1610 important generic drug manufacturer, Mylan, is headquartered
1611 in my district, and we want to make sure that any inspections
1612 they have to go through are equivalent to what takes place
1613 overseas. Now, my understanding is that based on the current
1614 statute, the FDA inspects domestic plants more frequently
1615 because they are looking for so-called ``known risks'' even
1616 if the plant has no history of problems but inspectors don't
1617 have the same body of knowledge about foreign factories
1618 because they haven't been there, and sometimes not in the
1619 last decade. So Dr. Woodcock, will you agree that inspectors
1620 have a certain comfort level visiting domestic factories
1621 because there is a record of inspection history that helps to
1622 identify known risks to these factories?

1623 Dr. {Woodcock.} My understanding is that we have a
1624 statutory requirement to inspect domestic facilities every 2

1625 years, and that is partly what drives the frequency of
1626 inspection. It is also that there is considerable logistical
1627 challenges to covering the globe. But the Center for Drugs
1628 has a risk-based approach to inspecting facilities. We try
1629 to identify the facilities that pose the most risk including
1630 the fact that we don't very much about them and try to target
1631 out inspections based on those risks. In addition, we do
1632 preapproval inspections, so that drives quite a few
1633 inspections because before a drug is released on the market,
1634 we want to know that the facility that is producing it and
1635 often it is multiple facilities are in compliance.

1636 Mr. {Murphy.} Thank you. I am just concerned here that
1637 if you go to a domestic factory, you see a problem, you can
1638 follow up or even a suspicion something might have happened
1639 but if we have long time delays--and I understand the global
1640 problems there but it is a concern that there is not the same
1641 follow-up. If Congress directs the FDA away from a statutory
1642 requirement to inspect facilities once every 2 years and
1643 instead allows the agency to adopt a risk-based approach,
1644 what factors might the agency consider using to determine
1645 what is a facility in need of inspection versus one that may
1646 not be?

1647 Dr. {Woodcock.} Well, we currently have a model.
1648 Obviously one of them is how recently have we been to the

1649 facility and how much do we know about it, and really, the
1650 less we know, the more important it is to know more and to
1651 visit the facility but also, for example, parenteral drugs
1652 that have to be sterile are a higher bar of manufacturing
1653 than tablets or capsules or creams, so that is a factor. The
1654 number of products that are produced in a facility ups the
1655 ante of risk, so to speak, because it is harder. There are
1656 more changes for mix-ups and so on if you have a lot of
1657 products made on the line. We have multiple factors like
1658 that that are technical on the challenges of manufacturing
1659 that go into the calculation as well as the history of the
1660 firm--have they been having problems, has that facility had
1661 problems in the past. That should prompt more frequent
1662 visits.

1663 Mr. {Murphy.} Well, thank you. I know that I am just
1664 about out of time but I wanted to also note that I am
1665 exploring putting guidance into the FDA for placing higher
1666 priority on inspecting foreign plants that have not been
1667 visited within the last 4 years. I could see this is
1668 beneficial for public safety because I think it would
1669 establish something of a psychology for plants that haven't
1670 been visited in the past 4 years that the FDA might be
1671 visiting soon, and I welcome your thoughts on that too, and
1672 also, in the goals letter for GDUFA, the FDA estimates that

1673 are 2,000 finished dosage form and active pharmaceutical
1674 ingredients manufacturing facilities that are associated with
1675 generic drug applications. I hope you can get to me in the
1676 future and let us know if this estimated all included the FDF
1677 and API facilities and does the FDA believe that there are
1678 other registered facilities under its jurisdiction that
1679 solely support branded applications. I will get you those
1680 questions in writing and I appreciate some feedback. Again,
1681 Doctor, thank you for your candor. I really respect your
1682 comments. I yield back.

1683 Dr. {Woodcock.} Thank you.

1684 Mr. {Pitts.} The chair thanks the gentleman and
1685 recognizes the gentleman from Utah, Mr. Matheson, 5 minutes
1686 for questions.

1687 Mr. {Matheson.} Thank you, Mr. Chairman. And Mr.
1688 Chairman, I want to acknowledge how you have been working in
1689 a bipartisan manner on the reauthorization of this. I really
1690 appreciate that.

1691 Over the past several years, I have worked with drug
1692 supply chain stakeholders in crafting legislation to develop
1693 a national system to better protect our Nation's drug supply
1694 against counterfeiting threats. Last year, I introduced
1695 legislation along with my colleague, Mr. Bilbray, to address
1696 this issue, and I certainly want to thank him for all the

1697 work he has done with me on that bill. Recently, a
1698 consortium of stakeholders from all sectors of the supply
1699 chain have come together to craft a proposal to address
1700 counterfeiting and supply chain safety. I am pleased to see
1701 that many of the elements of the legislation that I have
1702 worked on were included in this RxTEC proposal. I am
1703 supportive of this proposal, and I hope to see its inclusion
1704 in this year's user fee reauthorization, and I would like to
1705 note that the last time this committee attempted to work on a
1706 national track-and-trace system, we failed because there was
1707 no consensus among the supply chain stakeholders. The FDA
1708 has raised concerns over this proposal because it does not
1709 mandate a unit-level system by a date certain.

1710 Dr. Woodcock, in your written testimony, you note that
1711 Congress should provide FDA with the authority to require a
1712 ``cost-effective track-and-trace system in order to improve
1713 the security and integrity of the drug supply and show
1714 transparency and accountability in product manufacturing and
1715 distribution.'' However, many in the supply chain have
1716 raised concerns that a date-certain mandate approach would be
1717 cost-prohibitive and create a logistical challenge that could
1718 actually endanger the drug supply chain. So the question
1719 that I have for you, Dr. Woodcock, first, how do we ensure
1720 that a date-certain approach is in fact cost-effective and

1721 does not have unintended consequences such as job loss or
1722 further exacerbating the growing drug shortage problem in
1723 this country?

1724 Dr. {Woodcock.} Well, to start with, I would like to
1725 say again that we need to look at the problem we are trying
1726 to solve and make sure that any interventions we take will
1727 solve the problems that we are trying to address. My
1728 understanding with track and trace is, we are trying to deal
1729 with counterfeits, stolen drugs that are reintroduced,
1730 recalls, substandard drugs and so forth and prevent them from
1731 actually reaching patients and harming people. Our concern
1732 about the current proposal by the coalition, we have talked
1733 to them. As I said, I am happy to meet with them but that it
1734 will not meet the objectives of preventing those problems.
1735 It may help--in my analysis, it may help in reconstructing
1736 what went wrong after the fact, but if you want to interdict
1737 counterfeits and tampered drugs and so forth from reaching
1738 patients, then you have to be able to recognize it at the
1739 time it is introduced into the system, and so any system, any
1740 new requirements that don't accomplish that may not be worth
1741 the cost because they may be additional things that people
1742 have to do, but if they don't accomplish the objectives of
1743 protecting patients, they may not be worth it.

1744 Mr. {Matheson.} I am all for looking for the objective

1745 but you just mentioned cost, it may not be worth the cost, so
1746 I am suggesting that the concerns raised that if you want a
1747 date-certain mandate that that is going to have negative cost
1748 consequences, and so my question is, how do we evaluate, how
1749 do you intend to look at if there is going to be--the cost
1750 effect is not going to be a problem here?

1751 Dr. {Woodcock.} Well, we have been looking at this. We
1752 plan to develop and are developing voluntary standards that
1753 we would put out that people could use and hoping that the
1754 technology which many products in the market are tracked this
1755 way already, not pharmaceuticals, so hoping that the
1756 technology will reach a state where it will be cost-effective
1757 and not excessively burdensome.

1758 Mr. {Matheson.} I have to admit, hoping technology gets
1759 there and seeing date certain, those things in my mind are in
1760 conflict. I don't actually think that matches well.

1761 Noting some of the challenges that the California law is
1762 facing, I am trying to understand why this date-certain
1763 approach would work at a federal level when it has caused
1764 difficulties at the State level in California, and should we
1765 not look at the types of systems that are feasible across the
1766 supply chain system before we decide what and when to
1767 mandate?

1768 Dr. {Woodcock.} Well, I do believe that we should look

1769 at feasibility, absolutely. However, many of the
1770 stakeholders have told us they are worried about having 50
1771 different systems.

1772 Mr. {Matheson.} That is why I introduced my bill. I
1773 hear you. We need a national standard. I am just trying to
1774 figure out how we are going to manage it.

1775 Dr. {Woodcock.} But that means we have to settle on the
1776 technology if we do that, and what is going to be tracked and
1777 how it is going to be tracked, and that has been difficult
1778 because right now the costs have been fairly significant to
1779 some of the stakeholders because they don't do this now.
1780 They don't electronically track the products as they move
1781 through the supply chain and all the way to the patient. So
1782 I agree, there are tradeoffs here, and it will cost money to
1783 put such a system into place.

1784 Mr. {Matheson.} I will just close by saying I think the
1785 RxTEC proposal represents a consensus of a lot of the
1786 stakeholders. It does agree on a one-size-fits-all for the
1787 country and not 50 different State approaches. And I think
1788 we ought to continue this discussion about looking for if
1789 there is a way to accommodate this proposal without mandating
1790 a date-certain approach.

1791 With that, Mr. Chairman, I will yield back.

1792 Mr. {Pitts.} The chair thanks the gentleman and

1793 recognizes the gentleman from Ohio, Mr. Latta, for 5 minutes
1794 for questions.

1795 Mr. {Latta.} Thank you, Mr. Chairman, and welcome back
1796 to the committee. Great to see you again.

1797 Kind of going in a little bit different direction here.
1798 Dr. Woodcock, I know of a number of hospital systems that are
1799 coping with the hospital drug shortage by repackaging those
1800 drugs into smaller dosages, and these hospitals have also
1801 noted that the current law does not allow for the hospital to
1802 repackage a drug for use in another hospital within their own
1803 system, and we have quite a few systems, of course, not only
1804 in Ohio but across the country, and this appears to be an
1805 older regulation dating back to when hospitals were typically
1806 only in one building before they became the hospital systems.
1807 Has the FDA looked at updating this requirement to allow for
1808 repackaging within the same hospital system?

1809 Dr. {Woodcock.} I would have to get back to you on
1810 that. I do not think that we would object to such practices
1811 if they would help alleviate shortages but whether there is a
1812 law on the books that is being interpreted as prohibiting
1813 that, I am not aware of that.

1814 Mr. {Latta.} And again, I am glad to hear that because
1815 again, it seems a logical way to help solve it, because
1816 again, if one hospital has it, they could get it out to one

1817 or others in the same locale. That would be helpful because,
1818 again, it would help alleviate those shortages.

1819 Dr. {Woodcock.} If I may interject?

1820 Mr. {Latta.} Absolutely.

1821 Dr. {Woodcock.} We allow pharmacy compounding. Usually
1822 the hospital pharmacy would be handling these products and
1823 they would be the ones to put it into smaller vials or
1824 whatever. So that is why I am confused about why they feel
1825 that that isn't allowed, and we will get back to you on that.

1826 Mr. {Latta.} I appreciate that. And over time, it
1827 would help alleviate the problem, because again, we are
1828 talking about these shortages, I know you have been here
1829 before. We have quite a bit of discussion about that as to
1830 how to alleviate it, and when you have the situation that at
1831 least in the chain that one of the hospitals has the ability
1832 to supply the other ones, it would be very helpful, and so I
1833 look forward to your response on that. I would like to get
1834 back to these hospitals to be able to say that they can get
1835 this done and help alleviate that problem.

1836 And with that, Mr. Chairman, I yield back.

1837 Mr. {Pitts.} The chair thanks the gentleman and
1838 recognizes the gentleman from Louisiana, Dr. Cassidy, for 5
1839 minutes for questions.

1840 Dr. {Cassidy.} I always enjoy both your testimonies.

1841 Thank you. And as a practicing physician, I respect what you
1842 said earlier, Dr. Shuren, that the FDA's obligation is to
1843 protect patients' health. I thank you for that too.

1844 I would like to build upon, Dr. Woodcock, our
1845 conversation last time which was very good. The last time, I
1846 think we agreed that a valid prescription would be important
1847 to have, not just for controlled substances as currently but
1848 also for non-controlled drugs. So I just wanted to state
1849 that for the record.

1850 Dr. {Woodcock.} I agree.

1851 Dr. {Cassidy.} Secondly, we also spoke a lot about
1852 illegitimate online pharmacies. Now, you had mentioned the
1853 VIPPS program, which I had mentioned as a practicing
1854 physician married to a physician we did not know about, but
1855 since then we have kind of looked at it. I gather that this,
1856 although a good effort, only has about 30 pharmacies listed
1857 even though it is estimated there are about 1,500 legitimate
1858 pharmacies and just an explosion of illegitimate pharmacies.
1859 And secondly, that we still have, despite our conversation
1860 last time, there continues to be reports of adulterated drugs
1861 causing harmful effects to patients here in the United
1862 States. So with that said, Representative Ross and I in a
1863 companion bill to something that Senators Feinstein and
1864 Cornyn and others have introduced on the other side have an

1865 online pharmacy bill requesting that FDA compile a registry
1866 of legitimate online pharmacies so that I as a doc or I as a
1867 patient or I as a dad of a patient could log on and see, is
1868 this a legitimate online pharmacy. I gather FDA has some
1869 objections to that. Could you kind of go through those
1870 objections?

1871 Dr. {Woodcock.} Certainly. Basically there are
1872 practical difficulties in us doing that. As you said, there
1873 is a huge plethora of pharmacies that are probably not
1874 legitimate that consumers do order their drugs from and often
1875 they have no assurance that those are actual drugs.

1876 Dr. {Cassidy.} That is why we have the bill.

1877 Dr. {Woodcock.} Yes, so we are in agreement on the
1878 problem. We have trouble certifying Internet sites that
1879 would be legitimate. We have difficulties--

1880 Dr. {Cassidy.} But see, the National Association of
1881 Boards of Pharmacy, the NABP, currently does that.

1882 Dr. {Woodcock.} Yes.

1883 Dr. {Cassidy.} So why can they do it and the government
1884 cannot, or why could you just not contract with them to ask
1885 them to do it?

1886 Dr. {Woodcock.} I think it is worth discussion on how
1887 to establish a broader list of legitimate pharmacies. It is
1888 another work stream that we don't actually understand how we

1889 could accomplish very well.

1890 Dr. {Cassidy.} Now, in our bill, we allow you to
1891 contract that. I mean, I can tell you, Google can tell you
1892 who is legitimate and who is illegitimate, you know, Google,
1893 the big Internet--

1894 Dr. {Woodcock.} I know Google but we are talking about
1895 a pharmacy here and so--

1896 Dr. {Cassidy.} But they advertise via Google, and so I
1897 suspect that--I mean, it is not an impossibility to do it.
1898 You may not have expertise nor I but I promise you, NAPB has
1899 that expertise, and our bill allows you to contract out to
1900 them. Why not?

1901 Dr. {Woodcock.} Well, we are not sure that a
1902 certification by the federal government could--it would have
1903 to be very frequent inspection of the distribution center
1904 because you have a web page but there is not necessarily a
1905 brick-and-mortar entity behind that.

1906 Dr. {Cassidy.} Now, in there we do require to have some
1907 sort of U.S. asset, and we have spoken with NABP. Obviously,
1908 we weren't concerned if someone could come in as legitimate
1909 and flip to being rogue.

1910 Dr. {Woodcock.} Exactly. That is one of our concerns.

1911 Dr. {Cassidy.} NABP says that has never occurred in
1912 their experience.

1913 Dr. {Woodcock.} Of course, they only have 15 in there.

1914 Dr. {Cassidy.} Thirty. That said, at some point we
1915 have to move beyond existential fear, oh, my gosh, we don't
1916 know all the unknowns, and say if we are going to protect
1917 patient safety and we know this is an incredible problem, let
1918 us embrace the fear, if you will. Again, why do we allow
1919 existential fear to paralyze our efforts to protect our
1920 patients?

1921 Dr. {Woodcock.} I don't think it is existential fear.
1922 I believe that we are having difficulty conceiving of how we
1923 would add this program to our existing programs. So we would
1924 be very happy to work with you on this and talk to you about
1925 it.

1926 Dr. {Cassidy.} I would love it if you would support the
1927 bill because we will contract this out and there is someone
1928 out there that can do it, which I think is a logical thing.
1929 Someone out there knows how to do it even if the federal
1930 government doesn't. When I go through TSA, they know
1931 everything about me. To think that we can't figure who is
1932 legitimate and illegitimate just seems not quite to make
1933 sense to me.

1934 I have 2 seconds left but you have been giving everybody
1935 slack. Can I quickly ask one more question?

1936 Dr. Shuren, the unique identifier that has been

1937 suggested for medical devices, it is my understanding it has
1938 been held up at OMB for 5 years. That is what I was told.
1939 Maybe it not 5 years, maybe it is a shorter period of time.
1940 But even at the glacial pace at which government works, that
1941 seems a way to take a proposal and never get it out. Any
1942 thoughts about why OMB is holding up a unique ID system which
1943 really could help us improve safety of medical devices?

1944 Dr. {Shuren.} It is probably a question best put to the
1945 Administration. I will say the rule has been under review
1946 since July of 2011, so not 5 years.

1947 Dr. {Cassidy.} Oh, good. I am comforted by that.

1948 Dr. {Shuren.} Well, sometimes when people hear that
1949 things take longer, sometimes it is not always correct.

1950 Dr. {Cassidy.} Okay. So any idea? Is there ongoing
1951 discussion or is it just a wall of silence? Do you have any
1952 sense of is progress being made on this?

1953 Dr. {Shuren.} We continue to engage with OMB. We
1954 certainly believe it is important to have a unique device
1955 identification system in place in the United States. It will
1956 be critical to have a robust postmarket surveillance system.
1957 It will help in terms of recalls and adverse-event reporting
1958 but can also allow us to have a system in which we may get
1959 sufficiently good data that can be used to support new
1960 products coming to market. So it is not just about better

1961 understanding of benefit-risk profile once out the gate. It
1962 may actually be able to help companies in reducing the new
1963 evidence they need to generate to bring a new device to the
1964 United States.

1965 Dr. {Cassidy.} I yield back. Thank you.

1966 Mr. {Pitts.} The chair thanks the gentleman and
1967 recognizes the gentleman from Kentucky, Mr. Guthrie, for 5
1968 minutes for questions.

1969 Mr. {Guthrie.} Thank you, Mr. Chairman, and first, Dr.
1970 Shuren, I just have a comment. I know we have met in my
1971 office over medical device approval processes. I thought
1972 that was a very good, productive meeting, and you have talked
1973 today about the first-time approvals or the innovators and
1974 the least burdensome and getting it right, being safe and
1975 effective, but also efficient. I think that is important. I
1976 appreciate that, because it has been a big concern of mine
1977 that we are having people go overseas to get their products
1978 approved but not going to the least common denominator, going
1979 to the European Union and other areas and trying to get
1980 approved. And so we are interested as oversight monitor how
1981 that goes forward and appreciate your openness in meeting on
1982 that.

1983 Dr. Woodcock, there is a question I have. I talked to
1984 anesthesiologists and anesthesiologists and of course in the

1985 childcare cancer drugs of the shortages. When there is a
1986 shortage in a drug, I guess you can go to an alternative
1987 source if a manufacturer can't produce the drug. How does
1988 that process work? How do you actually make that happen?

1989 Dr. {Woodcock.} We hope usually we would get early
1990 notification from a manufacturer that they may be having to
1991 go out of production or reduce production and not meet the
1992 supply. We will then look around to all other manufacturers
1993 who have ever made that drug and see if they can ramp up so
1994 that we would avert the shortage. If that doesn't happen,
1995 then we might look outside the United States to people making
1996 a comparable drug elsewhere and we would check with other
1997 regulatory authorities to make sure their production was
1998 proper and the history of the drug so make sure we are not
1999 introducing a substandard drug into the United States, and
2000 then we would allow importation of that drug to cover if a
2001 shortage actually developed and we would talk to that
2002 manufacturer.

2003 Mr. {Guthrie.} Is there a formal process for that?

2004 Dr. {Woodcock.} A formal process?

2005 Mr. {Guthrie.} A formal process. Does somebody have to
2006 notify you when they know they are not going to make
2007 shipments and things like that or it is something that you
2008 have to react to?

2009 Dr. {Woodcock.} Well, there is some requirement to
2010 notify us but of course there is interest in more formalizing
2011 that notification process, and we think that would be
2012 helpful.

2013 Mr. {Guthrie.} And I have had people talking about
2014 having to delay surgeries for anesthesia and childhood
2015 cancers. Those are the two I mentioned. I know there are
2016 others. But since you have a handful that seem to be the
2017 bigger issue, do you have like a list of the people that can
2018 come online when you need to get them online?

2019 Dr. {Woodcock.} We have done extraordinary efforts to
2020 try and deal with this situation. The problem is that these
2021 are sterile injectables. There were only a few facilities in
2022 the United States that made these. They made large numbers
2023 of products so hundreds of products, and they had problems
2024 that they had to take their production offline and it almost
2025 sort of happened--it was like a perfect storm of problems.
2026 So we are having to look elsewhere and we are working with
2027 them as closely as possible to try to bring them back up into
2028 production of these medically necessary drugs.

2029 Mr. {Guthrie.} Do you think it would be helpful to have
2030 some kind of program that maybe manufacturers could
2031 voluntarily participate in? I know there are some areas you
2032 are just going to get blindsided because something happened

2033 in manufacturing. I know sometimes things happen in a
2034 manufacturing facility. But do you think if there would be a
2035 more formal program that maybe companies could volunteer to
2036 participate in, manufacturers could that could react quicker
2037 or do you think--

2038 Dr. {Woodcock.} We have heard from the private sector,
2039 and they are putting together some efforts on exchanging
2040 information and providing better information to us, and we
2041 think that things like that would help also. I would stress
2042 that we already have the flexibility. We will allow the
2043 manufacturers to continue in production even if they are
2044 having manufacturing problems. Maybe they will release batch
2045 by batch. We have even had manufacturers sent a filter with
2046 the product that had particulates in it which can't go into
2047 your veins, but we let them put a filter in after tests
2048 showed that would work and shipped that with the product so
2049 that that product so people could have anesthesia or they
2050 could have their cancer drugs. So we have a lot of
2051 flexibility. We do a lot of things now but it would probably
2052 help us to get more information earlier.

2053 Mr. {Guthrie.} Okay. Thanks. I appreciate that very
2054 much, and I yield back.

2055 Mr. {Pitts.} The chair thanks the gentleman and
2056 recognizes the gentlelady from Tennessee, Ms. Blackburn, for

2057 5 minutes for questions.

2058 Mrs. {Blackburn.} Thank you, Mr. Chairman.

2059 Dr. Shuren, I had a couple of questions for you. I
2060 really wanted to follow up on a letter that some of my
2061 colleagues and I sent to you earlier regarding the wireless
2062 medical devices and the mobile medical applications. You
2063 have talked a little bit about bringing technology and
2064 keeping technology-based jobs here in the country, talking to
2065 innovators. So I wish that you would take a couple of
2066 minutes and just detail what primary activities related to
2067 wireless health services and health devices are underway at
2068 the FDA including the independent and jointly with the FCC
2069 and the ONC, if you will, if you will just talk about what is
2070 underway there. And then I would also like to know who is
2071 tasked, if you have got one person that is tasked with
2072 overseeing the policy development in this area looking at
2073 regulations, guidance, documents, etc.

2074 Dr. {Shuren.} Certainly. For wireless technologies
2075 specifically, we are working on guidance to provide greater
2076 clarity to industry. We know this is a booming market and we
2077 want to make sure that innovators have the information they
2078 need to help bring those products to market. We have been
2079 working with the FCC. We sort of have split responsibility
2080 because they oversee what spectrum may be available and then

2081 we assure that when we are dealing with medical devices that
2082 they are safe and effective and so we have been getting
2083 together periodically to assure this good coordination where
2084 there are those areas in which we engage and to also make
2085 sure that we stay out of each other's way.

2086 Mrs. {Blackburn.} And do you have one specific point
2087 person that is handling that?

2088 Dr. {Shuren.} The person on our end who handles that
2089 engagement is Bakul Patel, and he is in my office.

2090 Mrs. {Blackburn.} Okay. And then is he handling the
2091 intra-agency coordination as well as the interagency?

2092 Dr. {Shuren.} Yes, that is correct, so one person.

2093 Mrs. {Blackburn.} So he is the guy in charge basically
2094 on that?

2095 Dr. {Shuren.} So to speak, yes.

2096 Mrs. {Blackburn.} And then could we get a listing or a
2097 memo that would give us more or less the primary activities
2098 related to these wireless devices that are underway? Could
2099 you give us a little bit more information or guidance on
2100 that? And you can submit that in writing.

2101 Dr. {Shuren.} We would be happy to do so. We can also
2102 provide more information regarding medical apps, an area
2103 where I think you know we took a position that while many of
2104 these apps could be under FDA authority, we actually made the

2105 decision that you know what, for the majority of these, they
2106 shouldn't come to us even if they should as a matter of law
2107 and we are willing now to--

2108 Mrs. {Blackburn.} So are you traveling then with your
2109 guidance to which--and this is one of my other questions for
2110 you. Realizing that there is a difference between medical
2111 devices and medical software, are you moving that direction
2112 to being able to provide that guidance?

2113 Dr. {Shuren.} So there is also guidance on clinical
2114 decision support software. Some software has been regulated
2115 as medical devices for years. What we are doing is going
2116 back for those kind of software to say some of these things,
2117 you know what, we shouldn't even look at even though they
2118 might fall under our purview and a lot of things that
2119 otherwise we would, we are going to come out with a policy
2120 that says we are leaving you alone.

2121 Mrs. {Blackburn.} So you are adjusting what would and
2122 would not fall under the Drug and Cosmetics Act of 1970?

2123 Dr. {Shuren.} We are going even further to say even if
2124 you fall under it, we may go out and say we will exercise
2125 enforcement discretion, don't worry about it, you don't have
2126 to come to us. We are going to narrow actually our purview
2127 even further than what the law may otherwise say. We are
2128 trying to adapt to the emerging technologies and adapt our

2129 approach to the business models for software, because we
2130 realize that even in those cases where it comes to us, you
2131 can't apply a traditional approach. There needs to be the
2132 ability to make frequent updates and for us not to get in the
2133 way of that technology.

2134 Mrs. {Blackburn.} Okay. Should we as legislators go in
2135 here and update the definitions of devices and software based
2136 on those advances in technology that you just touched on?

2137 Dr. {Shuren.} We don't think there is a need for it,
2138 and, you know, one of the challenges is, when you make the
2139 change in statute, it winds up having broad ramifications.
2140 It is very hard to put in something that applies the
2141 appropriate touch, if you will, and that is why we are able
2142 to do through a public process with policy changes where we
2143 can--

2144 Mrs. {Blackburn.} Okay. Let me ask you this then. You
2145 just talked about some of the software updates. I get
2146 notices for updates for different software packages all the
2147 time. I mean, it seems like almost a daily occurrence. So
2148 would each update that goes out, if it is under your
2149 jurisdiction, would each update need a separate approval
2150 process, or how do you envision that working?

2151 Dr. {Shuren.} No, and in fact, we are kind of looking
2152 to have an approach where you can make those kind of routine

2153 changes in software and not have to bother coming to us. It
2154 would only be certain things where you really change the
2155 technology itself and what it was about where that is an
2156 issue, and even there, the universe where we are going to be
2157 focusing is very, very narrow, even though more things might
2158 fall under our purview, so we are truly restricting where we
2159 would focus, and at the end of the day there is the value
2160 added, but you will see that the majority of the stuff out
2161 there, our intent is to just leave it alone.

2162 Mrs. {Blackburn.} Okay. Thank you. I yield back.

2163 Mr. {Pitts.} The chair thanks the gentlelady and
2164 recognizes the gentleman from Georgia, Dr. Gingrey, for 5
2165 minutes for questions.

2166 Dr. {Gingrey.} Mr. Chairman, thank you very much.

2167 I will address my first question to Dr. Woodcock. First
2168 of all, let me apologize for coming in at the last minute.
2169 We had a concurrent hearing that I chaired, so I apologize
2170 for that.

2171 In reference to antibiotic shortages in general and
2172 specifically the GAIN Act in particular, I know that my
2173 colleague on the other side of the aisle, the ranking member,
2174 Mr. Waxman, had talked about that a little earlier this
2175 morning in regard to this limited population antibiotic drug
2176 proposal. Staff at FDA told my staff just this Monday that

2177 the FDA has not officially endorsed the LPAD, if you can call
2178 it that, that proposal. Has the FDA officially endorsed the
2179 Limited Population Antibiotic Drug proposal as part of the
2180 GAIN Act or in any way?

2181 Dr. {Woodcock.} Well, the Commissioner, Dr. Hamburg,
2182 and I have talked about this, a program like this to many
2183 different stakeholders so we certainly feel that is something
2184 that should be considered by Congress. But of course, there
2185 is nothing specific in the GAIN Act right now that reflects
2186 this proposal. So we do feel that it would be beneficial.
2187 The GAIN Act provides long-term incentives for companies to
2188 move back into the antibiotic space. A shortened development
2189 program, a very narrow development program would provide that
2190 short-term incentive. In fact, I have already heard from a
2191 company that has written me a letter asking if they could be
2192 designated as one of these products because they would be
2193 interested in entering that space if they had a very clear
2194 development path to market.

2195 Dr. {Gingrey.} Well, I understand, and you said that
2196 you and Dr. Hamburg have discussed it and certainly I am not
2197 saying that the proposal does not have merit. I am just
2198 suggesting that at this late date, industry has some concerns
2199 in regard to making this part of the GAIN Act and
2200 subsequently of course part of PDUFA. I wanted to very

2201 specifically ask, and I will do that one more time. The FDA
2202 has not officially endorsed this. Is that correct?

2203 Dr. {Woodcock.} Well, the Administration has not put
2204 forth a proposal.

2205 Dr. {Gingrey.} Thank you very much, Dr. Woodcock.

2206 Dr. Shuren, there is a line in the FDA industry
2207 agreement that reads ``The FDA proposes to work with industry
2208 to develop a transitional IVD, in vitro diagnostics, approach
2209 for the regulation of emerging diagnostics.'' Dr. Shuren,
2210 explain to me what this means exactly.

2211 Dr. {Shuren.} Well, actually this is something that
2212 industry put on the table, and they put it after 13 months of
2213 negotiation back and forth. It actually came up in our
2214 second to last meeting, so it was at the very end. And even
2215 though we have committed in MDUFA III to talk about it, we
2216 have actually already been meeting with industry on it. What
2217 we have seen is to date a very broad brush proposal that
2218 needs a lot of work but we will work with industry and MDUFA
2219 III in putting it forward, and the broad brush strokes are
2220 for certain IVDs yet to kind of be determined. Would they
2221 come on the market under a lower standard than currently is
2222 in place for products to get on the market in the United
2223 States with the requirement that they provide the additional
2224 data to show that they are ultimately safe and effective at a

2225 later date in time, and if not, to then come off the market.
2226 Those are the broad brushstrokes. One of the issues we will
2227 also have to wrestle with are the implications for the FDA
2228 because even if we went down that path, it involves two
2229 reviews and two decisions on the part of the FDA for every
2230 single one of those devices going through as opposed to the
2231 one review and the one decision, and those kind of resource
2232 applications we didn't address in--

2233 Dr. {Gingrey.} Let me ask you this, Dr. Shuren. I am
2234 about to run out of time. I have one other question I wanted
2235 to ask. Does the FDA see the benefit and support
2236 transitional pathway approaches? Do you believe that such a
2237 pathway can benefit patients and industry?

2238 Dr. {Shuren.} Right now we need to work with industry
2239 on exactly what this is and what the ramifications would be.

2240 Dr. {Gingrey.} Will you keep the committee updated on
2241 the talks with industry in these coming months?

2242 Dr. {Shuren.} Yes.

2243 Dr. {Gingrey.} I very much appreciate that. And real
2244 quickly, Mr. Chairman, get it in under the line, and this is
2245 also Dr. Shuren. A review of the Office of Device
2246 Evaluation's annual report shows a decline in the percentage
2247 of IDEs approved on the first IDE review cycle. They dropped
2248 actually from 76 percent approval in fiscal year 2000 down to

2249 56 percent 9 years later, 2009. What is the explanation for
2250 the huge drop in IDEs approved on the first review cycle
2251 between 2009 and 2010? And real quickly, is it true that
2252 with each new review cycle, a company must pay an additional
2253 user fee for one product and these multiple review cycles are
2254 a strain on the FDA's valuable time and resources?

2255 Mr. Chairman, thank you for your indulgence, if maybe
2256 Dr. Shuren could quickly respond to that.

2257 Dr. {Shuren.} Certainly. There are no user fees tied
2258 to the review of IDEs, so we don't get any additional funding
2259 from industry for that. What has happened over time, and
2260 this is what we are addressing, is that we have got cases
2261 where we were not consistently applying the least-burdensome
2262 principle. So a decision was held up because a reviewer
2263 might be coming back to say we think you should be doing a
2264 better study when in fact the study was really good enough
2265 for its intended purpose moving forward. And the second is
2266 where approvals were being held up to get answers to
2267 questions that either did not need to be answered at that
2268 time, it may be something for later on, or there were
2269 questions that it would be nice to know but we don't need to
2270 know it, and that is why we put out draft policy in November
2271 of 2011 to sort of free that up to lay out very clearly here
2272 are all the different circumstances where we should approve

2273 that trial and these are other issues that can be put off to
2274 later, in fact, allowing for some cases where we never would
2275 have let the trial go through even in the past where we might
2276 actually do a staged approval, let some patients come in,
2277 make sure there is good data for safety and let it move
2278 forward. That is the kind of flexibility we are trying to--

2279 Dr. {Gingrey.} Well, I am real encouraged to hear that
2280 response, Dr. Shuren. Thank you.

2281 Mr. Chairman, thank you for your indulgence.

2282 Dr. {Shuren.} And if I can just add that the IDE first
2283 cycles have dropped. This year in 2012, they have actually
2284 been going upwards for the first time.

2285 Mr. {Pitts.} The chair thanks the gentleman. That
2286 concludes the subcommittee questioning. We have a couple of
2287 members on the full committee who would like to ask
2288 questions. Without objection, we will go to them at this
2289 time.

2290 Mr. Markey from Massachusetts, you are recognized for 5
2291 minutes for questions.

2292 Mr. {Markey.} Thank you, Mr. Chairman and Ranking
2293 Member Pallone, for allowing me to participate in today's
2294 legislative hearing. I also thank you for including the
2295 bipartisan Pediatric Research Equity Act and the Best
2296 Pharmaceuticals for Children Act that I was proud to work on

2297 with Mr. Rogers and Ms. Eshoo, and I look forward to
2298 continuing to work on these important bills.

2299 Dr. Shuren, I am concerned that the current discussion
2300 draft misses an important opportunity to improve the safety
2301 of medical devices. If a car is recalled because it had
2302 faulty brakes, no consumer would want to purchase a new car
2303 with the same brake problem. Yet when it comes to medical
2304 devices that are implanted in patients' bodies, companies can
2305 and do base their products on faulty predecessor
2306 technologies. The definition of insanity is doing the same
2307 thing over and over again and expecting a different result,
2308 but when it comes to medical devices, we have an insane
2309 policy that makes no sense. Devices have been recalled
2310 because they severely injured patients and they are used
2311 again and again as models for new devices with devastating,
2312 life-altering consequences for the patients who are injured
2313 by them.

2314 In fact, just last month, I issued a report that
2315 documented this problem in detail and shared the stories of
2316 patients whose lives were destroyed as a result of this
2317 federal loophole. Under current law, the vast majority of
2318 medical devices are not required to undergo clinical testing
2319 in humans before being sold. Instead, companies need only
2320 prove that their new device is substantially equivalent in

2321 technology in use to a device that FDA has previously
2322 cleared, known as the predicate technology. As we heard, Dr.
2323 Shuren, from your exchange with Dr. Burgess, if the device
2324 proves to be substantially equivalent to a device that is now
2325 known to be defective, the FDA has no choice. The FDA is
2326 legally obligated to clear that product for market. The law
2327 does not clearly provide the FDA the authority it needs to
2328 protect patient safety so that new victims are not created
2329 from a technology that we already known is defective.

2330 Dr. Shuren, if a new device proves substantial
2331 equivalence to a predicate technology that has been
2332 voluntarily recalled for a serious design flaw that could
2333 seriously injure people who used it, would FDA have the legal
2334 authority to reject that application?

2335 Dr. {Shuren.} We would have to find that it is
2336 substantially equivalent but we will then look for other
2337 opportunities to clarify this, use other mitigations to
2338 address it and protect the public. The challenge becomes
2339 more about having the ability to just get information.

2340 Mr. {Markey.} But if you found that it was
2341 substantially equivalent, would you be able to reject it?

2342 Dr. {Shuren.} Not for purposes of substantial
2343 equivalence determinations.

2344 Mr. {Markey.} You could not reject it even though you

2345 knew it was defective. Is that correct?

2346 Dr. {Shuren.} That is correct.

2347 Mr. {Markey.} Well, what if the FDA had knowledge that
2348 the new device repeated the same flaw as the predicate
2349 technology? Would the FDA still be required to find it
2350 substantially equivalent?

2351 Dr. {Shuren.} We would have to find it substantially
2352 equivalent. We oftentimes with the company at least try to
2353 look for changes in labeling or other things that--

2354 Mr. {Markey.} But that would be voluntary? You would
2355 not have the legal authority to reject it. Is that correct?

2356 Dr. {Shuren.} That is correct.

2357 Mr. {Markey.} Now, the device industry argues that FDA
2358 has complete authority to assure the safety and effectiveness
2359 of a product including demanding clinical trials when they
2360 deem it necessary. Is that true in a case where the product
2361 has been shown is substantially equivalent to its defective
2362 predicate technology?

2363 Dr. {Shuren.} No.

2364 Mr. {Markey.} You do not have that authority?

2365 Dr. {Shuren.} We don't.

2366 Mr. {Markey.} Does FDA currently have any authority to
2367 invalidate defective predicate technologies?

2368 Dr. {Shuren.} So to invalidate a predicate where there

2369 is a problem, we would either rescind the 510(k) as a matter
2370 of law. We could do that, a mandatory recall, or of by
2371 judicial order the device is found--

2372 Mr. {Markey.} So you can only do something after the
2373 fact, labeling, etc. right? That is what you can do? But
2374 you can't reject it. Is that correct?

2375 Dr. {Shuren.} Yes, and the labeling we will do before
2376 the product comes on the market.

2377 Mr. {Markey.} Does FDA--some have argued that to get
2378 around the lack of authority, FDA could just issue more
2379 mandatory recalls, thereby invalidating the defective device
2380 as a predicate. Why is that not a feasible response?

2381 Dr. {Shuren.} If there is sufficient justification to
2382 do a recall, we would actually work with the company on a
2383 voluntary recall, and companies generally comply with it. To
2384 run to a mandatory recall is profoundly resource-intensive,
2385 and because there is a formal hearing that can actually take
2386 years to do.

2387 Mr. {Markey.} You are saying it is a huge resource
2388 drain, not often the best use of FDA's limited resources, but
2389 a device recall voluntarily is still available to be cited as
2390 predicate. Is that not correct?

2391 Dr. {Shuren.} No, that is correct, and quite frankly,
2392 it is not a case of necessarily that predicate shouldn't be

2393 out there to be used as a predicate but rather having the
2394 ability to assure that if there was a problem, one, it is
2395 either not replicated in the device, or if it is replicated,
2396 there is adequate mitigation, and right now while we can try
2397 to work with the company--

2398 Mr. {Markey.} Final question. Would you like--

2399 Dr. {Shuren.} --having the ability to--

2400 Mr. {Markey.} --the authority to reject certain devices
2401 if they repeatedly had the same dangerous design flaws as
2402 other previously recalled defective devices? Would you like
2403 that authority?

2404 Dr. {Shuren.} We would be happy to work with the
2405 committee on what may be the best approach on how to deal
2406 with those--

2407 Mr. {Markey.} Would you like to have the authority or
2408 not have the authority?

2409 Dr. {Shuren.} We would like to have appropriately
2410 tailored authority.

2411 Mr. {Markey.} Okay. Great. I think I would like to
2412 work with you to hopefully accomplish that goal so you do
2413 have that appropriate authority.

2414 I thank you, Mr. Chairman.

2415 Mr. {Pitts.} The chair thanks the gentleman and now
2416 recognizes the gentleman from California, Mr. Bilbray, for 5

2417 minutes for questions.

2418 Mr. {Bilbray.} Following up on that line of
2419 questioning, Mr. Chairman, if you had an inhaler, let us just
2420 say an insulin inhaler, that was a new model that could be
2421 produced cheaper and was smaller than the original but gave
2422 the same dosage, same reliability, it was a different design
2423 but basically the outcome to the patient was the same. Do we
2424 have the ability to say yes, that is comparable, and thus you
2425 don't have to go through the entire review process over
2426 again?

2427 Dr. {Shuren.} It depends upon the changes you make. If
2428 those changes made would not significantly affect safety and
2429 effectiveness, then you don't have to--

2430 Mr. {Bilbray.} Basically, my point is, you have two
2431 little devices. One is this big and one is this big. Your
2432 doses are the same, the same insulin is being used, it is
2433 just a different--basically has been upgraded. You get a
2434 call from a flip phone or you get a call from an iPhone, same
2435 product, same delivery, different ways of doing it but the
2436 same deal. Do we have the ability for you to say okay, this
2437 is comparable and thus we can allow it to move forward or
2438 does the iPhone now have to go through the whole thing, the
2439 review process all over again?

2440 Dr. {Shuren.} So for some changes, size actually could

2441 affect safety and effectiveness. If it does, that
2442 modification comes to us. So you have things like certain
2443 joint replacements that when you change the size, that can
2444 actually affect--

2445 Mr. {Bilbray.} That is inside the body, though. I am
2446 talking about an external--

2447 Dr. {Shuren.} So some of the other things that may
2448 change in size--

2449 Mr. {Bilbray.} Like bringing an inhaler down from the
2450 size of a liter bottle down to the size, you know, smaller
2451 than a lighter. Do you have a comment on that?

2452 Dr. {Woodcock.} Yes. We have a lot of experience in
2453 inhaled drugs, regulating them, and--

2454 Mr. {Bilbray.} Well, I have a lot of family members
2455 that have that same problem, but that is a different issue.

2456 Dr. {Woodcock.} So the problem with the inhalation
2457 devices is that we do not have a good way to determine
2458 bioprevalance, and that has hampered us in fact in improving
2459 generics of, say, asthma drugs that are out there because we
2460 can't determine whether they deliver the same dose as the
2461 innovator, so that is the real question, okay. So if you
2462 move from one inhalation device to another, it may be the
2463 same plume--we do plume testing which is particle size,
2464 distribution, right? However, the user interface is very

2465 important in inhaled devices because some people--you know,
2466 we had some devices they were using upside down or sucking on
2467 the wrong end, and so there are a lot of issues with user
2468 interface with inhaled medicines that influence whether or
2469 not how equivalent we can determine them to be another
2470 version.

2471 Mr. {Bilbray.} Dr. Woodcock, the question that us
2472 Californians are talking about, and it has been a few years,
2473 the State of California is going to start putting mandates on
2474 the issue that had been talked about before, and that is the
2475 pedigree issue or the tracing. The fact is, they are talking
2476 about going to requiring every unit to be tagged and
2477 identified, and we are hearing from a lot of manufacturers
2478 that there is just no way they can follow that physically or
2479 cost-effectively. What is the possibility of us working on a
2480 compromise proposal with being able to trace lots and at
2481 least start the process down the road sooner rather than
2482 waiting for the crisis that is coming down the road in a
2483 couple years when you have a State like California that
2484 controls over 12 percent of the market, probably almost 20
2485 percent of the market all at once starting to have a standard
2486 that the rest of the country doesn't have?

2487 Dr. {Woodcock.} Well, number one, we agree that it is
2488 better to have uniform standards than develop 50 different

2489 standards, which would be a nightmare. Number two, you have
2490 to, I think, determine what problem you are trying to solve
2491 and then see if your solution will address the problem that
2492 you are trying to prevent or solve, and then think about how
2493 much it would cost to implement it and then you decide the
2494 tradeoffs between the costs and the investment you have to
2495 make and the benefits that it will bring. We are concerned
2496 that the coalition's proposal doesn't provide enough benefits
2497 to justify doing that, but you need to think about what else
2498 could be done, and I think we are willing to work on that.

2499 Mr. {Bilbray.} Are you willing to commit to work on
2500 that within this year so that we get some definitive approach
2501 or at least some unified strategy on this issue within the
2502 year?

2503 Dr. {Woodcock.} I am certainly willing to sit down and
2504 work with the coalition on this, absolutely.

2505 Mr. {Bilbray.} Thank you very much, Mr. Chairman.

2506 Mr. {Pitts.} The chair thanks the gentleman. That
2507 concludes the questioning. We have one follow-up on each
2508 side. We will go to Mr. Pallone for 5 minutes for follow-up.

2509 Mr. {Pallone.} So Mr. Chairman, I would like to yield
2510 time to Mr. Markey.

2511 Mr. {Markey.} It would be just Dr. Shuren, if you
2512 could. I had a woman that I brought to Washington and we had

2513 a press conference about 2 weeks ago, and it was a bladder
2514 mesh that she had surgically inserted into her body, and she
2515 was assured that it was safe and had been FDA approved, and
2516 since then, because of that faulty bladder mesh, she has lost
2517 her livelihood as a truck driver, had to undergo multiple
2518 corrective surgeries, and because of the medical bills is now
2519 being foreclosed upon by the bank, and she has a mother who
2520 is living with her, an elderly woman, and there are thousands
2521 of other people who have had this faulty bladder mesh
2522 inserted in them as well and it is all FDA approved because
2523 you cannot reject something that is based upon this predicate
2524 technology.

2525 So maybe you could explain a little bit about what
2526 happens out there in the real world because the FDA does not
2527 have this authority to protect women like that and thousands
2528 of others like them that have FDA approval on a technology
2529 that has a defect in it that you know about but you cannot
2530 take off the market.

2531 Dr. {Shuren.} First of all, we empathize with that
2532 patient and for other people who may have had adverse effects
2533 from medical devices. I will say in the case of surgical
2534 mesh, generally the issues we are dealing with may be more
2535 of, are they in the right regulatory framework, and we just
2536 went through in the case of surgical mesh for pelvic organ

2537 prolapse where in fact we held an advisory panel meeting to
2538 say should these actually be 510(k) devices or should they be
2539 subject to the more stringent requirements for a high-risk
2540 device or PMA, and that is a process we are moving forward
2541 towards. If we make that decision and if it is rulemaking,
2542 and that is the challenge. If we change classification and
2543 we up-classify, it is rulemaking.

2544 Mr. {Markey.} What do you say to this woman? What can
2545 you do for the thousands of other women out there? The
2546 device is still out on the market, so what can you say to all
2547 these tens of thousands of additional women who are being
2548 advised by their doctors right now that it is an FDA-approved
2549 technology. I mean, this is something that doesn't work and
2550 in fact it harms women. What should we say to that woman?

2551 Dr. {Shuren.} So I will tell you in the case of pelvic
2552 organ prolapse, one, we have gone out with information
2553 communications to patients. We have been working with the
2554 health care professional community.

2555 Mr. {Markey.} This woman is a truck driver, and her
2556 physician in some town in Colorado told her it was safe.
2557 What can we say to her in terms of other women who are just
2558 in the same similarly situated predicament?

2559 Dr. {Shuren.} Again, I empathize.

2560 Mr. {Markey.} I understand. Empathy is important, and

2561 we appreciate your empathy. But what can you say to her
2562 beyond empathy in terms of she is concerned and she is like a
2563 Paul Revere trying to warn these defective bladder meshes are
2564 coming?

2565 Dr. {Gingrey.} Would the gentleman yield?

2566 Mr. {Markey.} Sure, I would be glad to yield.

2567 Dr. {Gingrey.} And I appreciate the gentleman from
2568 Massachusetts yielding to me. Of course, as he knows, I am a
2569 physician member, and I am like Dr. Shuren, certainly
2570 tremendously empathetic to this individual's situation but,
2571 you know, meshes have been used in surgery for years and
2572 years, and whether it is an abdominal hernia situation where
2573 just a simple repair and trying to stitch things back
2574 together is not sufficient, you need that insert product to
2575 give a little strength to the repair. You know, again, in
2576 this particular situation, is it the product or could it have
2577 been an improperly placed stitch to sew the product in place?
2578 Could it have been an iatrogenic hospital-acquired infection
2579 that occasionally happens that made the procedure
2580 unsuccessful or it is really a defective product? Thank you
2581 for yielding. I just wanted to--

2582 Mr. {Markey.} Thank you, Doctor. In this particular
2583 case, it is in fact a recurrence of a defect in the
2584 technology that had already been identified and was in the

2585 original predicate technology that the FDA did not have the
2586 ability to take off the market as another company is making
2587 the same technology with the same defect in it that was
2588 correctable but the new company did not feel it had to
2589 correct it because the FDA was still approving it. So that
2590 was where the problem originated, and thousands of women are
2591 still having it inserted into them. Is that not correct?

2592 Dr. {Shuren.} Most of the issues we are dealing with
2593 with surgical mesh are probably not a matter of replicating a
2594 problem in the predicate. Many of the things we are seeing
2595 may be issues about, are they in the right framework to begin
2596 with, are we actually getting adequate assurances in the way
2597 they are currently regulated generally that they are in fact
2598 safe and effective.

2599 Mr. {Markey.} But you do need authority here, don't
2600 you? Don't you need stronger authority to protect women like
2601 this, or what do you say to a woman like that? You need
2602 appropriate authority here to make sure that a woman like
2603 this is not victimized and thousands of others. Don't you
2604 agree?

2605 Dr. {Shuren.} Again, in her particular case, I don't
2606 know what happened, and I know people don't want to hear
2607 ``empathize'' but I do. I do think the case, if we wind up
2608 making a change in surgical mesh, and again, we are looking

2609 at pelvic organ prolapse but also urinary incontinence, the
2610 challenge for us is, if we change classification, this is a
2611 slightly different issue but an important one, we go through
2612 a rulemaking process, and in those rare cases where that
2613 product based upon new evidence should move to a different
2614 classification, we have to take years to make that change.
2615 That is a challenge that we do face. We are going through
2616 questions now with metal-on-metal hips. You have raised it
2617 in terms of pre-amendment devices. Our barrier is actually
2618 in those cases statutory requirement to do rulemaking, and
2619 that makes it hard, and you want to know something? I don't
2620 know what you tell patients if you find a problem like that
2621 and you make a decision to up-classify, what you do for all
2622 that time and all those--

2623 Mr. {Markey.} This woman's life is ruined, and the only
2624 thing I could tell her is that her now ruined life in her own
2625 words, will now pay dividends for other women who won't be
2626 facing the same thing.

2627 Mr. {Pitts.} The chair thanks the gentleman.

2628 Mr. {Markey.} I thank you, Mr. Chairman.

2629 Mr. {Pitts.} We will proceed for a follow-up to Dr.
2630 Burgess.

2631 Dr. {Burgess.} I thank the chairman, and I have got
2632 some other things I want to ask, but I just feel obligated.

2633 Once again, substantial equivalence does not necessarily
2634 equate clearance, and your own information that you sent to a
2635 company that receives a substantial equivalence
2636 determination, ``Please be advised the FDA's issuance of a
2637 substantial equivalence determination does not mean that the
2638 FDA has made a determination that this complies with other
2639 requirements of the Act.'' They are referring to the Food,
2640 Drug and Cosmetic Act. I think you have authority there.
2641 Now, this situation is perhaps a little bit more ambiguous
2642 than an implantable pacemaker. I would be happy to work with
2643 you too on this issue of implantable mesh because I do think
2644 it is an important one. As the baby boom generation ages, we
2645 are going to see a lot of demand for these type of
2646 procedures, and as Mr. Markey points out, it is important
2647 that we get it right because the problems with defects down
2648 the road can be significant.

2649 Dr. Woodcock, let me just ask you a question. I know we
2650 visited drug shortages in these hearings, and I appreciate
2651 the work that you have done, and while I wish there were some
2652 single legislative product that would correct the defect, I
2653 am not sure that there is, and then the problem is with
2654 legislative products that we may make things worse if it
2655 leads to hoarding and that sort of activity. But it also
2656 seems like, you know, we brought specific examples in these

2657 hearings to your attention--methotrexate, doxorubicin--and
2658 things have happened then as a consequence, and I am very
2659 grateful for that. I am sure the patients are grateful. But
2660 it also makes me wonder if the problem isn't one of maybe if
2661 there were a little more flexibility or creativity on the
2662 part of the FDA that some of these shortages could be
2663 mitigated without having them become a national crisis. You
2664 provided us a long list at another hearing. Do you have
2665 someone on your staff who is looking at that? There may be
2666 unique ways to mitigate some of these shortages and perhaps
2667 we ought to get busy about doing that rather than trying to
2668 find ideal legislation.

2669 Dr. {Woodcock.} Well, we were working on methotrexate
2670 and doxorubicin for quite a long time and we had different
2671 solutions emerge for both of those. In every case, we are
2672 using almost every tool we have. We don't make the drugs.
2673 The manufacturers make the drugs, and we try to provide them
2674 with encouragement and flexibility and lot release, like we
2675 said, batch by batch. Even if their manufacturing isn't
2676 perfect, we can mitigate many of these things. So I think we
2677 have tools to do this. We think that additional notification
2678 may be helpful. We think the proposals by the private sector
2679 for more information sharing will be helpful. We feel that
2680 some of the proposed discussion draft legislative might have

2681 unintended consequences. For example, we have this expedited
2682 review. If we have a lot of people requesting that and we
2683 know that other companies are going to be able to come up and
2684 provide the product, because we have talked to them, then we
2685 don't want to be reviewing a lot of people or clamoring for
2686 expedited review if we feel there is not going to be a
2687 shortage and the company is in production. We think deeming
2688 compliance would be a problem, all right? Because people are
2689 either in compliance or not in compliance. If they are not
2690 in compliance with GMPs, we have flexibility and they don't
2691 have to be in full compliance to be producing these shortage
2692 drugs. They just have to be producing drugs that are of good
2693 enough quality that we feel comfortable with them going into
2694 the veins of our patients, right?

2695 Dr. {Burgess.} Right. Well, the only point I was
2696 trying to make is, it does seem like there are sometimes out
2697 there that if we just worked a little harder, we would come
2698 up with them, and I just encourage you to keep doing that.

2699 Dr. {Woodcock.} We are working very hard.

2700 Dr. {Burgess.} But one specific instance, of course, a
2701 shortage occurs right now today at any pharmacy across the
2702 country that an asthmatic cannot walk into a pharmacy and buy
2703 an over-the-counter asthma inhaler like they used to be able
2704 to before January 1st. So there is a solution there, and

2705 that would be to allow the manufacturer of the old CFC
2706 product to sell what stock they have left. This product was
2707 not deemed to be defective. It was an EPA requirement that
2708 they stop selling, not an FDA requirement, and I appreciate
2709 the fact that you are working through this problem with
2710 getting a new over-the-counter preparation available, but as
2711 you pointed out, you have difficulty with bioequivalency, and
2712 I will also readily admit that HFA is not nearly as good a
2713 propellant as CFC, and don't blame the victim. It was not
2714 because I was holding the thing upside down. It is just not
2715 as good. But having said all of that, could you help us with
2716 the EPA if you were to write Administrator Jackson that
2717 because of the difficulties you are having with assessing
2718 bioequivalence of these new products that it would be helpful
2719 to allow the company to sell the product that it already has
2720 manufactured. We are not asking them to make a single vial.
2721 All the CFC that is going to be put into vials has already
2722 been put in. The only problem is, we are preventing
2723 asthmatics from having it accessible. Can I get your help to
2724 write a letter to Administrator Jackson to let her know of
2725 your problem so that maybe she can help us with the problem
2726 that asthmatics are having?

2727 Dr. {Woodcock.} We have been discussing and working
2728 with the EPA on this matter.

2729 Dr. {Burgess.} Yes, but this is something that people
2730 just frankly do not understand why one federal agency and
2731 another federal agency cannot come together on a reasonable
2732 solution. That reasonable solution is, be able to sell the
2733 product as it exists in warehouses today. Again, not one
2734 single molecule of CFC is going to be produced that has not
2735 already been produced. The hole in the ozone is not going to
2736 get one millimeter bigger because we are allowing this
2737 product to be sold. Again, the CFC has already been produced
2738 and it is already in the canisters. One day it is going to
2739 come out by some mechanism or another. I just think it would
2740 helpful to the patients of America. We could eliminate this
2741 one drug shortage overnight if you could get some cooperation
2742 with the EPA.

2743 Mr. {Pitts.} The chair thanks the gentleman. Mr. Engel
2744 for 5 minutes for questions.

2745 Mr. {Engel.} Thank you, Mr. Chairman.

2746 Dr. Woodcock, I just have two quick questions. I want
2747 to get back to the issue of drug shortages again because
2748 during your last appearance before the subcommittee, I
2749 mentioned my concerns about drug shortages of medications
2750 that overlap with the DEA's controlled-substance
2751 jurisdiction, and I am pleased to see in this discussion
2752 draft there are provisions for the Attorney General to

2753 increase quotas as necessary within 30 days of a request from
2754 a manufacturer. So let me ask you this. Do you believe that
2755 the majority of drug shortages in the controlled-substance
2756 category can be effectively prevented if the Attorney General
2757 addresses this request within the 30-day window or do you
2758 believe a shorter window would be necessary to ensure patient
2759 access to needed medications?

2760 Dr. {Woodcock.} I am not familiar enough with DEA
2761 procedures to answer your question accurately. There are
2762 many causes of drug shortages, and certainly not all
2763 shortages of controlled substances may be related to DEA
2764 procedures or quotas or what have you. So I think it is a
2765 complicated issue and we would be glad to work with you.

2766 Mr. {Engel.} Okay. How about the 30 days, though? Do
2767 you think that is sufficient? It might be a little too long
2768 if someone really needs a medication.

2769 Dr. {Woodcock.} Again, it is very difficult for me to
2770 put that into--to understand what impact 30 versus a shorter
2771 time would have on an unfolding shortage situation.

2772 Mr. {Engel.} Okay. Well, we will work with you on it.

2773 During the last PDUFA reauthorization, I worked--this is
2774 a couple years ago--I worked with Congresswoman Blackburn and
2775 Congresswoman Giffords at that time to authorize critical
2776 path public-private partnerships, and to date, the Critical

2777 Path Institute in Arizona and the Clinical Data Interchange
2778 Standards Consortium have worked under this partnership to
2779 improve the regulatory science that FDA and industry depend
2780 on when developing and improving new pharmaceuticals and
2781 medical devices. So I am wondering if you could comment on
2782 that? It is sort of loaded question, but I want you to be on
2783 the record, because I feel strongly about the importance of
2784 the critical path public-private partnerships and the FDA's
2785 work, so I would like you to comment on that and what role
2786 you see for these partnerships in the future.

2787 Dr. {Woodcock.} Well, first of all, the Critical Path
2788 Institute has done a number of projects that are essential.
2789 For example, we have new biomarkers now being tested in the
2790 clinic for drug-induced renal failure, something we don't
2791 have any sensitive indicators for, and so this is a
2792 tremendous advance in regulatory science if we can get these.
2793 We have qualified them for animal studies. If we can use
2794 them in humans, that would be a tremendous advance for drug
2795 development.

2796 As far as the clinical data standards, as we move into
2797 developing electronic health records for the public and so
2798 forth, having unified standards for how you collect data in
2799 clinical trials not only will help companies, it will help
2800 the FDA and it will help all the investigators in efficiently

2801 performing clinical trials. Right now, we have a tremendous
2802 problem of loss of clinical studies from the United States
2803 and going elsewhere, and harmonized standards within the
2804 United States for clinical data are a tremendous requirement
2805 and would really help both drug development and understanding
2806 the role of medical products and their outcomes in our
2807 population. So this type of regulatory science that is being
2808 done by the Critical Path Institute and other public-private
2809 partnerships is really building for the future, and we really
2810 endorse it.

2811 Mr. {Engel.} Well, thank you. I couldn't agree with
2812 you, and you gave me the answer I wanted, so thank you very
2813 much.

2814 Mr. Chairman, I yield back the balance of my time.

2815 Mr. {Pitts.} The chair thanks the gentleman and yields
2816 to the ranking member for a unanimous consent request.

2817 Mr. {Pallone.} Thank you, Mr. Chairman. I just would
2818 like to make a unanimous consent request that the statement
2819 of Congresswoman Anna Eshoo as well as some questions that
2820 she is promulgating to Dr. Janet Woodcock be entered into the
2821 record.

2822 Mr. {Pitts.} Without objection, so ordered.

2823 [The information follows:]

2824 ***** COMMITTEE INSERT *****

|
2825 Mr. {Pitts.} We will make sure you get all of the
2826 questions for follow-up, if you would respond in writing.

2827 That concludes our first panel. Thank you, Dr.
2828 Woodcock, thank you, Dr. Shuren, for your testimony and your
2829 responses. The committee will recess for 5 minutes as we
2830 change for panel number two and we will reconvene in 5
2831 minutes.

2832 [Recess.]

2833 Mr. {Pitts.} The 5 minutes having expired, we will
2834 reconvene the subcommittee, and we now have panel number two.
2835 I would like to thank all of you for agreeing to testify
2836 before the subcommittee today. I would like to quickly
2837 introduce our expert panel.

2838 First, Dr. David Wheadon is Senior Vice President of
2839 Scientific and Regulatory Affairs at Pharmaceutical Research
2840 and Manufacturers of America. Dr. Sara Radcliffe is
2841 Executive Vice President of Health at Biotechnology Industry
2842 Organization. Mr. David Gaugh is Vice President of
2843 Regulatory Sciences at the Generic Pharmaceutical
2844 Association. Mr. Joseph Levitt is Partner at Hogan Lovells
2845 and is testifying on behalf of Advanced Medical Technology
2846 Association. And Mr. Allan Coukell is Director of Medical
2847 Programs of Pew Health Group at the Pew Charitable Trust.

2848 Again, thank you all for coming. We have your prepared
2849 statements. They will be entered into the record. We ask
2850 that you summarize your opening statements in 5 minutes. We
2851 are scheduled to vote in about 20 minutes. We will try to
2852 get through the presentations before having to go to the
2853 Floor for the vote.

2854 So with that, Dr. Wheadon, we will begin with you. You
2855 are recognized for 5 minutes to summarize your testimony.

|
2856 ^STATEMENTS OF DAVID E. WHEADON, M.D., SENIOR VICE PRESIDENT,
2857 SCIENTIFIC AND REGULATORY AFFAIRS, PHARMACEUTICAL RESEARCH
2858 AND MANUFACTURERS OF AMERICA; SARA RADCLIFFE, EXECUTIVE VICE
2859 PRESIDENT OF HEALTH, BIOTECHNOLOGY INDUSTRY ORGANIZATION;
2860 DAVID GAUGH, R.PH., VICE PRESIDENT, REGULATORY SCIENCES,
2861 GENERIC PHARMACEUTICAL ASSOCIATION; JOSEPH A. LEVITT, J.D.,
2862 PARTNER, HOGAN LOVELLS US LLP, ON BEHALF OF ADVANCED MEDICAL
2863 TECHNOLOGY ASSOCIATION; AND ALLAN COUKELL, DIRECTOR OF
2864 MEDICAL PROGRAMS, PEW HEALTH GROUP, THE PEW CHARITABLE TRUSTS

|
2865 ^STATEMENT OF DAVID E. WHEADON

2866 } Dr. {Wheadon.} Chairman Pitts, Ranking Member Pallone
2867 and members of the subcommittee, good afternoon. I am David
2868 Wheadon, Senior Vice President, Scientific and Regulatory
2869 Affairs, at the Pharmaceutical Research and Manufacturers of
2870 America, better known as PhRMA. PhRMA appreciates this
2871 opportunity to appear before you again today in order to
2872 share our views on the 5th reauthorization of the
2873 Prescription Drug User Fee Act and on the reauthorization of
2874 the Best Pharmaceuticals for Children Act and the Pediatric
2875 Research Equity Act.

2876 PhRMA and its member companies strongly support the

2877 original goals of PDUFA, namely to provide patients with
2878 faster access to innovative medicines, to preserve and
2879 strengthen FDA's high standards for safety, efficacy and
2880 quality, and to advance the scientific basis for the agency's
2881 regulatory oversight. PDUFA has advanced public health by
2882 accelerating the availability of innovative medicines to
2883 patients while helping to ensure patient safety. PDUFA has
2884 also played a role in improving America's competitiveness
2885 around the world.

2886 Since the passage of the original PDUFA in 1992, the
2887 United States has become the world leader in bringing new
2888 medicines to patients first, ensuring that the United States
2889 maintains a policy and regulatory environment that encourages
2890 an efficient, consistent and predictable drug review process
2891 is key to keeping America competitive in today's global
2892 economy.

2893 The PDUFA V performance goals letter was created with an
2894 impressive inner transparency and involvement from diverse
2895 stakeholders including patients, health care providers and
2896 academia. This agreement will provide FDA with the resources
2897 and tools required for further enhancing the timeliness,
2898 completeness and efficiency of the drug review process
2899 including provisions to advance regulatory science and
2900 modernize drug development, to improve benefit-risk decision

2901 making and to further strengthen FDA's focus on patient
2902 safety. PhRMA strongly endorses the recommendations of the
2903 PDUFA V performance goals letter and urges Congress to
2904 reauthorize this important legislation in a timely manner
2905 based on the negotiated agreement. Failure to reauthorize
2906 PDUFA in a timely fashion would have catastrophic effects on
2907 the ability of FDA to carry out its important role in
2908 bringing innovative medicines to patients.

2909 I would like to focus for a moment on one specific
2910 aspect of PDUFA. The enhanced New Molecular Entity review
2911 model, or NME review model, will improve the review process
2912 for new molecular entity drug and biologic applications.
2913 This will be particularly significant for patients because
2914 NMEs are novel compounds that have the potential to address
2915 unmet medical needs and advance patient care. Specifically,
2916 it is anticipated that earlier and more comprehensive
2917 communication between the agency and drug sponsors as
2918 required in this enhanced review model will improve the rate
2919 of on-time first-cycle successes. The success of the new
2920 review program and of the agency's ability to achieve its
2921 drug review goals will be independently assessed in 2015 and
2922 2017.

2923 PDUFA V will continue to provide FDA with the necessary
2924 tools and resources that are essential to support patient

2925 safety and promote medical innovation through enhanced
2926 timeliness, completeness and efficiency of the drug review
2927 process. PhRMA encourages Congress to reauthorize PDUFA in a
2928 timely manner based on the negotiated PDUFA V performance
2929 goals and to minimize the inclusion of additional provisions
2930 that may have the unintended consequences of distracting from
2931 the Act's original intent.

2932 The Best Pharmaceuticals for Children Act and the
2933 Pediatric Research Equity Act have been extraordinarily
2934 successful in improving medical care for children by driving
2935 research to create innovative medicines for use in pediatric
2936 patients. According to the FDA, the current pediatric
2937 exclusivity program has done more to spur research and create
2938 critical information about the use of medicines in pediatric
2939 patients than any other government initiative. Ensuring that
2940 the pediatric exclusivity incentive is preserved is key to
2941 continued innovation and improved pediatric medical care in
2942 the face of rising research costs.

2943 Since its initial enactment and subsequent
2944 reauthorizations, BPCA and PREA have been subject to a sunset
2945 clause under which their provisions expire after 5 years
2946 unless reauthorized by Congress. To build upon the
2947 tremendous success of BPCA and PREA in improving medical care
2948 for children, Congress should permanently reauthorize BPCA

2949 and PREA.

2950 We would particularly like to thank Representatives
2951 Eshoo, Rogers and Markey for their work towards a bipartisan
2952 effort for a permanent reauthorization of these important
2953 pieces of legislation.

2954 In summary, PhRMA and its member companies are committed
2955 to working closely with FDA, Congress and all stakeholders to
2956 ensure the continued success of PDUFA in bringing safe,
2957 effective and innovative medicines forward to address unmet
2958 medical needs for all patients including children. PhRMA
2959 therefore urges Congress to reauthorize PDUFA V and to
2960 permanently reauthorize BPCA and PREA in the most expeditious
2961 manner possible.

2962 Thank you, and I would be happy to entertain any
2963 questions.

2964 [The prepared statement of Dr. Wheadon follows:]

2965 ***** INSERT 3 *****

|

2966 Mr. {Pitts.} The chair thanks the gentleman.

2967 Ms. Radcliffe, you are recognized for 5 minutes.

|
2968 ^STATEMENT OF SARA RADCLIFFE

2969 } Ms. {Radcliffe.} Thank you. Chairman Pitts and Ranking
2970 Member Pallone, I appreciate the opportunity to be here
2971 today. I am Sara Radcliffe, Executive Vice President for
2972 Health for the Biotechnology Industry Organization, BIO. I
2973 led BIO's engagement in the Prescription Drug User Fee Act
2974 technical discussions with the Food and Drug Administration
2975 and managed BIO's involvement in the biosimilars user fee
2976 technical discussions as well.

2977 BIO supports quick enactment of the PDUFA V
2978 recommendations and we are supportive of the draft user fee
2979 package that the committee has released. This committee has
2980 reached strong bipartisan compromises on many issues that of
2981 critical importance to our industry. We believe that
2982 enhancements under PDUFA V will improve the drug development
2983 and review process through increased transparency and
2984 scientific dialog, advance regulatory science and strength
2985 postmarket surveillance. Most importantly, from the
2986 standpoint of young, innovative companies, our hope is that
2987 PDUFA V will provide patients and doctors with earlier access
2988 to the cures and treatments of tomorrow.

2989 The PDUFA V legislation will reinforce FDA's review

2990 performance and get back to basics for patients. These
2991 enhancements include a New Molecular Entity review program
2992 that will lead to fewer review cycles and earlier patient to
2993 needed treatment, enhanced communication during drug
2994 development, regulatory science modernization and robust drug
2995 safety and postmarket surveillance capacities.

2996 BIO supports FDA's ongoing implementation of a well-
2997 constructed, science-based pathway for the approval of
2998 biosimilar products. Establishing a sound BSUFA was also a
2999 priority for us. A transparent, predictable and balanced
3000 regulatory framework for the review and approval of
3001 biosimilars accompanied by reasonable performance goals and a
3002 dedicated independent funding stream will ensure that FDA can
3003 facilitate the development and evaluation of biosimilar
3004 products.

3005 There are a number of other important provisions
3006 included in the draft that are of critical importance to BIO.
3007 Modernizing the Accelerated Approval pathway has been a top
3008 priority, and we are extremely pleased that the draft
3009 included H.R. 4132, the Faster Access to Specialized
3010 Treatments, or FAST Act, introduced by Congressmen Cliff
3011 Stearns and Ed Towns. FAST will ensure that FDA can utilize
3012 the Accelerated Approval pathway as fully and frequently as
3013 possible while maintaining FDA's safety and effectiveness

3014 standards.

3015 The Accelerated Approval pathway has been a great
3016 success story. In certain disease areas such as cancer and
3017 HIV, the pathway has stimulated an explosion of investment in
3018 innovation and has brought immense benefit to patients. We
3019 appreciate Congress working to expand the pathway so that
3020 patients suffering from other life-threatening and rare
3021 diseases can benefit as well.

3022 The Best Pharmaceuticals for Children Act and Pediatric
3023 Research Equity Act have greatly improved health outcomes for
3024 children. However, the 5-year sunset periods have resulted
3025 in an uncertain regulatory environment for pediatric drug
3026 development that makes it difficult for our company and
3027 practically impossible for the FDA to issuance guidance to
3028 promote understanding of the current regulatory framework.
3029 BIO thanks Congressman Mike Rogers, Congresswoman Anna Eshoo
3030 and Congressman Ed Markey on their championship of this
3031 important issue and we support the inclusion of their
3032 legislation in the committee draft.

3033 It is also important that FDA has access to the most
3034 knowledgeable and most qualified scientific minds to help
3035 inform key public health decisions and evaluate the safety
3036 and effectiveness of innovative new cures and treatments for
3037 patients. BIO thanks Representative Burgess and Ranking

3038 Member Pallone for their work to enhance FDA's ability to
3039 impanel highly qualified external scientific advisors while
3040 maintaining the highest levels of integrity for these
3041 proceedings.

3042 Additionally, BIO looks forward to continuing to work
3043 with the committee to enhance oversight over the upstream
3044 supply chain for pharmaceutical ingredients and modernizing
3045 the downstream domestic supply chain for finished
3046 pharmaceutical products. BIO supports the establishment of
3047 strong, uniform national standards for serialization and
3048 tracing systems rather than relying on the emerging patchwork
3049 of individual State mandates. In this case, BIO believes
3050 that Congress should enact laws governing drug product
3051 serialization and traceability systems that regulators can
3052 leverage to hold supply chain member accountable for ensuring
3053 that legitimate product reaches the patient. A national
3054 system using existing and proven technologies would best
3055 protect supply chain integrity and patient safety.

3056 Thank you again for the opportunity to testify. We look
3057 forward to working with all of you to ensure that the user
3058 fee package is quickly enacted.

3059 [The prepared statement of Ms. Radcliffe follows:]

3060 ***** INSERT 4 *****

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3061 Mr. {Pitts.} The chair thanks the gentlelady.

3062 Mr. Gaugh, you are recognized for 5 minutes for an

3063 opening statement.

|
3064 ^STATEMENT OF DAVID GAUGH

3065 } Mr. {Gaugh.} Good afternoon, Chairman Pitts, Ranking
3066 Member Pallone and members of the subcommittee. I am David
3067 Gaugh, Vice President of Regulatory Science for the Generic
3068 Pharmaceutical Association and a Licensed Pharmacist. GPhA
3069 represents the manufacturers and distributors of finished
3070 dose pharmaceuticals and bulk pharmaceutical chemicals.

3071 Generic pharmaceuticals account for 80 percent of all
3072 prescription drugs dispensed in the United States but consume
3073 just 27 percent of the total drug spending for prescription
3074 medicines. Today's generic industry is one marked by
3075 diverse, innovative companies who have grown to become global
3076 leaders in providing equivalent medicines. At the same time,
3077 generic competition continues to play a vital role in driving
3078 pharmaceutical innovation. This growth in the generic
3079 industry has led to the creation of tens of thousands of new
3080 American jobs and dozens of States across the country. It
3081 has also served to underscore the critically important role
3082 of the Food and Drug Administration. However, the
3083 administration remains underfunded and responsibility of
3084 ensuring access to safe and affordable medicines is one that
3085 is shared with the rest of the entire pharmaceutical

3086 industry, not just the FDA. That is why the generic industry
3087 has stepped up to help provide the FDA with additional
3088 resources to address the ongoing challenges caused by an
3089 increasing global drug supply chain, the increase in the
3090 agency's workload and the regulation of complex technologies.

3091 Currently, more than 2,700 generic drug applications are
3092 awaiting approval from the FDA's Office of Generic Drugs, and
3093 the average approval time for an application is now
3094 stretching beyond 30 months, more than five times longer than
3095 the statutory six-month review time that was called for in
3096 Hatch-Waxman. Unfortunately, this backlog keeps safe, low-
3097 cost generic drugs off the market and reduces competition
3098 that may drive prices down even further.

3099 The proposed Generic Drug User Fee Act, or GDUFA, that
3100 we are discussing today will help alleviate this backlog and
3101 expedite consumer access to these generic drugs. GPhA also
3102 recognizes, however, that while providing early access to
3103 effective medicines is critical and is a key aim of the other
3104 user fee programs, an equally important pillar of FDA and
3105 industry is to ensure drug safety. That is why GDUFA takes
3106 the unprecedented step of holding all players contributing to
3107 the U.S. generic drug system both foreign and domestic to the
3108 same inspection standards and enhances FDA's ability to
3109 identify and require the registration of active

3110 pharmaceutical ingredients and finished fill dosage for
3111 manufacturers involved in each generic drug product that is
3112 sold in the United States. It is paramount that we work to
3113 shape the future of our country's generic drug industry. We
3114 also work to bring the FDA into the 21st century and ensure
3115 that the agency's authorities to achieve its mission in this
3116 global age are up to date.

3117 This is further exemplified by the other fee program we
3118 will discuss today, which is for generic biologic drugs or
3119 biosimilars. Biologic medicines are often the only
3120 lifesaving treatment for many of the more severe diseases
3121 encountered in patients today. In many respects, they
3122 represent the future of medicine. However, their price tag
3123 can keep these products out of the reach of many patients.

3124 During the biosimilar user fee negotiations, GPhA
3125 expressed its support for the user fee funding to provide FDA
3126 with the adequate resources to apply consistent regulatory
3127 standards to all biologics and review new applications as
3128 they are filed. Both industry and patients will benefit from
3129 this user fee program by gaining a higher degree of certainty
3130 in the timeliness of applications and their reviews. We
3131 applaud the FDA for recognizing the importance of the
3132 biosimilars and the need to apply state-of-the-art science in
3133 an agency activity governing the review and approval of these

3134 very important drugs.

3135 Now let me turn to drug shortages. The generic
3136 pharmaceutical industry has spearheaded the development of an
3137 unprecedented multi-stakeholder private sector collaboration
3138 which we believe will accelerate the recovery of certain
3139 critical drugs in short supply to the patients in need. This
3140 solution, which has been labeled the Accelerated Recovery
3141 Initiative, will play a crucial role in assisting the FDA
3142 with a more accurate, timely and comprehensive review of
3143 current potential drug shortages and in establishing
3144 practices to lessen or even eliminate in some cases current
3145 shortages.

3146 Finally, we urge the inclusion in the user fee
3147 legislation of a proposal introduced by Ranking Member
3148 Pallone and Representative Guthrie, H.R. 4332, the Generic
3149 Drug Application Review Fairness Act, which will ensure that
3150 generic drug manufacturers are not unfairly penalized for
3151 delays in the drug application approval process.

3152 In conclusion, Mr. Chairman, this is truly an historic
3153 time for GPhA. Nothing is more important to our industry
3154 than ensuring patients have access to lifesaving generic
3155 medications they require and these historic agreements will
3156 provide the critical step towards accomplishing that goal.
3157 Thank you.

3158 [The prepared statement of Mr. Gaugh follows:]

3159 ***** INSERTS 5, 6 *****

|

3160 Mr. {Pitts.} The chair thanks the gentleman.

3161 Mr. Levitt, you are recognized for 5 minutes.

|
3162 ^STATEMENT OF JOSEPH A. LEVITT

3163 } Mr. {Levitt.} Thank you. Chairman Pitts, Ranking
3164 Member Pallone and members of the committee, my name is Joe
3165 Levitt. I am a partner in the law firm of Hogan Lovells, and
3166 I am here today on behalf of AdvaMed, MDMA and MITA, the
3167 three trade associations who participated in the MDUFA
3168 negotiations with the FDA. I was on that negotiating team
3169 throughout that process, and I am pleased to be testifying
3170 with you here today. I also spent 25 year at the FDA and for
3171 6-1/2 of those years during the 1990s I held the senior
3172 position in FDA's Medical Device Center.

3173 As many of you know, the medical technology industry has
3174 been a true success story for patients and for the U.S.
3175 economy. Our industry truly leads the world but our
3176 leadership is slipping. One key reason, perhaps the most
3177 important reason, is the decline we have seen in FDA
3178 efficiency, consistency and predictability in recent years.
3179 To their credit, the FDA leadership has recognized the need
3180 to vigorously address the issues affecting the device center.
3181 The new user fee agreement has the potential to be a
3182 significant additional step in the right direction. It is
3183 good for industry, it is good for FDA, and most of all, it is

3184 good for American patients.

3185 The user fee agreement builds the conditions for success
3186 in a number of major ways. First, for the first time ever,
3187 this user fee agreement establishes average total time goals
3188 for FDA review. Our previous agreements had set goals only
3189 for terms of the FDA clock but what matters most to industry
3190 and to patients is the actual calendar, the time from
3191 beginning of submission to final FDA decision. By setting in
3192 place this new goal, efforts will be focused on the metric
3193 that truly matters.

3194 Second, the agreement also establishes improved goals
3195 for time on the FDA clock. These goals are a key management
3196 tool for the agency and they work in concert with the total
3197 time goal to produce better performance than either could
3198 achieve alone.

3199 Third, the agreement includes new procedures that we
3200 anticipate will improve the review process. These include
3201 before the review actually begins meaningful presubmission
3202 interactions between FDA and companies to be sure everybody
3203 is on the same wavelength going in, during the review process
3204 a mandatory mid-course substantive interaction between FDA
3205 and the company midway through the process to check in and be
3206 sure we are all on the right wavelength there, and finally at
3207 the tail end, a new procedure that we call ``no submission

3208 left behind'' so that if FDA time target is missed, that
3209 submission does not fall off the radar screen.

3210 Fourth, the agreement provides for greater
3211 accountability. Under the agreement, there will be quarterly
3212 and annual reporting on a variety of key metrics that both
3213 industry and FDA agree are important. In addition, the
3214 agreement provides an analysis of FDA's management of the
3215 review process by an independent consulting organization
3216 coupled with FDA corrective action plan to address
3217 opportunities for improvements. We see this as being
3218 critical. It is a way to bring fresh eyes to the issues and
3219 work constructively towards meaningful process improvements.

3220 Finally, to give FDA the additional tools to meet the
3221 new goals, the agreement provides for \$595 million in user
3222 fees over the life of the agreement. Additional reviewers,
3223 lower management-to-reviewer ratios, enhanced training and
3224 other resources totaling about 200 additional FTEs for the
3225 agency are provided by the agreement and will give FDA what
3226 it needs to improve performance.

3227 Of course, no agreement, no matter how good on paper, is
3228 self-executing. Making it work as intended will require the
3229 full efforts of all concerned. Continued oversight and
3230 interest from the Congress will also be important. Patients
3231 are depending on all of us.

3232 In conclusion, I should note that a number of
3233 legislation proposals have been introduced with the goal of
3234 improving FDA's operations also. We are appreciative of
3235 efforts by all members who seek to give FDA the tools and
3236 structure it needs to succeed. At the same time, I want to
3237 emphasize that we are strongly committed to the user fee
3238 agreement as negotiated and do not support any proposals that
3239 would change the terms of the agreement or undermine its
3240 goals. Just as the user fee agreement has the potential to
3241 help FDA move in a positive direction, failure to reauthorize
3242 the program in a timely way would be nothing short of
3243 catastrophic, as my colleagues on the panel have also echoed.

3244 So I thank the committee for the opportunity to testify
3245 and urge it act promptly to reauthorize the program which is
3246 so critical to patients, to FDA and to our industry.

3247 [The prepared statement of Mr. Levitt follows:]

3248 ***** INSERT 7 *****

|
3249 Mr. {Pitts.} The chair thanks the gentleman.

3250 We are in the middle of a vote on the Floor. We have
3251 about 10 minutes. We will take one more witness and then we
3252 will break for the vote.

3253 Mr. Coukell, you are recognized for 5 minutes.

|
3254 ^STATEMENT OF ALLAN COUKELL

3255 } Mr. {Coukell.} Thank you, Mr. Chairman, Ranking Member
3256 Pallone and committee members. I appreciate the opportunity
3257 to testify.

3258 My name is Allan Coukell, and I am the Director of
3259 Medical Programs for the Pew Health Group. Our research and
3260 analysis aim to improve the safety and well-being of American
3261 consumers with the major focus on drugs, medical devices and
3262 the FDA. I will focus today on the importance of the FDA
3263 user fee agreements to patients and public health and about
3264 three key policy areas that the committee is considering.

3265 Since 1992, PDUFA agreements have given FDA significant
3266 and sustained resources, allowing for faster reviews of new
3267 products. Indeed, preliminary results of a study that Pew
3268 has funded show that FDA reviews drugs faster than its
3269 counterparts in the E.U. and Canada. The development of new
3270 antibiotics is a particular focus for Pew's Antibiotics and
3271 Innovation Project, and we thank this committee for
3272 consideration of the GAIN Act, the bipartisan bill introduced
3273 by Mr. Gingrey that would grant extra market protection to
3274 certain antibiotics.

3275 Unlike other drugs, antibacterials lose their

3276 effectiveness over time as the bugs become resistant. That
3277 is why experts are so alarmed about the years-long decline in
3278 new antibiotics and the dearth of products in late-stage
3279 development. We look forward to working with this committee
3280 to see that this provision targets and incentivizes the drugs
3281 we most need, those that treat serious or life-threatening
3282 infections.

3283 Turning now to medical devices, we ask Congress to
3284 swiftly reauthorize MDUFA. Under this new agreement, FDA
3285 would add 200 device staff and nearly \$600 million for the
3286 review of device applications. Let me illustrate the
3287 importance of this funding with an analysis recently
3288 commissioned by Pew showing that FDA's Device Center has a
3289 higher attrition rate than the Centers for Drugs and
3290 Biologics or the Office of Regulatory Affairs. In fact,
3291 nearly 10 percent of FDA's device staff left in fiscal year
3292 2010, and the majority reported not having sufficient
3293 resources to get their job done. To function effectively,
3294 the center must have adequate funding.

3295 But let us never forget that true innovation is not just
3296 about speed to market but about developing products that are
3297 safer or more effective than existing drugs and devices, and
3298 because medical devices often enter the market with little or
3299 no clinical data, it is especially important that we have a

3300 robust system for postmarket surveillance, and we urge this
3301 committee to include legislation that will medical devices to
3302 FDA's Sentinel Surveillance System which is currently on for
3303 drugs, require that FDA issue and implement rules that assign
3304 a unique identifier like a barcode to each new device as we
3305 have on most other things that we buy, and clarify the
3306 agency's authority to order safety studies when necessary for
3307 high-risk devices. We must also ensure that these studies
3308 are completed in a timely way. Such a system would detect
3309 safety problems faster and would facilitate innovation by
3310 increasing the confidence of the public and the FDA on
3311 marketed devices.

3312 On safety, I am pleased to note that the landmark new
3313 generic drug user fee agreement while speeding the review of
3314 these products will also enhance safety by ensuring that FDA
3315 performs more inspections of overseas generic drug plants.
3316 As Pew's drug safety project has noted, 80 percent of the
3317 ingredients in our drug supply now come from overseas yet we
3318 inspect U.S.-based drug makers every 2 years, as the law
3319 requires. Meanwhile, the FDA inspections in China, for
3320 example, average out about every 17 years. Addressing this
3321 disparity will level the playing field for U.S.-based
3322 manufacturers and help to protect patients. Congress should
3323 hold FDA accountable by ensuring that no facility goes

3324 indefinitely without an inspection. But inspections are only
3325 part of the story. Several additional key measures would
3326 improve confidence in the supply chain.

3327 For example, we should ensure that every company takes
3328 responsibility for its own upstream suppliers, verifying that
3329 appropriate quality systems are in place. We should reward
3330 manufacturers who have strong systems. We support a national
3331 track-and-trace system for drugs but such a system must
3332 include standards that will detect counterfeits before they
3333 get to patients and, for example, provide law enforcement
3334 with the tools needed to address illegal-drug diversion.

3335 We thank the committee for its bipartisan work on the
3336 prescription drug supply chain. A poll we commissioned
3337 showed that Americans of all political persuasions recognize
3338 the risks and support Congressional action.

3339 I will conclude with a reference to FDA's mission
3340 statement, which acknowledges the agency's dual role:
3341 protecting patients and ensuring innovation. The user fee
3342 agreements support both aims, and we urge Congress to pass
3343 them quickly along with the three essential additions: drug
3344 supply chain safety, antibiotic development and medical
3345 device safety.

3346 Thank you, and I welcome your questions.

3347 [The prepared statement of Mr. Coukell follows:]

3348 ***** INSERT 8 *****

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3349 Mr. {Pitts.} The chair thanks the gentleman.

3350 That concludes the opening statements. We are in the
3351 middle of a vote. I think we have about 5 minutes left, so
3352 at this point the subcommittee will break until the third
3353 vote. Five minutes after the third vote, we will reconvene.
3354 The subcommittee stands in recess.

3355 [Recess.]

3356 Mr. {Pitts.} The recess having expired, we will
3357 reconvene the Subcommittee and go to the questioning. I will
3358 now begin the questioning and recognize myself for 5 minutes
3359 for that purpose.

3360 First of all, Dr. Wheadon, how does the PDUFA agreement
3361 help mitigate the issue of delayed reviews of drug
3362 applications at FDA and help America maintain their role as
3363 the leading innovator in the pharmaceutical space? If you
3364 would please elaborate on that.

3365 Dr. {Wheadon.} I will answer that, Chairman Pitts, on
3366 two fronts, focusing initially on the New Molecular Entity--

3367 Mr. {Pitts.} Is your microphone on? Just pull it down.
3368 Yeah.

3369 Dr. {Wheadon.} Focusing initially on the New Molecular
3370 Entity Review Program, that was really set up to enhance
3371 ongoing communication between drug sponsors and FDA such that

3372 sponsors would understand up front what FDA expectations may
3373 be as they enter into the review. As the review progresses,
3374 there would be feedback to the sponsor. There are questions
3375 that come out of the review that could be answered
3376 contemporaneously rather than waiting until the end of the
3377 review. The intention is that by the time you get to the end
3378 of the review, most of the issues could have been discussed
3379 and hopefully rectified, allowing for FDA to make a final
3380 action, hopefully an approval, thus allowing the drug to be
3381 approved in the first cycle and available to patients.

3382 Beyond that, the other aspects of the agreement, the
3383 availability of innovative medicines to patients, really
3384 looks at the regulatory science initiatives, things like
3385 benefit-risk, biomarker development, pharmacogenomic
3386 processes, enhancing the utilization of REMS in terms of
3387 standardizing that process rather than starting from square
3388 one with each necessity for utilizing of REMS for approval.

3389 So taken as a whole, the intention is to make the review
3390 process more efficient and more effective use of FDA
3391 resources, allowing for a thorough review but hopefully a
3392 one-cycle review and ultimately really addressing the issue
3393 that we started out looking at, and that is for roughly 50
3394 percent of applications, they don't get approved in the first
3395 cycle. They ultimately do get approved with following cycles

3396 of review. That is an inefficient use of FDA resources and
3397 that is really what we are trying to tackle with the
3398 agreement.

3399 Mr. {Pitts.} Ms. Radcliffe, would you like to add to
3400 that as far as bio is concerned?

3401 Ms. {Radcliffe.} Yes, I would. Thank you. I would
3402 like to support everything that Dr. Wheadon said about the
3403 weight of the PDUFA Technical Agreement will enhance the
3404 availability of products for patients but mention also one
3405 other thing. It was particularly important for our small
3406 companies and that was a provision to enhance timely
3407 interactive communication during the drug development phase.
3408 Our small companies tell us that very often they have simple,
3409 informal questions where they need timely answers in order to
3410 proceed. We were very pleased that the Agency agreed to
3411 state explicitly that they have a philosophy of timely,
3412 interactive communication with sponsors and also that we were
3413 able to agree to establish a liaison staff that would work to
3414 ensure that that communication occurs.

3415 Mr. {Pitts.} Thank you.

3416 Mr. Gaugh, the discussion draft includes a section on
3417 expediting manufacturing changes to alleviate a drug
3418 shortage. Would you comment on this provision, tell us how
3419 it would help?

3420 Mr. {Gaugh.} I am sorry. Could you repeat that?

3421 Mr. {Pitts.} Yes. The draft includes a section on
3422 expediting manufacturing changes to alleviate drug shortages.
3423 Comment on that provision.

3424 Mr. {Gaugh.} Yes, in today's environment it takes
3425 anywhere from 18 to 24 months for those review cycles to
3426 occur, so if you have a product that is in drug shortage,
3427 that is an additional time point with everything else that
3428 you are adding to it. The provisions in here are going to be
3429 for expedited review, which could be as quickly they say as 3
3430 to 6 months, which would help tremendously.

3431 Mr. {Pitts.} Mr. Levitt, can you explain IDEs, you
3432 know, what are they, what companies get IDEs traditionally,
3433 how does FDA evaluate IDEs? I understand FDA has a new
3434 policy on IDEs. How does that differ from previous policy
3435 and what is your opinion of the new policy?

3436 Mr. {Levitt.} Okay. An IDE stands for Investigational
3437 Device Exemption. What it basically means is that FDA
3438 reviews applications for new clinical studies. New clinical
3439 studies are needed generally for all Class 3 devices going
3440 through the premarket approval process and for a small
3441 minority of 510(k) products. But if a company wants to test
3442 their device in humans and it doesn't fit into one of the
3443 minor categories that they are exempt from submitting, then

3444 they submit an application to the FDA that includes the data
3445 to show that the device is safe enough to test in humans. So
3446 the first question is safety. And the second question is,
3447 what is the protocol that they are going to use during the
3448 study? They will submit those to FDA. FDA has 30 days only
3449 to review that, reflecting that FDA's review is really just
3450 to focus on is it safe and is this essentially a bona fide
3451 study where the potential benefits outweigh the potential
3452 risks. So that is the historical process.

3453 What has happened recently is that FDA has brought
3454 greater scrutiny to the clinical protocol part and they are
3455 trying to say that you can only do this clinical study if it
3456 is good enough to get final approval. And there is a lot of
3457 concern within the industry that that is much more than has
3458 ever been done in the past and is certainly much more than
3459 the regulations their statute require, that the process
3460 should be able to go forward at the pace that the company is
3461 prepared to undertake. It might be a preliminary study, it
3462 might be a study that will depend on how strong the results
3463 are, how big you need.

3464 And so I think the concern that you are hearing is that
3465 that study should not be the most robust possible, but
3466 instead, the FDA should allow the study to go forward if it
3467 is safe and if it is bona fide research where the potential

3468 benefits outweigh the potential risks and there is valid
3469 information to be learned from the study. That essentially
3470 is the company's call on how they want to investigate the
3471 device and develop the program.

3472 Mr. {Pitts.} The chair thanks the gentleman. My time
3473 is expired.

3474 The ranking member is recognized for 5 minutes for
3475 questions.

3476 Mr. {Pallone.} Thank you, Mr. Chairman.

3477 I wanted to start with Mr. Gaugh. I appreciated GPhA's
3478 support for the bill that Representative Guthrie and I
3479 recently introduced, the Generic Drug Application Review
3480 Fairness Act. We heard earlier from Dr. Woodcock about the
3481 long review times for generic drug applications that
3482 currently exist. If the median review time for generic drug
3483 applications currently exceeds 30 months, how does that
3484 impact the generic manufacturers and what are the
3485 consequences if you will?

3486 Mr. {Gaugh.} Well, you heard in earlier testimonies if
3487 you go back to the statute that it is 6-month review time,
3488 which we are well, well past that, 30 months, so almost 2
3489 years past the statute. So in that 2-year time point, once
3490 you have put your drug application in, market dynamics can
3491 change significantly in that additional 2 years. So it may

3492 be a situation where by the time the 30 months has expired,
3493 the market is not still effective for the company to get
3494 into. That is one issue.

3495 Mr. {Pallone.} And what about the significance of the
3496 180-day exclusivity period for generic firms?

3497 Mr. {Gaugh.} The 180-day exclusivity has become a real
3498 factor because in that approval process, it affects first-
3499 filers in paragraph 4 certifications, and if you don't have
3500 the product approved or tentatively approved by the FDA
3501 within that 30-day time point, you lose your 180-day
3502 exclusivity.

3503 Mr. {Pallone.} Do you know how many applications since
3504 maybe 2003 have unfairly lost the 180-day exclusivity because
3505 of the FDA review delay?

3506 Mr. {Gaugh.} Somewhere in the range of 8 to 10.

3507 Mr. {Pallone.} Okay. I mean it seems to me that the
3508 increasing meeting of approval time of generic drug
3509 applications is unintentionally placed into jeopardy the 180
3510 days of exclusivity rewarded to the generic applicants, and I
3511 am hopeful that my colleagues will support inclusion of the
3512 Generic Drug Application Fairness Act into the User Fee
3513 package, which is being considered, because this would at
3514 least temporarily fix the consequences that you discussed.

3515 Let me ask Mr. Wheadon, if you would, we heard from Dr.

3516 Woodcock a little bit ago that there is added language to the
3517 discussion draft that was not part of the negotiated PDUFA
3518 agreement, and in FDA's view, these extensive reporting
3519 requirements would place a burden on the Agency and could
3520 result in an unwarranted reshuffling of resources in other
3521 areas. What is PhRMA's view on this added provision?

3522 Dr. {Wheadon.} Well, there are two aspects to consider.
3523 In many meetings with the FDA we have asked for data going
3524 down to the division level so that we can see whether or not
3525 there were some learnings to be garnered in terms of
3526 divisions that actually are more efficient versus those that
3527 may not be as efficient. Having said that, we also recognize
3528 that we don't want to burden the Agency with a panoply of
3529 measurements coming out of the PDUFA agreement. As Dr.
3530 Woodcock described, that may have the unintended effect of
3531 diverting resources from the needed activities of reviewing
3532 applications and getting those applications acted upon. So
3533 it is a very nuanced position if you will that in terms of
3534 getting data down to the review division can be useful and we
3535 certainly have asked for such data, but we don't want to have
3536 so many measurements loaded onto the Agency such that they
3537 aren't able to do the basic work that they are there to do.

3538 Mr. {Pallone.} But I mean you said--and I think she
3539 said--that this wasn't part of your original agreement,

3540 correct?

3541 Dr. {Wheadon.} The review division data was not part of
3542 the original, no.

3543 Mr. {Pallone.} Okay. You are kind of answering it but,
3544 you know, I know you are trying to kind of--you are
3545 expressing your concern that we have to be careful but I
3546 guess my concern would be even if we knew that FDA could fail
3547 to accomplish other activities because of the need to shift
3548 their times and resources, you know, do you think that adding
3549 that would make sense if that were the consequence?

3550 Dr. {Wheadon.} Certainly if it was resource-neutral, if
3551 we could, for example, substitute review division data for
3552 other measurements that are currently being collected such
3553 that the resources are not diverted from needed activities
3554 along drug approval--

3555 Mr. {Pallone.} Yeah, but she said that is not likely,
3556 you know.

3557 Dr. {Wheadon.} But if they are ways that you can do it
3558 and not be overly burdensome, we would be supportive of
3559 getting review division data.

3560 Mr. {Pallone.} I mean I think that we all agree that we
3561 have to be careful. I mean if we were to tinker with the
3562 negotiated language that, you know, PhRMA signed off on, you
3563 know, we could very well hinder FDA's ability to accomplish

3564 their other performance goals. So I think you are basically
3565 expressing the view that you wish there were some way to
3566 accomplish this without jeopardizing, you know, the other.

3567 Dr. {Wheadon.} Exactly.

3568 Mr. {Pallone.} All right. Thanks. My time is
3569 completed. Thank you, Mr. Chairman.

3570 Mr. {Pitts.} The chair thanks the gentleman. I
3571 recognize the vice chairman of the subcommittee for 5 minutes
3572 for questions.

3573 Dr. {Burgess.} I thank the chairman for the
3574 recognition.

3575 Mr. Levitt, let me ask you a question just so I have my
3576 facts correct. Your previous experience was as a deputy
3577 director at the Center for Devices and Radiological Health?

3578 Mr. {Levitt.} That is correct. I was deputy director
3579 for regulations and policy

3580 Dr. {Burgess.} And currently, you are with the Medical
3581 Device Manufactures, is that correct?

3582 Mr. {Levitt.} Currently, I am a lawyer at the law firm
3583 Hogan Lovells, and I am representing AdvaMed and the other
3584 trade associations here today.

3585 Dr. {Burgess.} In either role, can you imagine a
3586 scenario where it would be a company's business plan to go to
3587 market with something that they knew was flawed and going to

3588 cause harm or damage to patients? Would that be a viable
3589 business strategy?

3590 Mr. {Levitt.} It is hard for me to imagine anybody
3591 having that business strategy.

3592 Dr. {Burgess.} But you have heard the exchanges this
3593 morning between Mr. Markey and Dr. Shuren, myself and Dr.
3594 Shuren. Do you have any thoughts on what you have heard this
3595 morning? Do you think there is a risk out there that rogue
3596 companies are going to be putting damaging products out there
3597 on the market that the FDA's hands are essentially tied and
3598 they can't do anything?

3599 Mr. {Levitt.} I think it is hard for me to believe that
3600 there is a significant issue, problem there that needs
3601 legislation. The reviewers have enormous latitude to ask
3602 questions on devices. There almost always are incremental
3603 differences between new devices and old ones, and as has been
3604 pointed out, even after a final 510(k) decision is made, the
3605 Agency has additional authorities to prevent adulterated or
3606 misbranded devices from going onto the market. It is hard
3607 for me to believe--and Dr. Shuren, I thought, said as much--
3608 that the Agency doesn't believe it has let out onto the
3609 market unsafe devices.

3610 Dr. {Burgess.} And, you know, just from where I sit
3611 here, that was pretty troubling. Even if there is only a

3612 handful, we really need to know those devices and where the
3613 system failed us if that is happening. And I am with you. I
3614 cannot believe that it actually is happening. In today's
3615 medical legal climate, I don't think a company could exist if
3616 it pursued such a strategy.

3617 Mr. {Levitt.} Right. I think we would have to see the
3618 examples, but I can't imagine any company going in with a
3619 business plan to say I am going to sell a flawed device.

3620 Dr. {Burgess.} Additionally--and of course your
3621 testimony and, Mr. Coukell, I think your testimony as well--
3622 the indication was that specifically the Center for Devices
3623 and Radiological Health required an additional 200 employees.
3624 Did I pick up that information correctly?

3625 Mr. {Coukell.} Yes, sir, that is a consequence of the
3626 User Fee Agreement that has been negotiated between the
3627 industry and FDA.

3628 Dr. {Burgess.} And will these 200 new employees, will
3629 they be housed at White Oak or will they be reviewers out
3630 somewhere else in the country or will they be put on the job
3631 inspecting manufacturing plants? Where do they go? I mean I
3632 visited Dr. Shuren. It is very lovely and spacious offices
3633 out there at White Oak, but I didn't see space for 200 more
3634 people.

3635 Mr. {Coukell.} Well, there is a lot of construction out

3636 there, sir, but I don't know the answer to that.

3637 Dr. {Burgess.} Okay. So we are expanding government in
3638 the process of doing this. And I am not disputing that they
3639 are not necessary, but at the same time, maybe, Mr. Chairman,
3640 we can, as a written question, follow up to Dr. Shuren. We
3641 can get a breakdown on the activities and duties of those 200
3642 new personnel that are going to be hired under the monies
3643 provided by the User Fee Agreement.

3644 Ms. Radcliffe, let me ask you a question. I have worked
3645 on the issue of conflicts. 2007, when the reauthorization
3646 was done that year, I thought the language on conflicts went
3647 a little bit too far and was too restrictive. Do you think
3648 that the concerns I had that day in June were justified about
3649 the conflicts language being a little too restrictive?

3650 Ms. {Radcliffe.} We do and we thank you very much for
3651 your work on that issue. The conflicts of interest are
3652 extremely important and we respect the need to ensure that
3653 conflicts of interest don't affect the way--

3654 Dr. {Burgess.} Correct.

3655 Ms. {Radcliffe.} --that FDA does its very important
3656 work. That being said, we have heard from many stakeholders
3657 that the provisions that were put in place have limited FDA's
3658 ability to put the right expertise on its advisory
3659 committees, and that is also I think of great concern to

3660 patients and certainly to industry. And so we appreciate the
3661 effort to return FDA to being governed by the same conflict-
3662 of-interest provisions that the rest of the U.S. Government
3663 is governed by.

3664 Dr. {Burgess.} And certainly, I want to thank you for
3665 working with committee staff to try to get that issue
3666 resolved.

3667 Mr. Gaugh, let me just ask you a question. I mean drug
3668 shortages come up every time we have a hearing such as this.
3669 Do you have an opinion as to is there enough in the User Fee
3670 Agreements, the draft that you have, is there enough in there
3671 to deal with the issue of drug shortages from the generic
3672 manufacturers' standpoint?

3673 Mr. {Gaugh.} We believe that the draft, including to
3674 the draft would be the private stakeholder group, the ARI,
3675 Accelerated Recovery Initiative. Between those two, there
3676 would be enough, yes.

3677 Dr. {Burgess.} Let me ask you this. Sometimes it
3678 occurs to me that maybe we have tightened things down too
3679 much, that the hyper-competition that has been introduced
3680 into the marketplace has made it unprofitable for a
3681 manufacturer to continue manufacture of something. And then
3682 if a problem occurs with their manufacturing floor, they just
3683 say forget it. I am out of the business. Is that in fact

3684 happening?

3685 Mr. {Gaugh.} I think part of the answer to that is, as
3686 Dr. Woodcock said today, the majority of the drug shortages
3687 in our environment as we see today is the sterile
3688 injectables, and sterile injectables are a highly
3689 sophisticated process and there is really only a handful in
3690 the United States that make the sterile injectables. So when
3691 an issue happens with the line, as you have said, that puts a
3692 severe crunch on the entire pipeline.

3693 Dr. {Burgess.} Okay. Thank you, Mr. Chairman. I will
3694 yield back.

3695 Mr. {Pitts.} The chair thanks the gentleman and
3696 recognizes the ranking member emeritus, Mr. Dingell, for 5
3697 minutes for questions.

3698 Mr. {Dingell.} Thank you, Mr. Chairman.

3699 And again, I want to thank you for this hearing but I
3700 also want to thank my colleague, Mr. Murphy, for working with
3701 me on the important system and issue of priority in
3702 inspections. These questions will go first to Mr. Gaugh.

3703 Mr. Gaugh, yes or no, under the User Fee Agreement
3704 negotiated by the generic drug industry, your industry is
3705 committed to paying additional fees to ensure that both
3706 foreign and domestic manufacturers are held to the same
3707 inspection standards? Is that correct? Yes or no?

3708 Mr. {Gaugh.} Yes.

3709 Mr. {Dingell.} And I believe that it is in good part
3710 because you are concerned that our domestic industry is
3711 inspected rather more and is policed rather more carefully
3712 than the foreigners, is that right?

3713 Mr. {Gaugh.} Yes.

3714 Mr. {Dingell.} Now, again, Mr. Gaugh, yes or no, these
3715 additional fees will ensure foreign and domestic
3716 manufacturers are held to the same inspection frequency and
3717 standards? Is that correct?

3718 Mr. {Gaugh.} Yes.

3719 Mr. {Dingell.} Now, again, if you please, the same
3720 inspection frequency as agreed to by FDA and the generic drug
3721 industry under the User Fee Agreement is routine inspection
3722 every 2 years, is that correct?

3723 Mr. {Gaugh.} That is correct, yes.

3724 Mr. {Dingell.} Now, again, do you agree routine
3725 inspections with parity between foreign and domestic
3726 manufacturers will help level the playing field for your
3727 industry? Yes or no?

3728 Mr. {Gaugh.} Yes.

3729 Mr. {Dingell.} Is it fair to say that those in your
3730 industry are comfortable with being inspected every 2 years?

3731 Mr. {Gaugh.} Yes.

3732 Mr. {Dingell.} Now, thank you for your kindness.

3733 Mr. Coukell, these questions for you, yes or no again to
3734 the degree you can. FDA is currently required by the Federal
3735 Food and Drug and Cosmetic Act to conduct a GMP inspection of
3736 domestic drug manufacturers every 2 years. Is that correct?

3737 Mr. {Coukell.} Yes, sir.

3738 Mr. {Dingell.} Many have proposed removing the
3739 requirement for biannual inspections and instead moving to a
3740 fully risk-based inspection system with no minimum inspection
3741 frequency. FDA currently uses a fully risk-based approach
3742 for inspections of foreign drug manufacturing facilities with
3743 no minimum inspection frequency. Is that correct?

3744 Mr. {Coukell.} Yes.

3745 Mr. {Dingell.} Under this approach, how is FDA
3746 currently inspecting foreign drug manufacturing facilities?

3747 Mr. {Coukell.} We look at all facilities outside the
3748 U.S. it is about every 9 years. If we look at China, for
3749 example, it is about every 17. Those are averages that come
3750 from the GAO.

3751 Mr. {Dingell.} Now, would a fully risk-based inspection
3752 schedule guarantee that no drug manufacturing facility went
3753 indefinitely without an inspection?

3754 Mr. {Coukell.} No.

3755 Mr. {Dingell.} But it could, could it not?

3756 Mr. {Coukell.} Would a fully risk-based system--

3757 Mr. {Dingell.} Yes.

3758 Mr. {Coukell.} --guarantee that--

3759 Mr. {Dingell.} Yeah, if it just says that we are going
3760 to do this on the basis of risk, they could say, well, we
3761 don't find any basis for inspecting this particular facility.

3762 Mr. {Coukell.} Yes, I agree with you.

3763 Mr. {Dingell.} Okay. Now, would a minimum inspection
3764 frequency provide regulatory certainty to our drug
3765 manufacturers, promote parity between our domestic and
3766 foreign drug manufacturers, and better protect the public's
3767 health and safety?

3768 Mr. {Coukell.} Yes, it would.

3769 Mr. {Dingell.} Mr. Chairman, I am giving you back a
3770 minute and 14 seconds.

3771 Mr. {Pitts.} The chair thanks the gentleman.

3772 Mr. {Dingell.} Thank you.

3773 Mr. {Pitts.} Recognizes the gentleman from Louisiana,
3774 Dr. Cassidy, for 5 minutes for questions.

3775 Dr. {Cassidy.} I see in your testimony you are
3776 concerned regarding the tracking of drugs in order to detect
3777 counterfeiting. One of my concerns though, and which Dr.
3778 Woodcock agreed, if somebody is buying from an illegitimate
3779 online pharmacy, they are buying straight from an overseas

3780 provider, then really the absence of an RID or something
3781 similar, a unique identifier, would not provide any benefit.
3782 The person is going to open up their package and they are
3783 going to open it and they are not going to look to see, oh,
3784 my gosh, is there something tracking it? Would you agree
3785 with that?

3786 Mr. {Coukell.} I think it is important to note that
3787 there are both legitimate and illegitimate online pharmacies
3788 and many of our big retail chains operate online pharmacies.
3789 So if a person is obtaining drugs from the legitimate supply,
3790 whether they are going to a brick-and-mortar pharmacy or
3791 online--

3792 Dr. {Cassidy.} Well, I agree with that totally--

3793 Mr. {Coukell.} --then it is difficult.

3794 Dr. {Cassidy.} --and I don't mean to interrupt; it is
3795 limited time.

3796 Mr. {Coukell.} But--

3797 Dr. {Cassidy.} In fact, that is my point. Right now,
3798 the consumer has limited ability to tell the difference
3799 between a legitimate and an illegitimate. And even though
3800 one of the things we can use to track counterfeits would be
3801 this unique ID system. Nonetheless, it still would not
3802 identify counterfeit drugs arriving in your mailbox from an
3803 illegitimate pharmacy.

3804 Mr. {Coukell.} That is correct.

3805 Dr. {Cassidy.} Yeah. So now, that said, Ms. Radcliffe
3806 and Dr. Wheadon, I am very interested in these rare pediatric
3807 diseases. Your heart tugs, they affect so few, it is hard to
3808 get an adequate in for a clinical trial, and there is never
3809 going to be a major investment by a pharmaceutical company if
3810 it is based upon return, okay. I read your testimony
3811 regarding the bills we have to promote pediatrics. What
3812 ideas do you have in order to encourage research into cures
3813 for these terribly tragic but rare diseases? You see where I
3814 am going with that.

3815 Ms. {Radcliffe.} This is an issue of extreme interest
3816 to many of our companies for the reason that you say. It
3817 tugs on the heartstrings when there are these very rare
3818 pediatric conditions and there are no cures for them. We
3819 have worked on this issue in a number of different ways.
3820 Specific to the issue at hand in this hearing today within
3821 the PDUFA agreement there is a provision for helping
3822 companies to move forward with drug development on rare
3823 conditions where FDA will have additional resources to hire
3824 expertise and to reach out to the community and gain input on
3825 how that may be done.

3826 Additionally, we support--as I said in my both written
3827 and oral testimony--the Faster Access to Specialized

3828 Treatments Act, which seeks to expand accelerated approval in
3829 a way that would allow the use of that pathway for more
3830 conditions by encouraging FDA to take advantage of modern
3831 tools, whether it is biomarkers, pharmacogenomics, predictive
3832 toxicology and so forth, and to expand these so that pathway
3833 to--

3834 Dr. {Cassidy.} Let me ask you because that seems as if
3835 those products would be a byproduct of research focused
3836 elsewhere. Does that make sense?

3837 Ms. {Radcliffe.} In some cases, yes, but that may be a
3838 very effective way of ensuring that those products do get
3839 developed.

3840 Dr. {Cassidy.} Is there a way to encourage the
3841 pharmaceutical companies in a market-based approach to focus
3842 resources on a particular illness? You are more likely to
3843 get to your destination if you go there directly
3844 theoretically than if you just kind of as a, you know,
3845 circuitous route end up there.

3846 Ms. {Radcliffe.} Right. That gets to a much broader
3847 discussion, I think, about the incentives that are available
3848 for research and development, whether it is R&D tax credits,
3849 whether it is the way the products are reimbursed and so
3850 forth, a very complicated decision that I think goes far
3851 beyond what FDA could accomplish. FDA, however, has a huge

3852 role in ensuring that companies have the information that
3853 they need to create drug development programs in rare disease
3854 which encounter challenges that are, honestly, not just
3855 related to the return that companies get--

3856 Dr. {Cassidy.} A friend of my who has such a child--so
3857 there is kind of a personal interest in mine--

3858 Ms. {Radcliffe.} Yeah.

3859 Dr. {Cassidy.} --he tells me that there is a bill being
3860 considered or proposed and if the company came up with such a
3861 drug for such a rare condition, they would get a
3862 transferrable sort of expedited review of any other drug.
3863 Now, would that be an effective way to do this or would that
3864 be--and I will open that up to the panel if anybody has a
3865 thought on this.

3866 Ms. {Radcliffe.} Sure. We are aware of that
3867 legislation and we haven't taken a position on it. That
3868 mechanism has been tried in other settings and we certainly
3869 think that where such a mechanism could be put in place, it
3870 is useful to do so, but it hasn't proven so far to really be
3871 a major incentive for this type of work.

3872 Dr. {Cassidy.} Thank you. I yield back. Thank you.

3873 Mr. {Pitts.} The chair thanks the gentleman and
3874 recognizes the ranking member of the full committee, Mr.
3875 Waxman, for 5 minutes for questions.

3876 Mr. {Waxman.} Thank you very much, Mr. Chairman.

3877 Mr. Coukell, I am going to ask you about antibiotics. I
3878 know that Pew has had a longstanding interest in making sure
3879 that we get more antibiotics, new antibiotics, so our arsenal
3880 is full, but I don't think we just want any antibiotics. We
3881 don't need two versions of the same antibiotics we already
3882 have. That would I am sure only serve to worsen the problem
3883 of antibiotic resistance. So I want to search your views on
3884 whether the language in the discussion draft for this hearing
3885 will achieve this goal.

3886 The bill, as it is currently written, would grant
3887 exclusivity for any antibiotic to treat essentially any
3888 resistant bacterial pathogen. Is that approach adequate to
3889 ensure that we get only the antibiotics that we truly need?
3890 And if not, is there another approach that you would suggest
3891 we take so that we can better target those drugs?

3892 Mr. {Coukell.} Thank you for that question, sir. I
3893 think the goal in the discussion draft is to make it more
3894 attractive for companies to be in the business of
3895 antibiotics. So that means they need predictability. We
3896 need to address the serious public health problem and we need
3897 to make sure that we are using taxpayer resources wisely.
3898 While we are on predictability, right now, the discussion
3899 draft has a list of bugs in it, and the question is if you

3900 get qualified early on as you do under the Orphan Drug Act as
3901 a qualified product, how does that carry through to you doing
3902 your clinical studies and coming to market? Bleach will kill
3903 resistant bugs; nobody would suggest it is a good drug. And
3904 so the question is, is there an established way to look at
3905 antibiotics and say here are the ones we need and here is how
3906 it would work through to market? And we think that looking
3907 at serious and life-threatening infections would be a very
3908 workable way to do it. It would address the public health
3909 need and provide great predictability.

3910 Mr. {Waxman.} So target it in that way and not have it
3911 more general--

3912 Mr. {Coukell.} In some ways that is broader in the
3913 sense that you don't have to have activity against the
3914 resistant organism but you are tackling the public health
3915 aide, which is a treatment for a serious or life-threatening
3916 infection.

3917 Mr. {Waxman.} Okay. Now, the LPAD offers an approach
3918 that I think should be given serious consideration because it
3919 has a potential to get important new antibiotics into market
3920 more quickly than usually possible. However, when we are
3921 getting products to market more quickly based on more limited
3922 clinical data they usually require, it becomes that much more
3923 important that we are confident that they will be used only

3924 in the small populations for which the drug was approved.

3925 With antibiotics, this concern is doubled. We must
3926 worry not only about patients receiving medications that
3927 could be dangerous to them because their safety has not been
3928 established in broader populations, we also need to act in a
3929 way that will preserve the efficacy of new antibiotics by
3930 using them only when truly necessary. Do you believe that
3931 the mechanism for limiting off-label use of antibiotics
3932 approved under LPAD will be effective in achieving both of
3933 these goals, and if not, do you have suggestions for
3934 additional mechanisms?

3935 Mr. {Coukell.} We think it is an interesting proposal.
3936 And let me make a couple of points about what we are thinking
3937 as we consider it. And we are still trying to understand how
3938 it would work. But first, it is attractive if you could have
3939 a faster pathway and then use the drugs only in patients that
3940 you couldn't treat with existing drugs. That would be good
3941 for public health and it would be good for the companies
3942 assuming there is a viable business model there. So one
3943 question is what does it take to get these drugs to market
3944 and get that particular designation?

3945 And then the limited population part of the Limited
3946 Population Provision is how do we ensure that if they are
3947 coming with a higher risk or lower evidence that they are

3948 used the way we intend--and there is nothing in the statutory
3949 language that ensure that--so the question is how would
3950 individual providers, how would payers, how would hospital
3951 formulary committees use these drugs and ensure that they
3952 were used only on label. And that is something that we are
3953 still trying to understand.

3954 And then the other thing I think you would want to know
3955 is if you are approving drugs based on less evidence, do we
3956 have a mechanism of post-market surveillance so we can
3957 continue to learn as they are in clinical use?

3958 Mr. {Waxman.} Well, what is your reaction to what is in
3959 the draft?

3960 Mr. {Coukell.} We are still studying. We think it is
3961 interesting, but as I say, we are trying to understand--

3962 Mr. {Waxman.} You are still thinking but it needs to be
3963 refined in some way. You are trying to think it through?

3964 Mr. {Coukell.} Trying to think it through.

3965 Mr. {Waxman.} Is that it? Okay. Well, we are, too,
3966 and so we would appreciate your suggestions.

3967 Mr. Chairman, I am going to yield back my time. Thank
3968 you.

3969 Mr. {Pitts.} The chair thanks the gentleman and
3970 recognizes the gentleman from Illinois, Mr. Shimkus, for 5
3971 minutes for questions.

3972 Mr. {Shimkus.} Thank you, Mr. Chairman.

3973 And it may have been noted before but I see Dr. Shuren
3974 is still in the committee room. Thank you for being here.
3975 This is important. Even my follow-up is going to be on the,
3976 again, working on the IDEs and the 510(k) a little bit more.
3977 Most of my questions will be directed to Mr. Levitt, but I do
3978 appreciate you being here. I did like Dr. Woodcock's
3979 statement Congress needs to define a problem that we want to
3980 address, and we really do think there is a problem with the
3981 change in the process in these two areas.

3982 So with that, Mr. Levitt, you said in the explanation to
3983 the chairman's question about--kind of explain the
3984 Investigative Device Exemption, safety and protocol were the
3985 two primary issues. And then the FDA's change in the
3986 processing, that it has to be good enough for final approval.
3987 Are there benefits to going through the Investigational
3988 Device Exemption process even though you might not eventually
3989 get to a final approval in the process? Are there positives
3990 going through this process?

3991 Mr. {Levitt.} Well, I think there are positives any
3992 time you are learning new information in a structured setting
3993 under informed consent of course about the performance of new
3994 devices or improved devices both for safety and for
3995 effectiveness. Very often, a company may want to try

3996 something and if it is not working have a small trial and
3997 learn that quickly and pursue another direction. Or they may
3998 want to proceed in a more robust way because they have
3999 greater confidence. So I think there is value in any
4000 clinical study that is safe and that has a bona fide research
4001 protocol to greater learning.

4002 Mr. {Shimkus.} So the FDA's change in focus--I do think
4003 there are benefits from going through--if you meet the two
4004 criteria of safety and bona fide protocol--and that the
4005 information you learn may help you or may help the sector
4006 move in a more robust path forward or to change course and
4007 start anew. That is summarizing what you said?

4008 Mr. {Levitt.} Yes.

4009 Mr. {Shimkus.} I am not going to go over the issue of
4010 what is the legal law and what is the--what was the other
4011 thing I had here on the Administrative Procedures Act? And
4012 there are some, I think, legal concerns with the change
4013 without it being bona fide. You might have some experience
4014 in your legal background and your other history with that,
4015 but I think I addressed that enough.

4016 On the 510(k) process, can you walk us through what
4017 currently happens when a company makes a modification to
4018 existing 510(k)?

4019 Mr. {Levitt.} Yes. When companies often make changes

4020 to their devices, FDA has a flowchart to help companies walk
4021 through is this a significant change affecting safety and
4022 effectiveness? If it is, then the company submits a new
4023 510(k). If it isn't, the company documents what their
4024 decision and a basis is. They make the change and they move
4025 on. That information is available to FDA during an FDA
4026 inspection so there is still transparency.

4027 Mr. {Shimkus.} So have you heard--obviously, from the
4028 sector now that you are representing--the concern that with
4029 the changed rules, there may be a projected backlog of 300 to
4030 500 percent and that this is harmful to the process, not
4031 helpful?

4032 Mr. {Levitt.} Yes, I have certainly heard that. I mean
4033 what Dr. Shuren testified this morning, if I heard him
4034 correctly, was that FDA really was just trying to affect a
4035 little gray zone, a small number around the margin. But as
4036 companies went back and applied the examples, companies
4037 saying oh, no. You, FDA, really missed the mark. This would
4038 result in just a flood of new 510(k)s where there really is
4039 not a significant change. But the examples that FDA gave led
4040 them to believe they would have to submit this. So there is
4041 clearly a gap between what FDA intended and how the industry
4042 is perceiving it. And I think Dr. Shuren testified he
4043 recognized that and he needs to address that.

4044 Mr. {Shimkus.} I appreciate you all being here today
4045 and, Dr. Shuren, that is why I appreciate you remaining in
4046 the committee room because, you know, the other issue is
4047 resources, which we can agree to disagree. But I do think we
4048 want to improve the system. This is our one opportunity to
4049 do that.

4050 And my time is expired, Mr. Chairman. Thank you.

4051 Mr. {Pitts.} The chair thanks the gentleman.

4052 That concludes the questioning. I would like to thank
4053 the panel. This has been an extremely valuable hearing, very
4054 important information.

4055 I have a unanimous consent request to enter into the
4056 record statements from the National Alliance on Mental
4057 Illness and the California Healthcare Institute. That has
4058 been shared without objection, so ordered.

4059 [The information follows:]

4060 ***** COMMITTEE INSERT *****

|
4061 Mr. {Pitts.} I remind Members that they have 10
4062 business days to submit questions for the record, and I ask
4063 all witnesses to respond to questions promptly. Members
4064 should submit their questions by the close of business on
4065 Wednesday, May the 2nd.

4066 Without objection, the Subcommittee is adjourned.

4067 [Whereupon, at 2:44 p.m., the Subcommittee was
4068 adjourned.]