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4 ``REAUTHORIZATION OF PDUFA: WHAT IT MEANS FOR JOBS,

5 INNOVATION, AND PATIENTS''

6 WEDNESDAY, FEBRUARY 1, 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 10:02 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, Gingrey, Latta, Lance,
16 Cassidy, Guthrie, Griffith, Bilbray, Pallone, Dingell, Towns,
17 Capps, Schakowsky, Gonzalez, Ross, Matheson, Markey,
18 Christensen, Eshoo and Waxman (ex officio).

19 Staff present: Clay Alspach, Counsel, Health; Michael
20 Beckerman, Deputy Staff Director; Mike Bloomquist, General
21 Counsel; Anita Bradley, Senior Policy Advisor to Chairman
22 Emeritus; Andy Duberstein, Deputy Press Secretary; Paul
23 Edattel, Professional Staff Member, Health; Debbie Keller,
24 Press Secretary; Ryan Long, Chief Counsel, Health; Carly
25 McWilliams, Legislative Clerk; John O'Shea, Professional
26 Staff Member, Health; Heidi Stirrup, Health Policy
27 Coordinator; Alli Corr, Democratic Policy Analyst; Eric
28 Flamm, FDA Detailee; Karen Lightfoot, Democratic
29 Communications Director, and Senior Policy Advisor; Karen
30 Nelson, Democratic Deputy Committee Staff Director for
31 Health; and Rachel Sher, Democratic Senior Counsel.

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

35 Today, we will discuss reauthorizations of the
36 Prescription Drug User Fee Act, PDUFA, the Best
37 Pharmaceuticals for Children Act, BPCA, and the Pediatric
38 Research Equity Act, PREA, all of which expire September 30
39 of this year. We will also discuss pharmaceutical supply
40 chain issues.

41 PDUFA was first authorized by Congress in 1992 with the
42 goal of expediting human drug applications through the FDA
43 approval process. Under the act and its subsequent
44 reauthorizations, the drug industry pays user fees to FDA,
45 and FDA commits to meet certain performance goals. I am
46 pleased that the industry and FDA have reached an agreement
47 for PDUFA V, and I look forward to hearing more of the
48 details from our witnesses. Under the agreement, industry
49 would pay over \$700 million in fiscal year 2013, and higher
50 amounts in the remaining 4 years.

51 The PDUFA V agreement is designed to speed new drugs to
52 patients awaiting treatments and cures, while ensuring the
53 highest safety standards. It is also designed to make the
54 approval process more timely, predictable, and certain for

55 drug sponsors and the venture capitalists who fund new drug
56 research.

57 Among the highlights, the agreement increases the
58 communication between FDA and drug sponsors, specifically
59 building contacts and meetings into the regulatory review
60 process. To increase the efficiency and predictability of
61 the review process, a new 60-day validation period will be
62 used for FDA and drug sponsors to communicate, interact and
63 plan before the clock officially starts.

64 We are also here to discuss the Best Pharmaceuticals for
65 Children Act and the Pediatric Research Equity Act. BPCA
66 gives FDA the authority to extend a 6-month period of market
67 exclusivity to a manufacturer in return for specific studies
68 on pediatric use. Under PREA, a manufacturer of a new drug
69 or biologic is required to submit studies of a drug's safety
70 and effectiveness when used by children.

71 Most prescription drugs have never been the subject of
72 studies specifically designed to test their effects on
73 children. Yet, when no pediatric-approved drugs exist for an
74 illness, doctors often prescribe these medications to
75 children, relying on the safety and effectiveness
76 demonstrated with adults, in the absence of clinical data on
77 how the drug may work in a child. As a father and
78 grandfather, I view reauthorizing BPCA and PREA as a step

79 toward obtaining that data and ensuring that our children and
80 grandchildren receive the correct medications and correct
81 dosages when they are ill.

82 We should not forget that Americans are the most
83 innovative people on earth, and the United States leads the
84 world in new drug development. Some 4 million jobs in the
85 United States are directly or indirectly supported by the
86 drug industry.

87 If the goals of the PDUFA V agreement are realized, we
88 will continue to be the world leader in new, safe and
89 effective life-saving and life-enhancing drugs; American
90 patients will have timely access to treatments and cures for
91 everyday maladies, chronic illnesses, and terminal diseases;
92 and we will keep good, well-paying jobs here in the United
93 States.

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

95 ***** COMMITTEE INSERT *****

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96 Mr. {Pitts.} I would like to thank all of our witnesses
97 for coming today and now yield to the vice chairman, Dr.
98 Burgess.

99 Dr. {Burgess.} Thank you, Mr. Chairman and Madam
100 Chairwoman. Thank you very much for being here. Thank you
101 for the hospitality you have shown to me and my staff on the
102 two times we ventured out to the FDA during your tenure. I
103 certainly appreciate the time you spent with us.

104 We are here to talk about the User Fee Act
105 reauthorizations, but we are also here to ask some questions
106 about how the FDA as a whole is successfully accomplishing
107 its mission. If we don't understand where we are, it is hard
108 to know where we are trying to go, and this committee has
109 already laid an aggressive schedule and foundation for the
110 user fee reauthorizations. Certainly, today's hearing is
111 going to be a big part of that because it is an issue of
112 patient safety, and we are all for patient safety. That is
113 not a partisan issue. We are also all for creation of
114 American jobs. That is not a partisan issue, or should not
115 be a partisan issue either.

116 And the big question I have is the lack of
117 predictability driving American drug manufacturers out of the
118 country. We are trying to encourage job growth and

119 innovation in this country. Does the FDA's slow approval
120 process send venture capitalists elsewhere where they can
121 find more stability? Is there a way to continue to
122 streamline the approval process of single-molecule drugs
123 where you have the most regulatory experience?

124 The FDA must have the infrastructure and programs in
125 place in order that innovations are dealt with in a fashion
126 that assures safety for the patient and a straightforward and
127 streamlined approved process.

128 Mr. Chairman, I thank you for the recognition. I will
129 yield back the balance of my time.

130 [The prepared statement of Dr. Burgess follows:]

131 ***** COMMITTEE INSERT *****

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132 Mr. {Pitts.} The chair thanks the gentleman and
133 recognizes the ranking member of the full committee, Mr.
134 Waxman, for 5 minutes.

135 Mr. {Waxman.} Thank you, Mr. Chairman, and thank you,
136 Mr. Pallone, for allowing me to give my statement at this
137 point.

138 Today, we begin, once again, the process of
139 reauthorizing the UFAs and our pediatric drug testing laws.
140 I have been a part of this process since the inception of
141 each of these programs, starting first with the Prescription
142 Drug User Fee Act in 1992. In every reauthorization, we have
143 worked together on a bipartisan basis. Of course, that is
144 how it should be, given the role these laws play in helping
145 FDA fulfill its vital public health mission.

146 The drug and device user fee programs ensure that FDA
147 gets critical dollars to allow the agency to complete its
148 premarket review in a timely manner so that patients have
149 access to therapies at the earliest possible time. The Best
150 Pharmaceuticals for Children Act and the Pediatric Research
151 Equity Act give FDA the authority to obtain information about
152 the use of drugs in children. And this year, for the first
153 time, we will be establishing two new programs to help speed
154 FDA's review of low-cost generics and biosimilars.

155 As we begin this process, these are the primary goals we
156 need to keep in mind. We must reauthorize and establish
157 these essential programs in a timely way so that FDA can do
158 its job protecting the health and safety of American
159 patients. It would be irresponsible to allow this
160 legislation to become a vehicle for the wish lists of members
161 seeking to move their own controversial bills. I hope we
162 should continue the long tradition of UFA bipartisanship and
163 work together to ensure this does not happen.

164 I am concerned, however, about some of the bills our
165 counterparts across the aisle have suggested will be under
166 consideration. Some of these bills would prevent FDA from
167 insisting on adequate data from clinical trials and forcing
168 it to approve drugs and devices on an incomplete record.
169 These proposals would prove disastrous for the safety and
170 efficacy of our drugs and devices. Another would enrich the
171 pharmaceutical industry by gutting the time-tested system of
172 incentives provided under Hatch-Waxman. The cost of this
173 windfall would fall on the backs of American patients who
174 under that proposal would be forced to pay monopoly drug
175 prices for 15 years.

176 Another controversial proposal the majority intends to
177 consider would fundamentally reform FDA's mission by adding
178 things like ``economic growth, innovation, competitiveness,

179 and job creation'' to the agency's priorities. The title of
180 this hearing suggested our colleagues across the aisle also
181 believe that creating jobs should be one of FDA's many
182 responsibilities. I hope we would all agree that FDA should
183 not take jobs into consideration when it is reviewing the
184 safety and effectiveness of a new medicine. We want FDA to
185 ensure that our drugs and devices are safe and effective.
186 Whether jobs will be created is simply not a part of that
187 scientific public health equation. As a matter of fact, some
188 of the new drugs, if they are higher priced and don't do any
189 more than the older drugs, may be a financial burden and one
190 could then evaluate that at FDA, which is also not FDA's
191 appropriate role.

192 It appears that many of these proposals are driven by
193 rhetoric insisting that FDA has become too demanding of
194 companies seeking to market their drugs and devices. As a
195 result, innovation and jobs are being driven abroad. When we
196 examine claims as serious as these, we must insist on data
197 and on facts. Biased anecdotes from individual constituent
198 companies do not qualify as fact. I am aware of no reliable
199 data showing that these claims are true. To the contrary, I
200 am aware of some studies showing, for example, that FDA
201 actually approves drugs faster than our counterparts in
202 Europe. I am also aware of a study showing that FDA is quite

203 flexible in its requirements in reviewing orphan drug
204 applications. NORD is here today and will testify on this
205 study.

206 We should all be united in the goal of ensuring that we
207 have a strong, well-resourced FDA that is armed with a full
208 complement of authorities to protect us from unsafe drugs and
209 to assure that those drugs work. That is FDA's fundamental
210 mission, and it is in no one's interest to have a weak FDA.
211 American consumers depend on FDA. If Americans lose
212 confidence in the FDA, they will lose confidence in the
213 pharmaceutical and medical device industries as well.

214 One final point. I appreciate that we are looking at
215 the increasing globalization of our drug supply a feature of
216 our hearing. It is critically important issue. FDA has
217 indicated that it needs an updated set of tools to deal with
218 this dramatically different marketplace, and I look forward
219 to hearing more on this issue from our witnesses today.

220 Mr. Dingell, Mr. Pallone, Ms. DeGette and I have
221 proposed legislation, the Drug Safety Enhancement Act, that
222 will go a long way toward providing FDA with these much-
223 needed resources and authorities.

224 Thank you, Mr. Chairman. I yield back the balance of my
225 time.

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

227 ***** COMMITTEE INSERT *****

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228 Mr. {Pitts.} The chair thanks the gentleman and now
229 recognizes the gentleman from New Jersey, Mr. Lance, for 5
230 minutes.

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

232 Congress first authorized PDUFA in response to lagging
233 approval times for prescription drugs at the FDA. Under the
234 agreement, the FDA collects funds from drug sponsors to help
235 expedite the human drug approval process. Not only has PDUFA
236 improved the approval times of drugs, but the past
237 authorizations have led to improved safety policies, better
238 communication and improved regulatory processes at the FDA.

239 The current reauthorization, PDUFA V, includes
240 provisions to provide the FDA with tools to make safe and
241 effective new medicines available to patients in a more
242 efficient, consistent and timely manner while maintaining the
243 high review standards for safety and efficacy. Additionally,
244 the agreement contains new provisions to address problems
245 that have arisen since PDUFA IV. This includes the
246 implementation of a new benefit risk framework, patient-
247 focused drug development, standardization of the risk
248 evaluation and mitigation strategies, and a new
249 implementation plan for the rare-disease program, something
250 that is close to my heart.

251 I look forward to hearing from the panels on their views
252 on the agreement and working with my colleagues on both sides
253 of the aisle on the committee to reauthorize this vitally
254 important legislation.

255 Thank you, Mr. Chairman, and I yield the balance of my
256 time to Dr. Murphy.

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

258 ***** COMMITTEE INSERT *****

|
259 Mr. {Murphy.} I thank the gentleman for yielding.

260 As this committee begins the processing of reauthorizing
261 the Prescription Drug User Fee Act, it is important to look
262 back at where we were when this was first enacted.

263 Prior to the first PDUFA agreement in 1992, it took
264 almost 2 years for the FDA to review new drug applications
265 and roughly 70 percent of all new drugs were entering the
266 market overseas before they became available to U.S.
267 patients. By 2007, review time for new drugs had been
268 reduced to just over one year. The backlog of applications
269 that had been built up prior to PDUFA had been cleared, and
270 today, 50 percent of new drugs are now marketed in the United
271 States first, making us the world leader in bringing new
272 treatments to market.

273 The certainty and transparency provided to drug
274 manufacturers as a result of PDUFA have been key drivers of
275 economic development in the biopharmaceutical sector. In
276 2009, the industry was directly supporting almost 650,000
277 jobs and as many as 4 million jobs indirectly while boasting
278 a total economic impact of \$918 billion annually.

279 Now industry and the FDA have come together and
280 negotiated an agreement that seeks to expand transparency and
281 consistency in the drug approval process while continuing to

282 ensure patient safety. As this committee reviews this
283 agreement, we must have three priority goals: one, ensuring
284 the safety of patients; two, facilitating access to new
285 treatments for patients as soon and as safely as possible;
286 and three, establishing a review process that continues to
287 allow U.S. pharmaceutical jobs to flourish. Let us gather
288 the facts on these three essential goals and work together
289 towards a bill that saves lives and saves jobs.

290 With that, Mr. Chairman, I will yield to Dr. Gingrey of
291 Georgia.

292 [The prepared statement of Mr. Murphy follows:]

293 ***** COMMITTEE INSERT *****

|
294 Dr. {Gingrey.} Mr. Chairman, I thank the gentleman from
295 Pennsylvania for yielding to me.

296 The reauthorization of the FDA user fee program presents
297 Congress with the opportunity to improve upon the current
298 U.S. drug and device approval pathway. These hearings also
299 present us with an opportunity to work together for patients
300 and businesses back home in our districts who tell us that
301 reform is long overdue. I look forward to working with my
302 colleagues on both sides of the aisle to accomplish this
303 worthy goal.

304 To Dr. Hamburg, a special welcome. It is good to see
305 you before this subcommittee again, Dr. Hamburg. You and I
306 have spent time talking over the past year and a half about
307 the potential that regulatory science holds as well as the
308 need to spur antibiotic drug development, and I want to
309 commend you for your leadership in these fields and
310 personally thank you for your support of our efforts on
311 Generating Antibiotic Incentives Now, the GAIN Act, H.R.
312 2182. My GAIN Act original cosponsors, Gene Green, Ed
313 Whitfield, Diana DeGette, John Shimkus, Anna Eshoo, Mike
314 Rogers, and the latest edition, and not the least, Ed Markey,
315 thank you for your efforts and that of your staff on the GAIN
316 Act. This is truly a bipartisan piece of legislation. We

317 created it together. We have advocated for it together, and
318 it is because of our combined efforts that it has a real
319 chance of becoming law.

320 Finally, thank you to the long list of GAIN Act
321 supporters, and specifically, the Pew Charitable Trust, which
322 I see will be testifying on the second panel.

323 With that, Mr. Chairman, I thank you for the time and I
324 yield back.

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

326 ***** COMMITTEE INSERT *****

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327 Mr. {Pitts.} The chair thanks the gentleman and yields
328 to the ranking member of the subcommittee, Mr. Pallone, for 5
329 minutes.

330 Mr. {Pallone.} Thank you, Chairman Pitts, and I welcome
331 today's hearing and I am very much looking forward to working
332 together on the critical business of this subcommittee.

333 This is the beginning of a multi-month process in this
334 subcommittee that will involve many hearings, lengthy
335 deliberations, negotiations amongst members and staff, and
336 final legislation on critical FDA policy.

337 The User Fee Acts, which has become known as the UFAs,
338 will include reauthorizations of some successful and some not
339 as successful FDA programs. This will be our subcommittee's
340 opportunity of working alongside the FDA, industry and other
341 stakeholders to build upon and improve these critical
342 programs. It will also include some new programs such as a
343 generic drug user fee program that I am optimistic will help
344 to advance generic drug utilization in this country.

345 But today's hearing will focus on the reauthorization of
346 the Prescription Drug User Fee Act, otherwise known as PDUFA.
347 Originally authorized in 1992, PDUFA has provided FDA with
348 the additional resources it needs to efficiently review an
349 application for a new drug or biologic to enter the

350 marketplace.

351 I would like to first applaud the FDA and the brand drug
352 industry for coming together on this thorough and responsible
353 agreement. PDUFA has been a remarkable success, giving
354 patients access to safe, effective and breakthrough medical
355 treatments while supporting the advancement of science and
356 promoting a thriving pharmaceutical industry in the United
357 States, and I know that we all agree that failure to
358 reauthorize PDUFA in a timely manner would be extraordinarily
359 disruptive and a misstep for all parties involved, so I look
360 forward to hearing from our witnesses about the important
361 compromises made in this agreement and how it will help to
362 strengthen the PDUFA program overall.

363 That said, I would like to note that as we set out to
364 reauthorize this program for a fourth time, an important
365 issue remains unresolved, and that is the growing
366 globalization of the drug marketplace. I believe that
367 Americans deserve the confidence that the drugs they rely on
368 will help them get better and not make them more sick. That
369 is why along with Mr. Dingell, Mr. Waxman and Ms. DeGette, I
370 will be advocating for critical provisions of the Drug Safety
371 Enhancement Act to be included in these reauthorizations.
372 The bill would equip the FDA with the increased authorities
373 and resources it needs to keep pace with an increasingly

374 international marketplace of products. It is imperative that
375 the FDA play a role in improving quality and safety standards
376 of manufacturing facilities abroad. This legislation process
377 presents a unique opportunity for this subcommittee to make
378 extraordinary changes to enhance our drug safety laws, and it
379 is my hope that my colleagues on both sides of the aisle,
380 consumer advocates and the regulated industry, can all come
381 together to ensure we address the safety of the Nation's drug
382 supply in a meaningful way.

383 Also under discussion today is the reauthorization of
384 two pediatric programs, the Best Pharmaceuticals for Children
385 Act, BPCA, and the Pediatric Research Equity Act, PREA, which
386 are designed to provide necessary research on the appropriate
387 use of prescription drugs in pediatric populations. These
388 programs have been crucial in the successful cultivation of
389 important research used by doctors and parents to better
390 determine what kind of drug therapy is safest and most
391 appropriate for a child. Above all else, we must ensure that
392 the prescriptions our children use are tested appropriately
393 and deemed safe. I believe that we can all agree that we
394 have an enormous responsibility to our children to make
395 certain that they have access to the best possible medical
396 treatment. BPCA and PREA are two different but complementary
397 approaches towards accomplishing that goal.

398 Now, the regulatory authority granted to FDA under PREA
399 is linked to the expiration of BPCA and thus will also expire
400 at the end of this fiscal year. I understand there are
401 proposals being offered by some members on the subcommittee
402 that would sunset the expirations on both programs, and I
403 have some concerns with that approach, so I am eager to hear
404 from our witnesses about their views on the linkage and
405 expiration of these programs.

406 Now it is time for us to get to work on these critical
407 issues. It is my hope that our subcommittee can work in a
408 bipartisan manner and produce strong consensus legislation,
409 and again, I want to thank all our witnesses for being here
410 today, including Dr. Hamburg, who I have to say with regard
411 to Dr. Hamburg, she has been incredibly cooperative, come to
412 my district and I know other districts to talk about the FDA,
413 and I do believe we have made substantial progress under your
414 leadership, so I want to commend you for that. Thanks.

415 I yield back, Mr. Chairman.

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

417 ***** COMMITTEE INSERT *****

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

419 We have two panels today. Our first panel will have
420 just one witness, Dr. Margaret Hamburg, the Commissioner of
421 FDA, and we are happy to have you with us today.

422 Dr. Hamburg, you are recognized for 5 minutes for your
423 opening statement.

|
424 ^STATEMENT OF HON. MARGARET A. HAMBURG, M.D., COMMISSIONER,
425 U.S. FOOD AND DRUG ADMINISTRATION

426 } Dr. {Hamburg.} Good morning, Mr. Chairman and members
427 of the subcommittee. I am Dr. Margaret Hamburg, Commissioner
428 of Food and Drugs, and I really do appreciate this
429 opportunity to discuss the reauthorization of both the
430 Prescription Drug User Fee Act and legislation to promote
431 pediatric drug testing, laws that will expire if not
432 reauthorized this year. I will also talk about FDA's efforts
433 to promote science and innovation as well as the continuing
434 challenges of ensuring the safety of medical products in a
435 global marketplace.

436 I am joined today by Dr. Theresa Mullin, who is the
437 Director of the Office of Planning and Informatics in the
438 Center for Drug Evaluation and Research, and Deborah Autor,
439 Deputy Commissioner for Global Regulatory Operations and
440 Policy. Dr. Mullin actually served as FDA's lead negotiator
441 during the recent PDUFA reauthorization discussions and leads
442 our long-range planning efforts within the Center for Drug
443 Evaluation and Research. I have also charged Ms. Autor, Deb
444 Autor, in a new role recently to really help the agency to
445 adapt to the challenges of globalization and import safety as

446 the Deputy Commissioner of a newly organized entity to really
447 focus on these important challenges. Both are very
448 distinguished and they are available to help answer some of
449 the questions that you may have based on their ample
450 experience and knowledge.

451 I am pleased to report that we have transmitted our
452 recommendations for three user fee programs to help fund our
453 prescription drug, generic drug and biosimilar review
454 programs to Congress ahead of schedule. I am also very
455 pleased to announce this morning that FDA and industry have
456 also agreed in principle to a user fee program for medical
457 devices.

458 Congress first enacted the Prescription Drug User Fee
459 Act, also known as PDUFA, back in 1992, as was noted. Before
460 PDUFA, FDA's review process was understaffed, unpredictable
461 and slow. Patients in the United States often had to wait
462 for new products that were already available in foreign
463 countries. PDUFA revolutionized the drug approval process by
464 providing the funding necessary for us to conduct faster,
465 more predictable reviews.

466 In the nearly 20 years since PDUFA was first enacted,
467 FDA has approved over 1,500 new drugs and biologics. In the
468 last fiscal year, FDA approved 35 new groundbreaking
469 medicines, actually the largest number second to only one

470 other year in the last couple of decades. We were able to
471 approve two new treatments for hepatitis C, groundbreaking
472 medicines using more advanced science, targeting molecular
473 targets linking diagnostics and therapeutics. We approved
474 the first drug for Hodgkin's lymphoma in 30 years and the
475 first drug for lupus in 50 years, and just this week we
476 approved innovative new drugs to treat cystic fibrosis and
477 skin cancer, and we did it ahead of our PDUFA performance
478 goals. The United States now in fact leads the world in the
479 introduction of novel drugs.

480 We look forward to working with the subcommittee on the
481 fifth authorization of PDUFA. In keeping with the
482 requirements Congress put into place, we negotiated this new
483 PDUFA agreement with industry while regularly consulting
484 consumer, patients and health care professional
485 organizations. The agreement contains several enhancements
486 that address the concerns raised by industry and public
487 stakeholders as well as the agency's priorities. These
488 enhancements include initiatives to improve communication
489 between FDA and industry to speed up drug development,
490 advance the science behind drug regulation, particularly
491 around rare diseases, enhance the way FDA evaluates the risks
492 and benefits of therapies, modernize FDA's drug safety
493 system, and require electronic submission and standardize the

494 format of the data that we receive. Together, these
495 improvements along with additional funding industry will be
496 providing under the agreement, will allow us to maintain our
497 Nation's leadership in drug development while preserving our
498 high standards for safety and efficacy.

499 On the same timetable for reauthorization as PDUFA are
500 two laws designed to ensure that drugs are appropriately
501 tested for their use in children, entitled the Best
502 Pharmaceuticals for Children Act and the Pediatric Research
503 Equity Act, also known as BPCA and PREA. These two laws have
504 dramatically improved our understanding of the safety and
505 efficacy of drugs prescribed for our children, and I want to
506 thank Representatives Mike Rogers and Anna Eshoo, who are
507 leading the reauthorization efforts on these important laws.

508 Before enactment of BPCA in 1997, all too often, health
509 care professionals were forced to rely on imprecise and
510 ineffective methods to provide medications for children such
511 as adjusting dosing based on weight or crushing pills and
512 mixing them in food. But today, as a result of BPCA and
513 PREA, approximately 400 drugs have been studied and labeled
514 specifically for pediatric use. We welcome the opportunity
515 to work with Congress to reauthorize these successful
516 programs.

517 Lastly, I will turn to the challenges posed by

518 globalization and FDA's efforts to meet these challenges.
519 Today, approximately 40 percent of the drugs Americans take
520 are manufactured outside our borders and up to 80 percent of
521 the active pharmaceutical ingredients in those drugs come
522 from foreign sources. Over the next decade, FDA will
523 transform itself from a domestic agency operating in a
524 globalized world to a truly global agency fully prepared for
525 a regulatory environment in which product safety and quality
526 knows no borders.

527 To achieve this transformation, the agency is developing
528 a new, more international operating model that relies on
529 strengthening collaboration, improved information sharing and
530 gathering, data-driven risk analytics, and the smart
531 allocation of resources. We are eager to work with Congress
532 to ensure that our regulatory authorities keep pace with an
533 increasingly globalized world.

534 So I thank you for the opportunity to testify today and
535 I am happy to address any questions that you may have.

536 [The prepared statement of Dr. Hamburg follows:]

537 ***** INSERT 1 *****

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538 Mr. {Pitts.} The chair thanks the gentlelady and I will
539 now begin the questioning and recognize myself for 5 minutes
540 for that purpose.

541 Commissioner, I believe the PDUFA agreement contains
542 helpful improvements to the drug review process, and I am
543 particularly interested in the process improvements for the
544 review of new molecular entities. Would you explain these
545 improvements and how they will add to the predictability and
546 transparency of the review process?

547 Dr. {Hamburg.} Well, there are a number of important
548 elements. One is, you know, to really focus on the
549 transparency, consistency and predictability issues that are
550 so important to industry that you mentioned through enhanced
551 communication and sitting down early in the process and
552 midway through the process to really make sure that we all
553 understand where we are, where we are going, what are the
554 expectations, and to be able to, you know, much more rapidly
555 surface issues as they emerge and address them so that we
556 can, you know, really streamline the process and avoid
557 unnecessary delays or confusion.

558 Mr. {Pitts.} I understand that FDA and the industry
559 have a tentative agreement on the medical device user fees.
560 As you know, Chairman Upton and I have set a deadline of

561 reauthorizing the user fees by the end of June. I think my
562 colleagues on the other side of the aisle would agree that
563 reauthorizing the user fees by the end of June is in the best
564 interest of the FDA and the American people. We received the
565 three other user fee proposals by January 15 but we did not
566 receive the medical device user fee proposal as required
567 under statute. Given the need to reauthorize the user fees
568 as soon as possible, when will the FDA send us the
569 legislative language and the proposed agreement for the
570 Medical Device User Fee Act so this committee can begin its
571 work? Could you give us a specific date? And how does the
572 Administration plan to expedite the process so the committee
573 can get the device information as soon as possible?

574 Dr. {Hamburg.} Well, we are really delighted to be able
575 to come before you this morning and say that we have an
576 agreement in principle, and that was actually just announced
577 within the last hours. There are still some i's to dot and
578 t's to cross. We will move as swiftly as we can to be able
579 to present it to all of you to begin to work on it. We do
580 want to follow the process that Congress laid for us of
581 course, though, which does require that the recommendations
582 be presented at a public meeting and also that a docket be
583 opened with at least 30 days of comment. As soon as we have
584 finalized this agreement and we are very nearly there, we

585 will begin that process, and while I can't specify an exact
586 date, we are very mindful of the timeframe that you have set
587 forward and are very appreciative of that timeframe that you
588 have set forward, and we are very eager to move this as
589 swiftly and as surely as possible. This is an important
590 agreement and one that we are very, very pleased to be able
591 soon to finalize and move to this next stage.

592 Mr. {Pitts.} Thank you. Companies that want to
593 manufacture prescription drugs in the United States are at a
594 competitive disadvantage because there are manufacturing
595 plants in China with very little oversight. Now, there is a
596 2-year inspection requirement for domestic manufacturers but
597 no similar requirement for foreign manufacturers including
598 those located in China. Shouldn't we ensure that our
599 regulatory oversight system does not create an uneven playing
600 field for American manufacturers? Wouldn't a risk-based
601 inspections approach make more sense in ensuring resources
602 are spent inspecting higher-risk facilities like those in
603 China rather than setting arbitrary statutory requirements?

604 Dr. {Hamburg.} Well, I think the issue of how we can
605 really respond to the globalized world that we live in where
606 there are manufacturing facilities around the world that are
607 making products coming into the United States is one of the
608 most important challenges before us and certainly one of the

609 priorities that I have taken on during my tenure as
610 Commissioner. We very much need to rethink many of the ways
611 that we have traditionally done business. Many of our
612 authorities were actually put in place in a world that looks
613 very different back when President Roosevelt created the
614 modern FDA in 1938. Most drugs were in fact produced in this
615 country and that is certainly not the case anymore.

616 So we are both trying to expand our ability to do
617 inspections internationally, which are more complex and a bit
618 more costly. We certainly are trying to introduce risk-based
619 approaches so that we use our limited resources as widely as
620 possible. We are also trying to work more closely with
621 regulatory counterparts who share this challenge of having to
622 do inspections in many more places and many more countries so
623 that we can actually share information and begin to in many
624 instances, you know, rely on the work of others to leverage
625 resources towards the goal of expanding our presence
626 internationally and, as you say, leveling the playing field
627 so that people who have manufacturing overseas don't have to
628 wait longer than those that are producing domestically. We
629 also think that by more coordination with regulatory
630 authorities, we can reduce the burden on industry by having
631 more harmonization of standards, approaches and expectations
632 and perhaps reducing the overall number of inspections that

633 they will be subject to.

634 Mr. {Pitts.} The chair thanks the gentlelady and yields
635 to the ranking member, Mr. Pallone, for 5 minutes for
636 questions.

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

638 Dr. Hamburg, in your testimony you mention the
639 challenges posed by increasing the global marketplace. As
640 you know, Mr. Dingell, Ms. DeGette, Mr. Waxman and I have
641 introduced a bill, the Drug Safety Enhancement Act, that
642 gives FDA some authorities and an infusion of resources to
643 address these challenges. Could you comment on the bill and
644 whether FDA supports the bill? Some have asserted that FDA
645 already has the authority to do some of the things that are
646 included in the bill and that FDA could just proceed with its
647 current authority. Can you comment to what extent that is
648 true and whether having explicit new authority would be
649 helpful?

650 Dr. {Hamburg.} You know, we really do feel, as I
651 mentioned, that the ability to respond to the challenges of a
652 globalized world is among the most important issues before us
653 and that we really have increased vulnerabilities and
654 increased demands that, you know, really threaten our ability
655 to fulfill our critical mission to ensure the safety of
656 products that the American people use and count on, so we are

657 very eager to work with the members of this committee and
658 Members of Congress more broadly to identify authorities that
659 will make a difference in our ability to better ensure the
660 safety of the supply chain and these important products that
661 are being manufactured and distributed on a global basis to
662 enable us to do better screening of products coming into this
663 country, to be able to act when we identify products that are
664 coming in that may pose a risk in terms of safety and
665 quality, so we are very, very interested in the work that you
666 are doing, appreciate your leadership and stand ready to
667 provide whatever information that we can.

668 Mr. {Pallone.} Thank you. A topic that has garnered a
669 lot of attention over the years is the issue surrounding
670 conflicts of interest on FDA's advisory panels. Obviously,
671 if the advisory committee is to be credible and useful, it
672 has to have a limited number of members who have conflicts.
673 In the 2007 legislation, we included a provision that
674 prohibited FDA from seating more than a certain percentage of
675 conflicted advisory committee members, but both before and
676 since the 2007 law, FDA has encountered difficulty trying to
677 fill advisory committees with qualified and unconflicted
678 members, and many have asserted that the waiver caps are to
679 blame, but my understanding is that FDA has not come close to
680 hitting those caps. So I am concerned about reports of

681 weakened advisory committees because I think they are very
682 important.

683 I wanted to ask you, do you agree that FDA has indeed
684 encountered problems in filling advisory committees in recent
685 years, and what is the impact, if so, of these vacancies on
686 the ability of FDA to obtain expertise? Have there been
687 instances in which the advisory committee meetings were
688 delayed because FDA could not identify a sufficient number of
689 outside experts, and to what extent are the waiver caps the
690 problem or, you know, related to this?

691 Dr. {Hamburg.} Well, this is a very important issue and
692 one, you know, that very much goes to our ability to bring
693 the best possible science to bear on our decision making. We
694 also must have a process that has integrity, and so we have
695 been, you know, working on this issue, talking with
696 stakeholders and reviewing our policies and experience. It
697 is one of those issues unfortunately in a way that the more
698 you get into it, the thornier and more complex it gets, and
699 on the one hand, there are people who would like to see us
700 step away and relax some of our conflict-of-interest policies
701 so that we can bring those individuals who are most expert to
702 the table to serve on our advisory committees, and there are
703 others on the other end of the spectrum who are very, very
704 concerned that we need to have individuals who do not have--

705 Mr. {Pallone.} I am just trying to--because my time--
706 specifically, have there been problems filling these advisory
707 committees in recent years?

708 Dr. {Hamburg.} At the present time, as you noted, we
709 are not bumping up against our cap in terms of waivers, and
710 we have actually been making an aggressive effort to fill
711 empty slots on our advisory committees and have made
712 progress. It is a challenge to get people on our advisory
713 committees for many reasons, both that it is a huge time
714 commitment and--

715 Mr. {Pallone.} Do you have any ideas about what you
716 could do to improve it--

717 Dr. {Hamburg.} Well, I think--

718 Mr. {Pallone.} --and whether we could help in some way
719 with the legislation?

720 Dr. {Hamburg.} You know, we have been looking at this
721 pretty closely and we don't at the moment see major areas
722 where a legislative fix is required but I think it is
723 something that we want to continue to work on. The input and
724 engagement with our various stakeholders is absolutely
725 crucial, and, you know, the role of the advisory committees
726 is, you know, very foundational to a lot of what we do and so
727 we want to make sure that we have the right balance of
728 expertise without conflict of interest that might compromise

729 the value of the input of those individuals, and we do think
730 that transparency is a very important aspect of moving
731 forward on this, and that is a strategy that enables often
732 individuals to be able to bring their expertise with fuller
733 understanding also though of their engagement either with
734 sponsors of a product or an industry or positions that they
735 have taken in the past on related issues.

736 Mr. {Pallone.} I thank you.

737 Mr. {Pitts.} The chair thanks the gentleman and
738 recognizes the gentleman from New Jersey, Mr. Lance, for 5
739 minutes for questions.

740 Mr. {Lance.} Thank you, Mr. Chairman, and good morning
741 to you, Dr. Hamburg. I have not had the privilege of meeting
742 you previously, and it is my honor to do so.

743 On the front of advancing personalized medicine, what
744 steps might the FDA be taking to modernize the current
745 regulatory structure? I have a bill in the hopper, the
746 Modern Cures Act, that I believe might be able to be helpful
747 in this area.

748 Dr. {Hamburg.} Well, it is such an important area and
749 we certainly are on the cusp of dramatic advances in terms of
750 opportunities for care and treatment, and we are already
751 seeing breakthroughs including a new therapy that was
752 announced yesterday for cystic fibrosis where we are able to

753 really see a therapy targeted to individuals with a
754 particular genetic marker and really treat the underlying
755 pathway of a disease in a new way.

756 With respect to activities at the FDA to enable us to
757 really realize the potential of personalized medicine, a
758 major area of focus is the investments in advancing
759 regulatory science that we have embarked on with our
760 colleagues in industry and academia, and I am very happy that
761 a focus on new investments in regulatory science is part of
762 the PDUFA V agreement because I think that will enable us to
763 further develop the tools that will matter to both drug
764 development and regulatory review and enable us to really
765 target therapies for the people who will respond or for the
766 people who will have unacceptable adverse consequences of
767 therapy. We can also stratify populations and learn who will
768 benefit and who will perhaps have unacceptable risks.

769 Mr. {Lance.} Thank you.

770 Dr. {Hamburg.} There is one other thing. I have also
771 reorganized the agency in order to try to bring new
772 leadership in, and we have a Deputy Commissioner for Medical
773 Products who has a background in personalized medicine, and
774 he will be working across drugs, biologics and devices to
775 coordinate activities, which is very important to make
776 personalized medicine real.

777 Mr. {Lance.} Thank you.

778 Dr. {Hamburg.} I am sorry.

779 Mr. {Lance.} I look forward to working with you on
780 that.

781 Section 9 of the goals letter, enhancing regulatory
782 science and expediting drug development, includes a
783 subsection on advancing development of drugs for rare
784 diseases. Specifically, the proposal provides for by the end
785 of fiscal year 2013 that the FDA will complete a staffing and
786 implementation plan for the CDER rare disease program within
787 the office of new drugs and a CBER rare disease liaison
788 within the Office of Center Director, and the FDA will
789 increase by five the staff of the CDER rare disease program
790 and will establish and fill the CBER rare disease liaison
791 position. Would you please indicate to the committee
792 assurances that you can provide that these additional staff
793 will lead to greater efficiency and not create an additional
794 layer of delay with no or limited value?

795 Dr. {Hamburg.} You know, I think that we are moving in
796 a direction that is very positive and will help support and
797 extend our efforts in the rare and neglected disease area. I
798 think it is an area where we have made terrific progress in
799 terms of being able to work with sponsors to identify new
800 promising drug candidates and move them through the system

801 where we have been able to apply new and better science and
802 more flexible regulatory tools, innovative clinical trial
803 designs being one important aspect of that, and I think you
804 will have the opportunity to hear more about that.

805 But I think the new proposal in the PDUFA agreement will
806 enable us to have some individuals who are really focused on
807 some of the unique needs and concerns in the rare and
808 neglected disease areas and to be able to work across many
809 components of the agency to ensure that we are doing all that
810 we can, bringing the best possible science to bear and never
811 forgetting this important aspect of drug development and
812 getting new products to the people who need them.

813 Mr. {Lance.} Thank you, Commissioner. And finally, on
814 biomarkers, innovative drug development is increasingly
815 dependent on the use of new biomarkers of disease to target
816 the right patients. What is the FDA doing to encourage the
817 use of biomarkers in drug development?

818 Dr. {Hamburg.} It is such a key aspect of how we can
819 bring new and better science to bear on drug development and
820 drug review. We already have been, you know, quite involved
821 in biomarker development including through the biomarker
822 consortium that brings industry and academic together with
823 government, both FDA and NIH, to try to identify and validate
824 biomarkers for regulatory use. Biomarkers have an essential

825 role to play in identifying potential toxicities so that if a
826 drug is going to fail, it can fail early and we can speed the
827 process. Biomarkers have a critical role to play in terms of
828 serving as surrogate end points for clinical trials so that
829 we can get important information about whether a drug is
830 working or not without having to have extended trials and
831 follow the whole course of the disease to give us early
832 indications, and in other ways, you know, really gives us
833 tools to accelerate the drug development process and the
834 review process. It is an area that industry shares our
835 excitement and enthusiasm about the opportunities in science,
836 and I think its inclusion in the PDUFA V agreement reflects
837 that we think that by focusing on this area, we can really
838 make huge strides forward.

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

840 Mr. {Pitts.} The chair thanks the gentleman and
841 recognizes the gentlelady from California, Ms. Capps, for 5
842 minutes for questions.

843 Mrs. {Capps.} Thank you, Mr. Chairman.

844 Thank you so much for your testimony, Dr. Hamburg, and
845 for being with us today. You and your team have done such
846 terrific work coming together on the PDUFA V agreement, and I
847 look forward to working with you to move this bill forward.
848 I also wanted to acknowledge that while these user fee

849 agreements are a critical piece to ensuring that the FDA has
850 the resources to do its job and continue to be the goal
851 standard in this work around the world, at the same time we
852 here in Congress must not shirk our responsibility to
853 adequately fund the agency so that you can do that work, and
854 I hope that in our bipartisan agreement that we will also
855 work across the aisle during the appropriations time to do
856 just that.

857 I hope to get to two topics in this very fast-moving 5
858 minutes that I have. In your testimony, Dr. Hamburg, you
859 mentioned the Sentinel system for postmarket surveillance.
860 This program holds great promise for more efficient and
861 effective postmarket surveillance to protect the public's
862 health, save money on research and curb potential drug
863 recalls. Your testimony says that PDUFA V will allow user
864 fees, and this is a quote, ``to determine the feasibility of
865 using Sentinel to evaluate drug safety issues that may
866 require regulatory action.'' Would you explain just a little
867 bit more, not too long, about what that means? How do the
868 goals described in PDUFA V differ or expand upon the pilot
869 projects that have already been completed in PDUFA IV?

870 Dr. {Hamburg.} Well, of course, FDOB began us on the
871 path of really strengthening our postmarketing surveillance
872 capabilities and focusing on safety in the postmarket

873 setting, and what we hope to be able to accomplish now with
874 PDUFA V is to really use the data available in the postmarket
875 setting and the data management and analytic tools to be able
876 to very quickly ask and get answers to questions of an
877 emerging drug safety concern. If we hear that a particular
878 drug might be associated with an elevated risk of another
879 kind of problem, we can query the database, and we are now up
880 to 100 million patient lives in the database, and can answer
881 that will help us to determine the level of concern
882 associated with an emerging safety issue and help us decide,
883 do we really need to ask for additional clinical studies to
884 further evaluate the safety risk or are we comfortable with
885 a determination that it doesn't appear to be a true
886 correlation.

887 Mrs. {Capps.} I understand. That is important. Do you
888 have the authority--should you need to expand the scale of
889 this program, do you have the authority on your own to
890 evaluate and make decisions along the way?

891 Dr. {Hamburg.} I believe that we have all the
892 authorities that we need, and obviously PDUFA V will help to
893 give us additional resources that we need, and part of what
894 is exciting about what we are doing as well is that it is a
895 real partnership working with the private sector and the
896 broader patient community in terms of being able to access

897 important data, which of course is utilized in a patient-
898 confidential manner but--

899 Mrs. {Capps.} Great.

900 Dr. {Hamburg.} --we do now have these large information
901 resources that enable us to do things that we couldn't do
902 before.

903 Mrs. {Capps.} Great. Another topic, in your testimony
904 you touched on the scale-up of electronic submissions to the
905 agency, and in July I asked your colleague, Janet Woodcock,
906 about reports that clinical trial data be submitted to the
907 FDA do not routinely reporting based on sex or other
908 important demographics. As you may know, this issue is one
909 we have long struggled with. It is a key component of a bill
910 that I have, my Heart for Women Act. In her response, she
911 noted that while she couldn't confirm these reports, the use
912 of electronic submissions would make it easier for the FDA to
913 identify if companies are indeed submitting the disaggregated
914 data as required by law. Can you tell me where the agency is
915 at this moment on moving toward an electronic-only submission
916 system and what are the benchmarks put forward in PDUFA V for
917 that kind of adoption?

918 Dr. {Hamburg.} Yeah. Well, we are very excited about
919 this component of PDUFA V. It has many benefits, both
920 streamlining and modernizing our systems to help speed review

921 and reduce burdens ultimately on both industry and our staff,
922 but it has the additional benefit that it will enable us to
923 deal with data in much more targeted ways and to be able to
924 ask and answer critical questions around such important
925 matters as gender and race and age and other factors that we
926 very much need to understand more deeply to be able to
927 provide the best possible products and the best possible care
928 to our citizens.

929 Mrs. {Capps.} Thank you very much. I yield back.

930 Mr. {Pitts.} The chair thanks the gentlelady and
931 recognizes the gentleman, Dr. Burgess, for 5 minutes for
932 questions.

933 Dr. {Burgess.} Thank you, Commissioner, again for being
934 here.

935 Commissioner, we need your help. Last year, February
936 2011, this committee sent a letter regarding documents from
937 the Food and Drug Administration relating to the issue of
938 contaminated heparin, and you recall that national tragedy
939 was prior to your becoming Commissioner but at the same time
940 we are having difficulty coming to a conclusion on that, and
941 while I recognize that you talked about the issues of
942 globalization, you are no longer going to be a domestic
943 agency but a global agency, I mean, here is where you have to
944 show value because you had a compound manufactured in

945 communist China that was used to adulterate a biologically
946 derived product, heparin, a blood thinner. This
947 hypersulfated chondroitin sulfate that was used to
948 contaminate the heparin was a molecule that was produced in a
949 lab and patented in the People's Republic of China and found
950 its way into our drug supply with loss of life in dialysis
951 centers when people were administered a bolus of heparin.

952 Last year, February 23rd, the committee sent a letter.
953 Your Office of Legislative Affairs has documents from at
954 least four employees but we don't have them at the committee
955 level. In November, your agency committed to a timetable to
956 complete the production of heparin documents by the end of
957 January 2012. We are there but we don't have any documents.
958 So what has been happening over at your Office of Legislative
959 Affairs for over 6 months? This is a poor reflection on the
960 agency and one where our committee and you all need to work
961 together and it is not happening.

962 Dr. {Hamburg.} Well, as you point out, heparin was a
963 very serious event that we all take very seriously in terms
964 of the initial response at the time but also making sure that
965 we have the systems in place to prevent that particular
966 problem from occurring again or other similar problems. I am
967 surprised by what you say. I am eager to work directly with
968 you to make sure you are getting what you need because my

969 sense was that our staff was spending literally thousands of
970 hours culling through documents for you, answering questions,
971 briefing committee staff on these issues, that we had sent up
972 some 50,000 pages of documents. But if you--

973 Dr. {Burgess.} If I may interrupt, that may be the case
974 but we don't have them, so over the next 2 weeks can we
975 elicit your help in getting this committee and the
976 Subcommittee on Oversight and Investigation the information
977 that it needs?

978 Dr. {Hamburg.} Absolutely. I commit to working very
979 closely with you to make sure that you are getting the
980 materials that you are requesting and need.

981 Dr. {Burgess.} Well, we are grateful for the more
982 sophisticated testing that would reveal this problem in the
983 future for new heparin but if there is someone out there who
984 seeks value in contaminating our drug supply chain, it may
985 not be heparin next time, it may be something else, and I
986 don't have a sense that we understand what happened when this
987 adulteration occurred.

988 We are all concerned about drug shortages. You hear
989 about it. It is in the newspapers. There is a particular
990 chemotherapeutic agent named Doxil which you are probably
991 familiar with that has the company apparently involved in the
992 manufacture of Doxil has said they are not going to make any

993 more, so now we are in a tough spot because other companies
994 are willing to take up that slack but all remaining Doxil has
995 to be used for treating patients. It can't be used for doing
996 the clinical trials, randomized clinical trials that would be
997 necessary. So what options do we have in this very rare
998 situation to allow the patients who are depending upon that
999 chemotherapeutic agent to continue to receive it and at the
1000 same time speed the approval of generic doses of Doxil?

1001 Dr. {Hamburg.} Well, I am not familiar with all the
1002 details of the particular case of Doxil that you raise. But
1003 it is speaks to a set of important issues around drug
1004 shortages in terms of, you know, really needing to work
1005 closely with companies to get early warning when decisions
1006 are made to discontinue manufacture or if they believe that
1007 there is an emerging quality or manufacturing concern to help
1008 identify other sources of available product to treat the
1009 conditions that patients may have when there are potential
1010 shortages and to help work with sponsors to expedite the
1011 standing up of manufacturing capability.

1012 Dr. {Burgess.} Right. We appreciate this is a complex
1013 problem, a multifactorial problem, but in this specific
1014 instance what we're asking is, can you use your flexibility
1015 on the issue of bioequivalents to help get these patients the
1016 drugs that they so desperately need?

1017 Dr. {Hamburg.} You know, as I said, I don't know enough
1018 about the specifics in terms of the option in that case so I
1019 would not want to comment in the setting. I will certainly
1020 go back and make sure that the people with the direct
1021 knowledge and expertise address that.

1022 Dr. {Burgess.} We will follow up with that. Thank you.

1023 Mr. {Pitts.} The chair thanks the gentleman and
1024 recognizes the gentlelady from Illinois, Ms. Schakowsky, for
1025 5 minutes for questions.

1026 Ms. {Schakowsky.} Thank you, Mr. Chairman, and thank
1027 you, Dr. Hamburg, for being here. I have four questions and
1028 I am going to get right to them, but I do want to associate
1029 myself with Ms. Capps' complimentary remarks to you and also
1030 the need to make sure that we adequately fund the FDA.

1031 My first question is this. There was a 2010 report from
1032 the HHS Office of Inspector General which found that ``80
1033 percent of approved marketing applications for drugs and
1034 biologics contain data from foreign clinical trials.'' So my
1035 question is, does the FDA have adequate resources to do
1036 clinical trial oversight in places like China and Peru?

1037 Dr. {Hamburg.} Well, this is part of the overall
1038 growing demands on FDA in terms of oversight of both foreign
1039 manufacturing facilities and research that is being done in
1040 other countries. It certainly is something that we are

1041 putting time and attention to. We are working both with the
1042 regulatory authorities in a wide range of countries--

1043 Ms. {Schakowsky.} Do you have the resources to--

1044 Dr. {Hamburg.} We need additional resources in order to
1045 be really provide the level of oversight that we think is
1046 necessary and appropriate, and we need some new models for
1047 doing business as well in terms of coordination with
1048 regulatory authorities sharing information and also
1049 increasing regulatory oversight capacity in many countries to
1050 ensure good clinical practice.

1051 Ms. {Schakowsky.} So it is authority and resources,
1052 right?

1053 Dr. {Hamburg.} Indeed.

1054 Ms. {Schakowsky.} I have been very interested in the
1055 issue of cosmetic safety, and here is my question. It
1056 relates to authority. If the FDA had reason to believe a
1057 cosmetic product was harmful, could it issue a mandatory
1058 recall of that product?

1059 Dr. {Hamburg.} I believe that we could work with the
1060 company to encourage a voluntary recall, but in order to
1061 pursue a mandatory recall, we would have to engage with the
1062 court system and pursue it through that venue.

1063 Ms. {Schakowsky.} There has been a lot of publicity
1064 around the product, the hair straightener product, Brazilian

1065 Blowout, and I know that the FDA wrote to the manufacturer to
1066 inform them they had determined their products to be both
1067 misbranded and adulterated, but apparently it is still being
1068 used in salons across the United States. So do you plan any
1069 further actions against the manufacturer of Brazilian
1070 Blowout?

1071 Dr. {Hamburg.} It is my understanding that we are
1072 involved in some continuing discussions with the
1073 manufacturers trying to better understand the issues involved
1074 and working with them around our concerns. I also believe
1075 that OSHA is engaged on this issue in terms of some of the
1076 workplace health concerns around the people that are
1077 providing the services in those beauty salons.

1078 Ms. {Schakowsky.} Right, the employees there, OSHA has
1079 moved in on their behalf.

1080 Now, I want to ask you about the ubiquitous advertising,
1081 direct-to-consumer advertising that we see on television.
1082 Some of them, I have to tell you, seem like if you really
1083 listen to all the cautionary things, it is like ``and death
1084 could result'' it seems like always at the end. It is almost
1085 humorous to me while you see people skipping through the
1086 flower fields. Anyway, what I am asking is that do you
1087 actually have any resources for direct-to-consumer
1088 advertising monitoring to ensure that consumers do have a

1089 balanced understanding of the drugs and the risks advertised
1090 to them, the accuracy of those? Where are with monitoring
1091 those direct-to-consumer ads?

1092 Dr. {Hamburg.} Well, we do have a group that is charged
1093 with working on the oversight of direct-to-consumer
1094 advertising and there is a process that involves the
1095 screening of the direct-to-consumer advertisements.

1096 Ms. {Schakowsky.} But you didn't fees for that, right?

1097 Dr. {Hamburg.} We don't have fees associated with that.
1098 I gather that in the last PDUFA negotiation, this has been
1099 identified as possible area of focus, but actually including
1100 it was moved away from for a number of reasons that I think
1101 may have included the willingness to match or include budget
1102 authority. I am not sure of all the details but it was
1103 considered in PDUFA IV but--

1104 Ms. {Schakowsky.} Let me just say--

1105 Dr. {Hamburg.} --but it is not part of PDUFA V.

1106 Ms. {Schakowsky.} Given the prevalence of those ads on
1107 television, it seems to me that that would be a major focus,
1108 and I hope we can work together to make that happen. Thank
1109 you.

1110 Dr. {Hamburg.} Thank you.

1111 Mr. {Pitts.} The chair thanks the gentlelady and
1112 recognizes the gentleman from Kentucky, Mr. Guthrie, for 5

1113 minutes for questions.

1114 Mr. {Guthrie.} Thanks, Dr. Hamburg. Thanks for coming.
1115 It is nice to have you here today. I have a related
1116 question, I want to get to another question, and it is
1117 related because it is user fee related. On the Tobacco
1118 Control Act, I have a question on that. The concern is,
1119 there is a user fee by tobacco companies to fund the Center
1120 for Tobacco Products, and my understanding, there is not
1121 transparency in the use of that money in terms of performance
1122 reporting or financial reporting like it is in PDUFA, you
1123 have to account for where that money is being used. My
1124 understanding is, there is not a report, not required
1125 statutorily for you to issue a report. I wonder if you have
1126 any comment on the transparency or use of those funds.

1127 Dr. {Hamburg.} Well, the user fees that are involved in
1128 supporting the tobacco program and its activities are
1129 scrutinized, and we have developed, you know, very strict
1130 oversight mechanisms and firewalls in terms of their targeted
1131 use for tobacco program activities, but you are correct that
1132 the legislation did not require the same kind of performance
1133 reporting as for other user fees, and, you know, I think that
1134 are obviously--I would certainly understand that Congress
1135 would like to know more about how those user fees are being
1136 utilized. I would say that, you know, we take, as I said,

1137 the oversight of those resources and their appropriate very
1138 seriously and do have a stringent process that is involved
1139 with that.

1140 Mr. {Guthrie.} Yeah, I don't think anybody has
1141 commented that you all were using it improperly, just that
1142 they don't have the access to the information that you do.
1143 So if I implied that, I apologize. But just the idea that
1144 other user fee programs, and maybe we should have financial
1145 reporting. Of course, Congress didn't ask you to do that
1146 when we passed that bill before.

1147 The one thing, and I have been kind of focused on a
1148 little bit is this use of guidance documents, so I know it is
1149 not right on PDUFA but while we are here talking about that,
1150 and just a couple of examples, and I'm not getting into the
1151 details of specifics, but just like draft guidance for
1152 industry and FDA staff commercially distributed in vitro
1153 diagnostic products. I know that is very detailed. But when
1154 that was issued and it went forward, there were citations
1155 about 2 weeks after guidance document. Well, first it was
1156 brought forth as nonbonding, not for implementation, but my
1157 understanding is that the FDA has to take an action citing
1158 that guidance document I guess 2 weeks after implementation.
1159 So the question is, and I want to leave you time to respond,
1160 essentially the Administrative Procedures Act has the

1161 rulemaking process and there is some concern that FDA is
1162 using the guidance documents in a way that should be through
1163 the whole rulemaking process and comments. A lot of
1164 stakeholders have brought that to our attention. Do you have
1165 any comment on the use of guidance documents as binding even
1166 though they say nonbinding?

1167 Dr. {Hamburg.} Well, you know, we have found a lot of
1168 interest from the industries that we regulate in the role of
1169 guidance. There may be some mixed views, but I will tell you
1170 that what I generally hear is that guidance is very useful in
1171 giving an indication of where the agency is, where we are
1172 going and thinking about a particular problem. While they
1173 are not binding in the same way that rulemaking is, they are
1174 much quicker to put forward and they are welcomed. In fact,
1175 one of the things that I think came up in the PDUFA
1176 negotiations was examining ways to actually support the
1177 guidance production system because there are a lot of areas,
1178 personalized medicine being one, where it would be helpful to
1179 sponsors of products to have more guidance in order to know
1180 what directions to pursue and get the insight into our
1181 thinking and approaches. So I think that it is overall my
1182 sense is very useful but I think it does sometimes create an
1183 uncomfortable situation where people don't know whether it is
1184 an enforcement document or whether it is simply guidance.

1185 Mr. {Guthrie.} See, I don't disagree with anything you
1186 said there at all. I think that you are absolutely right.
1187 People want some direction because the rulemaking process
1188 does take time so where is the direction we need to go in the
1189 interim, but I guess the concern is when they become treated
1190 like rules, that they didn't actually go through the
1191 Procedures Act, and that is a just a concern that we have.

1192 Thanks. I yield back.

1193 Mr. {Pitts.} The chair thanks the gentleman and yields
1194 to the ranking member emeritus from Michigan, Mr. Dingell,
1195 for 5 minutes for questions.

1196 Mr. {Dingell.} Mr. Chairman, I thank you. I commend
1197 you for this hearing. It is very much needed, and
1198 significant reform of food and drug laws is very much needed.

1199 I ask unanimous consent my opening statement be inserted
1200 into the record at this point.

1201 Mr. {Pitts.} Without objection.

1202 [The prepared statement of Mr. Dingell follows:]

1203 ***** COMMITTEE INSERT *****

|
1204 Mr. {Dingell.} I would like to begin by making a couple
1205 of observations. We have renewed PDUFA on a number of
1206 occasions and have expanded to a number of other activities
1207 by Food and Drug for a fee is now paid willingly by the
1208 industry. Each time this legislation has been extended, it
1209 has been extended with the active support of the industry. I
1210 authored PDUFA for some very interesting reasons. This
1211 committee conducted an extensive investigation of Food and
1212 Drug involving some serious misbehavior, accepting of
1213 gratuities and things of that kind, because of the fact that
1214 the agency did not have the resources to properly handle the
1215 issuance of permits for new pharmaceuticals, and the end
1216 result was, there were huge numbers of complaints from
1217 industry and some very unfortunate corruption existed in the
1218 agency.

1219 One of the interesting things, and I hope my colleagues
1220 will listen to this, about PDUFA and one of the reasons that
1221 it and its half sisters and brothers have been supported by
1222 the industry is that a good pharmaceutical brings into the
1223 manufacturer, or did at the time it was first put in place,
1224 about \$250 million a year, and if each time that a company
1225 found that it is delayed in putting a pharmaceutical to work
1226 and getting approved, that company finds that it has massive

1227 losses, massive losses stemming from the fact that it cannot
1228 market while its patent, which exists for 17 years, is
1229 running. Food and Drug does not have the resources to do
1230 this.

1231 Now, Food and Drug is also moving forward to see to it
1232 that they have legislation which would enable them to begin
1233 to collect fees for certain changes in the law with regard to
1234 other pharmaceutical regulatory activities by that agency.
1235 These would impose the same burden on foreign manufacturers,
1236 who are now bringing in huge amounts of counterfeits and
1237 other unfortunate things into this country, to the great
1238 detriment and the hurt not only of our law but also of
1239 American manufacturers and Americans who are being poisoned.
1240 I would observe that we had a rather hideous example of this
1241 when a lot of Americans were killed or seriously hurt by
1242 heparin which came in.

1243 So these questions first of all to Commissioner Hamburg.
1244 Has the law kept up with the changing environment? Yes or
1245 no.

1246 Dr. {Hamburg.} No.

1247 Mr. {Dingell.} It is badly in need of change, is it
1248 not?

1249 Dr. {Hamburg.} Yes.

1250 Mr. {Dingell.} And you have a number of changes which

1251 you will suggest for the record on this matter. Is that not
1252 so?

1253 Dr. {Hamburg.} We would love to work with you on this.

1254 Mr. {Dingell.} But the answer is yes?

1255 Dr. {Hamburg.} Yes.

1256 Mr. {Dingell.} It is also so that these will enable you
1257 to address not only changes in domestic production and the
1258 law as regards to domestic production but also with regard to
1259 the foreigners who are now sending in huge amounts of unsafe
1260 pharmaceuticals that you simply do not have the resources to
1261 address. Is that not so?

1262 Dr. {Hamburg.} It is correct.

1263 Mr. {Dingell.} Unfortunately, yes. Now, does Food and
1264 Drug have the authorities, the resources to adequately
1265 oversee such a heavily outsourced drug industry?

1266 Dr. {Hamburg.} We don't currently have the resources--

1267 Mr. {Dingell.} You don't have the resources, do you?

1268 Dr. {Hamburg.} --to fulfill as we would like our
1269 mission.

1270 Mr. {Dingell.} Good. I am giving you easy questions.
1271 These are all yeses or nos.

1272 Dr. {Hamburg.} It is hard to answer just yes or no.

1273 Mr. {Dingell.} Unless I indicate otherwise.

1274 Now, will you submit for the record the key authorities

1275 that FDA needs to oversee the drug supply chain?

1276 Dr. {Hamburg.} With pleasure.

1277 Mr. {Dingell.} Now, one of the additional problems that
1278 you have is that the components are now coming in from
1279 overseas. In the case of heparin, it was the components
1280 which caused the damage to the health of the American people,
1281 was it not?

1282 Dr. {Hamburg.} We believe that the contaminant was
1283 introduced into the crude heparin preparation, yes.

1284 Mr. {Dingell.} Thank you.

1285 Now, I have, Mr. Chairman, an analysis of H.R. 1483, the
1286 Drug Safety Enhancement Act of 2011, and I would ask
1287 unanimous consent that it be inserted into the record at this
1288 point.

1289 Mr. {Pitts.} Without objection.

1290 [The information follows:]

1291 ***** COMMITTEE INSERT *****

|
1292 Mr. {Dingell.} Madam Commissioner, one last question.
1293 You are familiar with the provisions of 1483. They are
1294 significantly similar to the additional powers and resources
1295 that Food and Drug received in the last couple Congresses ago
1296 to address the question of food safety, and you are finding
1297 that those new authorities are working very well there, are
1298 you not?

1299 Dr. {Hamburg.} Those new authorities are very, very
1300 important. We of course are struggling to fully implement
1301 the demands of the Food Safety Modernization Act but we are
1302 moving forward, and the additional authorities really are
1303 able to put us in a position to do things that are very, very
1304 important to prevent problems and address them swiftly.

1305 Mr. {Dingell.} And they particularly allow you to
1306 control imports and to address the question of possible
1307 seizure of unsafe pharmaceuticals which you had previously no
1308 capacity to address. Is that not so?

1309 Dr. {Hamburg.} That is correct.

1310 Mr. {Dingell.} Mr. Chairman, I have used more time than
1311 I am entitled to. Thank you for your courtesy.

1312 Mr. {Pitts.} The chair thanks the gentleman and
1313 recognizes the gentleman from Georgia, Dr. Gingrey, for 5
1314 minutes for questions.

1315 Dr. {Gingrey.} Mr. Chairman, thank you.

1316 Dr. Hamburg, I love you just as much as the chairman
1317 emeritus does. He said he had some easy questions for you.
1318 In that spirit, I definitely have one that I think is easy
1319 but another one that may not be quite so easy. First, for
1320 the easier of the two, I am holding in my hand a news report
1321 that ran yesterday from U.S. News and World Report, and it
1322 reads, ``Antibiotic-resistant bacteria found in 37 United
1323 States states.'' Can you tell me your thoughts on the
1324 magnitude of the threat that antibiotic-resistant bacteria
1325 pose to the United States patients?

1326 Dr. {Hamburg.} Antibiotic resistance, as you well know,
1327 is a huge and growing problem and one that we must take very
1328 seriously. We are seeing across various, you know, classes
1329 of antibiotics more and more resistance. That is greatly
1330 worrisome in terms of, you know, rendering important tools
1331 for controlling disease and preventing spread. We are seeing
1332 them, you know, rendered useless, increasing the burden of
1333 disease and the costs of care and potentially putting us in a
1334 position in some instances where we don't have the kinds of
1335 therapeutic interventions that we have come to expect, so it
1336 is something we need to address and we need to address it
1337 together, and FDA has a critical role to play.

1338 Dr. {Gingrey.} And I really appreciate that. I will

1339 put in more plug for the GAIN Act. So much for the easier of
1340 the two.

1341 Now, this next question is not meant to be unfriendly at
1342 all but I think it is very important. Ranking Member of the
1343 Health Subcommittee, Mr. Pallone, sort of addressed this
1344 earlier. I want to follow up on what he said, though.

1345 A number of constituencies, both patients' groups and
1346 industry, recognize there are great advancements in our
1347 understanding of the human genome and science behind
1348 biologics. These same constituencies, however, have shared
1349 with me their concerns regarding current conflict-of-interest
1350 rules governing the FDA. Their contention is this: If the
1351 rules are not changed to take into these emerging sciences
1352 nor the limited number of individuals who understand these
1353 emerging sciences, these sciences may progress beyond the
1354 FDA's ability to understand how to properly assess the
1355 science. And I understand that currently the cap on the
1356 waivers for these conflict-of-interest rules has not been
1357 reached but I also understand that there are maybe a number
1358 of obesity drugs, as an example, within the FDA review
1359 process that have been stalled because of a preconceived lack
1360 of understanding of the science behind the drugs. I will cut
1361 right to the chase. Simply put, I do not believe the FDA cap
1362 is the issue here. I just want to understand this. Is it

1363 the FDA's contention that changes to the current conflict-of-
1364 interest rules governing the FDA advisory panels would not
1365 benefit the FDA, patient groups or businesses when
1366 considering whether to invest in new drug development?

1367 Dr. {Hamburg.} Well, I think your question raises a
1368 number of really important points and of course goes beyond
1369 simply the conflict-of-interest rules and the advisory
1370 committees but how do we bring in the best possible expertise
1371 as we pursue our regulatory oversight of critical products to
1372 address critical medical and public health needs, and
1373 advisory committees are one important element of that but
1374 there are other ways that we do it as well.

1375 You know, for example, you mentioned obesity drugs.
1376 Well, we have a working relationship now spearheaded out of
1377 George Washington University where we are trying to bring
1378 together critical partners to help us think through how we
1379 can really improve our regulatory pathways for obesity
1380 reduction drugs including, you know, health care providers,
1381 scientific experts and patients. So I think there are
1382 different ways to bring in expertise, and part of what is
1383 exciting in PDUFA V, I think, is the focus on investments in
1384 regulatory science, which is an important venue for bringing
1385 the right expertise together, framing the right questions and
1386 making sure that we bring the best minds to bear in getting

1387 the critical answers.

1388 Dr. {Gingrey.} Well, let me interrupt you because I am
1389 just about out of time, and I am encouraged to hear that and
1390 I thank you for that response, but that is why I am
1391 supportive, quite honestly, of my colleague from Texas, Dr.
1392 Burgess's bill in regard to lifting these caps on waiver so
1393 that we have that expertise and maybe we approach it from two
1394 aspects, but thank you very much, Dr. Hamburg, and Mr.
1395 Chairman, I yield back.

1396 Mr. {Pitts.} The chair thanks the gentleman and
1397 recognizes the gentleman from Arkansas, Mr. Ross, for 5
1398 minutes for questions.

1399 Mr. {Ross.} Thank you, Mr. Chairman, and Commissioner
1400 Hamburg, thank you for joining us today.

1401 I believe that keeping a safe, affordable emergency
1402 inhaler available without a prescription, specifically
1403 Primatene Mist, is critical for asthmatics. Therefore, I am
1404 a little confused as to why the FDA took Primatene Mist off
1405 the market after December 31st of last year. Primatene has
1406 been available for over 40 years, and now, because of an
1407 environmental issue, not a health issue but an EPA
1408 environmental issue, the FDA has pulled Primatene from retail
1409 shelves and will not allow the existing supply chain to be
1410 sold. Here is why this concerns me. If the FDA allowed the

1411 existing supply to be sold, asthmatics could have access to
1412 an over-the-counter emergency inhaler for at least the next
1413 few months until another affordable over-the-counter
1414 emergency inhaler without harmful environmental impacts, as
1415 alleged by the EPA, is approved. Not only did the FDA deny
1416 access to the Primatene Mist in our supply chain but you have
1417 now stopped the phase III studies for development of an over-
1418 the-counter replacement for Primatene, and now Americans are
1419 without an OTC emergency inhaler and probably will be for the
1420 rest of the year when there are at least a million units of
1421 this inhaler sitting in a warehouse in California.

1422 So Americans now have to go see a doctor. If they get a
1423 prescription, then they have got to get it filled if they can
1424 afford it as a substitute for this over-the-counter product,
1425 and here is where it really hits home for me. I represent a
1426 very large, a very rural, a very poor district, and Primatene
1427 Mist can be purchased over the counter for asthmatic patients
1428 for 20 bucks and prescription albuterol is costing those same
1429 patients 50 to 65 bucks, and the cost is not only to
1430 consumers but also to the government. It is estimated it is
1431 costing our government, the federal government, between \$300
1432 million and \$1.1 billion due to asthmatics' increased
1433 hospitalizations, ER visits and an increased cost of going
1434 from the over-the-counter inhaler to one that requires a

1435 prescription, and of course, much of this cost of the \$300
1436 million to \$1.1 billion obviously is coming from Medicare and
1437 Medicaid because there is not another OTC emergency inhaler.

1438 So these figures are taken from the FDA's final rule
1439 ordering the removal of Primatene Mist based on not 2012 but
1440 2008 cost estimates. So when we say it is costing the
1441 government \$300 million to \$1.1 billion, those are probably
1442 low numbers, and I believe that the denial letter from the
1443 EPA states it deferred to the FDA in denying the sale of the
1444 last remaining units. In other words, the EPA left it up to
1445 FDA. FDA chose not to. A lot of folks where I come from,
1446 they can't afford a \$50 substitute for a \$20 product that
1447 they have been taking for way too many years because of their
1448 asthmatic condition.

1449 And so I would ask or suggest that you look into
1450 resolving this issue by considering releasing the remaining
1451 units of Primatene Mist and expedite the development of an
1452 emergency over-the-counter inhaler for asthma that is
1453 affordable and back on the U.S. market as soon as possible,
1454 and I would love to get your comments and thoughts on that.

1455 Dr. {Hamburg.} Well, it is obviously a complicated
1456 issue, but I think it is important to understand the broader
1457 context and the medical issues here. As part of the Montreal
1458 convention, there was a move--there was an environmental

1459 issue, as you point out, to remove chlorofluorocarbons from
1460 various products including asthma inhalers. It has been a
1461 very long transition period and we have been working with the
1462 various manufacturers of asthma inhalers to transition
1463 towards other delivery vehicles that don't have the CFCs. Of
1464 course, the manufacturer of Primatene Mist has been part of
1465 these discussions and they were given an extended period,
1466 some additional time for transition and we had indicated that
1467 we would welcome an application for another product.

1468 But in terms of the concerns you raise about the public
1469 health of individuals, I want to make it clear that there
1470 really is--we engaged in a very broad process of consensus
1471 development about the medical necessity of this product,
1472 talking with health care providers, scientific experts,
1473 public health professionals and patients and patient groups,
1474 and there is great concern about Primatene Mist or over-the-
1475 counter epinephrine-based--solely epinephrine asthma inhaler
1476 being used without the oversight and management of a medical
1477 provider and is really in the best interest of patients that
1478 have asthma, which can be a very serious and life-threatening
1479 condition, to have a medical provider. There are better
1480 treatments for the management of asthma overall. The
1481 epinephrine inhaler is a transient effect that briefly
1482 improves moderate symptoms but doesn't address the underlying

1483 cause of the asthma, and so we really think that in the best
1484 interest of individuals having access to a medical provider,
1485 going to a community health center where you pay on the basis
1486 of your ability to pay, local free clinic or public hospital
1487 or there are also sponsored programs to make medicines
1488 available at cheaper rates by various companies is important
1489 to the overall health and wellbeing of individuals suffering
1490 from asthma.

1491 I recognize the inconvenience of not being able to get
1492 an over-the-counter product for immediate relief if you don't
1493 have your prescription inhaler with you, etc. We really
1494 tried to make it a smooth phase-out process with ample
1495 warning and information, both to enable patients to find
1496 alternative products and health care providers and to ensure
1497 that the health of individuals would be protected. But I
1498 understand the issues that you are raising and the concerns
1499 that you have.

1500 Mr. {Ross.} Well, it is not about convenience, it is
1501 not about trying to sell these million units that are in a
1502 warehouse in California. It is about having a product that
1503 people can afford. Too many of my folks can't afford to go
1504 to a doctor. They can't afford a \$50 inhaler. They are
1505 having a tough time affording a \$20 inhaler. I am just
1506 saying we ought to continue--whatever CFCs are out there,

1507 they have been out there and people have been on this stuff
1508 forever in order to be able to breathe, and we ought to find
1509 a way to be able to let them continue to get it until another
1510 over-the-counter product that is EPA approved can be
1511 developed. Otherwise they can't afford it. They are going
1512 without it. They are showing up in the emergency room and it
1513 is costing our government well over a billion dollars as we
1514 make this transition.

1515 Mr. {Pitts.} The gentleman's time is expired. The
1516 chairman thanks the gentleman and recognizes the gentleman
1517 from Ohio, Mr. Latta, for 5 minutes for questions.

1518 Mr. {Latta.} Well, thank you, Mr. Chairman, and
1519 Commissioner, thanks very much for being with us today. I
1520 really appreciate it, and very interesting testimony today.

1521 I would like to just kind of switch a little bit over on
1522 the pediatric side, and I see in your testimony you state,
1523 you know, that both these statutes, the BPCA and the PREA,
1524 continue to foster an environment that promotes pediatric
1525 studies and build an infrastructure for pediatric trials that
1526 previously were nonexistence. If I could, I would just like
1527 of like to--from experience I have had, I have talked to a
1528 lot of pediatric docs, researchers, hospitals and parents of
1529 children that have severe illnesses, and I guess I would like
1530 to ask you, first of all, what they see is that the adult

1531 side sometimes is getting more of the dollars that are going
1532 in for the research, and on the second question, when these
1533 drugs are coming through, are they getting equal treatment as
1534 the adult medicines that are going--when the FDA is making
1535 its determination decisions?

1536 Dr. {Hamburg.} Well, I think that the BPCA and PREA
1537 legislation have been enormously helpful in creating a
1538 framework to really focus attention on the importance of
1539 doing pediatric studies on drugs that had previously really
1540 been only studied in adult populations and providing some
1541 incentives to move in that direction. We still have a
1542 considerable ways to go. There are, I think, reasons why
1543 pediatric trials often are not as likely to be done as adult
1544 trials that include both the recruitment issues of getting
1545 kids into trials, both logistics and ethics issues, and--

1546 Mr. {Latta.} Can I interrupt you right there? To solve
1547 that then, when you are talking about getting the kids into
1548 the trials and also the ethics issue, how should we go about
1549 trying to get that changed or promote to get more children
1550 into them so that these drugs can be--

1551 Dr. {Hamburg.} Well, I think that this path is a good
1552 one and we need to continue these programs and strengthen
1553 them as it becomes more routine for drug sponsors to be
1554 expected to also examine the drugs in pediatric populations,

1555 you know, both creates a very different climate where there
1556 is now an expectation and a commitment and accountability for
1557 doing so, and it also, I think, helps to expand the
1558 opportunities and the expertise for doing pediatric clinical
1559 trials. But I think it is an area--obviously it is not
1560 exclusively within the realm of FDA but where we need to as a
1561 nation be continuing to put more attention and resources to
1562 create pediatric clinical trial networks, to train the
1563 clinical researchers to do that work, and to encourage both
1564 on the medical product and the medical device side more
1565 innovation and attention to the needs of pediatric
1566 populations.

1567 Mr. {Latta.} Let me ask then, in your testimony you say
1568 there is slow but deliberate process that is being made in
1569 setting the safety and the efficiency of the approved
1570 therapies for certain ages. Would you say that would be the
1571 same thing, it is trying to get these--getting the children
1572 into these tests, or how would you address that statement in
1573 your testimony?

1574 Dr. {Hamburg.} You know, to be honest, I am not quite
1575 sure the question you are asking, but--

1576 Mr. {Latta.} You state that slow but deliberate
1577 progress is being made in these studies and again, is that
1578 going back to the whole issue of trying to get the children

1579 and maybe infants into some of these studies and the ethics
1580 side?

1581 Dr. {Hamburg.} I see. There definitely are some
1582 additional barriers I think to recruiting pediatric patients
1583 into clinical trials, and we need to work on those, and it
1584 is--I think it is, as I said, a broader issue of really
1585 having the support for the clinical trial networks, the
1586 training of the pediatric researchers, the education of both
1587 families and pediatric community providers about the
1588 importance of pediatric clinical trials and the opportunities
1589 that they can represent for both individual patients and for
1590 extending knowledge about appropriate pediatric care, so I
1591 think it is something that we really do need to work on and
1592 we need to work on it together.

1593 Mr. {Latta.} Thank you.

1594 Mr. Chairman, my time is expired and I yield back.

1595 Mr. {Pitts.} The chair thanks the gentleman and
1596 recognizes the gentleman from New York, Mr. Towns, for 5
1597 minutes for questions.

1598 Mr. {Towns.} Thank you very much, Mr. Chairman, and
1599 also the ranking member for holding this hearing today.
1600 Also, thank you very much, Commissioner, for being here.

1601 PDUFA has been an effective and essential tool in
1602 assuring that safe, effective drugs are brought to the market

1603 in a timely fashion. However, we must be certain that we are
1604 striking the proper balance between the benefits of speedy
1605 approval of new treatments and the risk that different
1606 patient populations are willing to accept in order to gain
1607 access to them.

1608 Let us also keep in mind that different patient groups
1609 may be willing to tolerate different degrees of risk. This
1610 is why it is crucial for FDA to communicate with the affected
1611 patient population when reviewing new treatments.

1612 In your written testimony, Commissioner, you indicated
1613 that the FDA takes into consideration the benefits and risks
1614 of new drugs on a case-by-case basis. Considering the degree
1615 of unmet medical needs and the severe or morbidity of the
1616 conditions the drugs intended to treat when conducting this
1617 assessment, do you see the input of the patient population
1618 affected by the condition?

1619 Dr. {Hamburg.} Well, we do, and one of the exciting
1620 things about the PDUFA V framework also is a real focus on
1621 developing better strategies to formalize and systematize how
1622 we think about benefit-risk and importantly the engagement of
1623 patients and their perspectives, and part of what we hope to
1624 accomplish over the next 5 years, if this PDUFA agreement is
1625 reauthorized, is to in a formal way through a series of
1626 public meetings, four a year over the 5-year period to really

1627 target different disease conditions and engage with the
1628 patient community about their perspectives of the available
1629 drugs, their experience of benefits and risks, what kind of
1630 risks they are willing to tolerate, etc., and that will be, I
1631 think, very, very useful, in addition, you know, really
1632 building on work that we do every day as we look at important
1633 products in terms of thinking about what are the other
1634 options available to patients and how serious, life-
1635 threatening, life-disrupting is the condition, and we do
1636 weigh risks and balance them with benefits, and in our
1637 approvals we are often willing to accept a considerably high
1638 level of risk in some cases when there is true benefit to the
1639 patient.

1640 Mr. {Towns.} Thank you very much, and let me say to my
1641 colleagues, I hope we recognize the importance of making
1642 certain that we fund you adequately as we make some demands
1643 as we move forward.

1644 I applaud the agency for instituting the accelerated
1645 approval process in 1992. Do you feel that the program has
1646 been successful, particularly in the rare disease space?

1647 Dr. {Hamburg.} You know, it has been a very valuable
1648 program and we have seen, you know, a high number of drugs
1649 move forward through the accelerated approval process. We
1650 also--and many of them, a large percentage have been in the

1651 rare and neglected disease space. We also often give a full
1652 approval straightaway to rare and neglected diseases when we
1653 have, you know, good science, a good product and an impact on
1654 the underlying condition that is meaningful. So I think we
1655 have made enormous progress in the last couple of decades
1656 moving forward in orphan drugs, rare and neglected diseases
1657 and have been able to apply a lot of regulatory flexibility
1658 in how we approve those drugs, and I think you may be able to
1659 hear more about that in the second panel from the NORD
1660 representative.

1661 Mr. {Towns.} Let me ask you, what challenges do you
1662 face with orphan drugs? What challenges do you actually
1663 face? Very quickly.

1664 Dr. {Hamburg.} Well, very often, the challenge is how
1665 to do the science that enables us to get the answers that we
1666 need. If you are talking about small numbers of patients,
1667 how can you tailor the clinical studies so that you can get
1668 robust, meaningful answers with only a small number of
1669 patients. I think historically also there were concerns
1670 about incentivizing industry to want to work on some of these
1671 disease areas where there would be limited patient numbers,
1672 and I think that the orphan drug program and the incentive
1673 structure there has helped to shift that dynamic, and I think
1674 that as we really begin to draw on the advances in science

1675 and technology today, there are very special opportunities in
1676 the rare and neglected disease areas to produce the kinds of
1677 product like the way we were able to approve yesterday for
1678 cystic fibrosis. We were able to really see a targeted
1679 therapy for a particular underlying genetic marker and really
1680 provide a breakthrough treatment, even though the number of
1681 patients with that particular condition is quite limited. In
1682 this case, we are estimating about 1,200 cystic fibrosis
1683 patients.

1684 It is a very exciting time and it is an area where I
1685 think there is a lot of opportunity, and PDUFA obviously has
1686 identified that as an area where we can make some real
1687 progress.

1688 Mr. {Towns.} Thank you, Mr. Chairman. I yield back.

1689 Mr. {Pitts.} The chair thanks the gentleman and
1690 recognizes the gentlelady from North Carolina, Ms. Myrick,
1691 for 5 minutes for questions.

1692 Mrs. {Myrick.} Thank you, Mr. Chairman.

1693 I appreciate you being here today, and that is kind of
1694 along the same lines of what I wanted to talk about and that,
1695 is, the guidelines for approval of certain drugs. While the
1696 FDA is tasked with protecting public health, I don't think it
1697 should be in a position of withholding or removing approval
1698 of drugs that treat fatal illnesses. When a patient is

1699 expected to die imminently from a disease, the FDA's decision
1700 of whether or not to approve that drug should be made on a
1701 different metric than the approval of a drug that is intended
1702 to treat a less serious condition.

1703 Your agency does claim to factor this in, and I know you
1704 see it as part of your mission to move treatment forward for
1705 patients, but it doesn't seem to me that you give enough
1706 weigh to the fact that dying patients will tolerate a riskier
1707 drug. Sometimes they won't respond and will succumb to the
1708 disease but sometimes they respond well, and aggregate
1709 clinical data doesn't always reflect that properly. So can
1710 you just tell me why the FDA shouldn't have a separate metric
1711 for determining approvals for diseases like metastatic or
1712 otherwise fatal cancers, ALS and other deadly illnesses?

1713 Dr. {Hamburg.} Well, we do, as we were discussing
1714 earlier, you know, really take very seriously the importance
1715 of balancing risk and benefit and recognizing when you have a
1716 serious life-threatening illness with no or limited other
1717 treatment options. The proposed drug must be viewed in a
1718 very different context than if it is one of six potential
1719 drugs for a disease, you know, that has only a very minor
1720 impact on the tasks of daily living. So we do take that
1721 very, very seriously, and if you look at our approvals, it is
1722 clear that as I said, in some instances, there is significant

1723 risk associated with a drug that we will approve, but we do
1724 at the end of the day have to ask the question of, is there
1725 an overall benefit to the patient, and that can be very
1726 difficult and challenging. But that is, you know, an
1727 important part of what we are charged with.

1728 I think, again, you mentioned the sort of stratified
1729 populations, that there may be some who respond and some who
1730 don't, and that is why the deepening of the scientific
1731 understanding is so important and to continue to work as
1732 PDUFA V, you know, has indicated in the area of regulatory
1733 science and really identifying how we identify--we need to
1734 really define who are the subpopulations of responders so
1735 that we can target the benefits to the people.

1736 Mrs. {Myrick.} No, I understand. We have talked about
1737 that before. That is one that I refer to simply because of
1738 people that I know who are very successfully being treated
1739 with that for other than the uses that you had approved.

1740 Also, with the compassionate use process for terminally
1741 ill patients who have very few other clinical options, it
1742 doesn't always work very well. Companies understandably
1743 worry that patients who don't fit the trial guidelines who
1744 have completed the trial for their drug will negatively alter
1745 their clinical data if they are allowed to take an
1746 experimental treatment under a compassionate use exception.

1747 Yesterday, a 41-year-old ALS patient was in our office, and
1748 he saw significant symptom improvement while involved in a
1749 clinical trial, but his participation in the trial ended and
1750 then he was denied access to the drug under compassionate use
1751 because of these concerns.

1752 So in your opinion, what else can FDA or Congress, for
1753 that matter, do to improve the likelihood that patients with
1754 no other clinical option can access treatment through
1755 compassionate use? I mean, this is an ongoing problem. I
1756 understand where you come from but it is also pretty hard to
1757 look somebody in the face and say I am sorry, I can't help.

1758 Dr. {Hamburg.} Well, it is, you know, a huge issue and
1759 one that certainly without knowing the specifics of that
1760 instance, you know, we do try to work with patients' families
1761 and providers under those kinds of circumstances to see if we
1762 can help facilitate access to a product.

1763 Mrs. {Myrick.} Can we refer him to you?

1764 Dr. {Hamburg.} Pardon me?

1765 Mrs. {Myrick.} Can we refer him to you?

1766 Dr. {Hamburg.} You know, I think you could. You know,
1767 I can't make any promises but--

1768 Mrs. {Myrick.} No, I understand.

1769 Dr. {Hamburg.} --absolutely and we can--

1770 Mrs. {Myrick.} He is so young, you know.

1771 Dr. {Hamburg.} Yeah, no, and, you know, it is an area
1772 that we need as a society to continue to work on.

1773 Mrs. {Myrick.} Well, my time is almost up so I will
1774 yield back, Mr. Chairman.

1775 Mr. {Pitts.} The chair thanks the gentlelady and yields
1776 to the gentleman from Utah, Mr. Matheson, 5 minutes for
1777 questioning.

1778 Mr. {Matheson.} Thank you, Mr. Chairman, and Dr.
1779 Hamburg, welcome. Thank you for coming today.

1780 I would like to focus my questions on a national track
1781 and trace program or a drug pedigree issue, which I know Mr.
1782 Dingell talked about and some others as well. You probably
1783 know, I have worked with my colleague, Mr. Bilbray, and a lot
1784 of stakeholders on crafting legislation to implement a single
1785 national pedigree standard. Last year, February 2011, the
1786 FDA held a 2-day track and trace public workshop. One of the
1787 reoccurring concerns from stakeholders at the workshop was
1788 the need for timely guidance on a single national pedigree
1789 standard prior to States going off and implementing their own
1790 systems. Implementation of a national standard could take
1791 years to implement. Could you speak to the timeframe
1792 necessary for Congress, the FDA and industry to act on this?
1793 And in speaking on that also, if PDUFA passes without a
1794 national pedigree solution included, what are the

1795 implications for where we are going to be in terms of our
1796 domestic pharmaceutical supply chain over the next 5 or 10
1797 years?

1798 Dr. {Hamburg.} Well, it is a very important question,
1799 and since I happen to be sitting next to an expert on this
1800 topic and you have been hearing me talk an awful lot, I think
1801 I may actually let my colleague, Deputy Commissioner Deb
1802 Autor, respond to that because she really has been working on
1803 those important issue for a very long time.

1804 Mr. {Matheson.} Great.

1805 Ms. {Autor.} Thank you. Congressman, as you mentioned,
1806 we did hold a public workshop on track and trace and we have
1807 had over 120 participants in that workshop and a lot of
1808 comments that have been submitted to the docket on a track
1809 and trace system. We are working hard on working on those
1810 standards, and I would be happy to talk to you more about how
1811 we can work together towards a national uniform pedigree
1812 system. We are concerned that if a national system doesn't
1813 go into place, we run the risk of having a patchwork of State
1814 laws including California's law that is scheduled to go into
1815 effect in 2015. We believe track and trace provides very
1816 important assurances to the integrity of the drug supply by
1817 giving us and industry and pharmacies and consumers the
1818 information they need to know to be assured that their drugs

1819 are safe and effective.

1820 Mr. {Matheson.} Do you think the FDA needs further
1821 authority from Congress in order to implement a national
1822 standard?

1823 Ms. {Autor.} Yes. We have authority now to implement
1824 standards but it is not clear in the law that those standards
1825 will be binding on everybody in the industry, and it is not
1826 clear that they would effectively preempt State law, so in
1827 fact, I think national legislation on this would be useful.

1828 Mr. {Matheson.} That is good to know.

1829 Now, the safety of our pharmaceutical supply chain has
1830 an important overlap with the drug shortage issue that we
1831 have been talking about. I saw a survey by the American
1832 Hospital Association that showed 42 percent of those
1833 hospitals facing shortages purchased a more expensive product
1834 from a new distributor. However, in this instance, there is
1835 no meaningful way for that hospital to be sure the drug they
1836 are buying has traveled a safe and secure path. Do you think
1837 a single national pedigree standard would help hospitals
1838 ensure the integrity of products bought outside their normal
1839 source of supply?

1840 Dr. {Hamburg.} I think, you know, that the issue of
1841 supply chain and shortages are linked but they also have many
1842 distinct characteristics, and I think that as we are grappling

1843 with the drug shortage problem, which is, as you know, a very
1844 real problem and growing, you know, we are trying to look at
1845 all the critical factors that are involved and, you know,
1846 they range from issues of limited numbers of manufacturers of
1847 a given product to aging production facilities, to cost
1848 reimbursement issues, and some of the issues around
1849 consolidation of providers and manufacturers.

1850 The issue of the security of the supply chain and
1851 quality being built into both manufacturing and assurances of
1852 quality throughout the supply chain obviously play a role in
1853 shortages to some degree, and also understanding the supply
1854 chain is important in understanding what kinds of products
1855 and quality products people might be accessing in relation to
1856 a shortage. So it is a complicated issue.

1857 Mr. {Matheson.} And I know there are a lot of separate
1858 issues in the two. It just seems to me that in a shortage
1859 situation, that--

1860 Dr. {Hamburg.} In a shortage situation, it is
1861 absolutely critical that whatever you are using as an
1862 alternative product, we can know is safe and high quality.

1863 Mr. {Matheson.} Yes, shortages create stress on the
1864 system, and stress creates opportunity for bad things to
1865 happen.

1866 Mr. Chairman, my time is up. I will yield back.

1867 Thanks.

1868 Mr. {Pitts.} The chair thanks the gentleman and yields
1869 to the gentleman from Louisiana, Dr. Cassidy, for 5 minutes
1870 for questions.

1871 Dr. {Cassidy.} Dr. Hamburg, thank you for being here.

1872 Now, I have learned to say in this job, I know what I
1873 have been told, not what I know, so let me just preface this
1874 by this. I am told that there is a difference between
1875 calendar days and FDA days, so on page 4 of your testimony
1876 where you mention that the FDA approval phase of new drug
1877 development has shrunk. I heard previously people come and
1878 say you have got to be kidding, they kick it back to us, they
1879 don't include this, and actually the time has grown. I have
1880 learned to say what I have been told, not what I know, so I
1881 come to the front, if you will, to say is that true? Is
1882 calendar days actually longer even though FDA days are
1883 theoretically shorter?

1884 Dr. {Hamburg.} Well, in terms of the way the
1885 performance goals have historically been structured, you
1886 know, in fact, one is looking at the FDA time and the clock
1887 can be stopped for different kinds of activities and
1888 ultimately what matters to patients and, you know, truly what
1889 matters to all of us involved in the process is how long does
1890 it take for a product to actually get to the person who needs

1891 it. But I think one of the things that has been very, very
1892 encouraging as we have watched the PDUFA process really take
1893 hold in terms of the resources capacities and focus of our
1894 review activities is that we have seen the number of drugs
1895 approved in the first cycle increase and it is over 60
1896 percent now, I think, which means that we are getting drugs
1897 to people in the first review process, which is really
1898 critical because--

1899 Dr. {Cassidy.} Now, your answer suggests to me that
1900 indeed calendar days may have increased for any given drug
1901 but it doesn't go through two cycles so maybe net it is less.

1902 Dr. {Hamburg.} On the drug side, I don't believe that
1903 that is the case. The device side, it is a little bit of a
1904 different scenario, and that is why I was sort of avoiding
1905 speaking to specific details, but on the drug side, we are
1906 seeing changes in the absolute time that it takes to get a
1907 product to market in really across-the-board way,
1908 particularly for priority review.

1909 Dr. {Cassidy.} Let me go to my next question. I thank
1910 you. We will later here testimony from the Pew Health Group,
1911 which kind of relates to something which we previously spoke
1912 about, that if you are a domestic pharmaceutical, you are
1913 getting reviewed every 2 years, and if you are overseas, it
1914 may be every decade. And I understand here we are now

1915 creating resources but in a previous conversation, you
1916 mentioned that union contracts limit the ability of FDA to
1917 assign people to go overseas to inspect. Now, does this
1918 address that issue as well?

1919 Dr. {Hamburg.} You know, I think that the union issue
1920 is really not central to the discussion. The issue about the
1921 increased cost complexity demands on the system of increasing
1922 the numbers of international inspections is, and we are
1923 really embarked on a series of activities to be able to
1924 strengthen our capacity to have a global presence and either
1925 directly inspect or get inspectional information.

1926 Dr. {Cassidy.} So you imply that, if you will, as a
1927 workaround so even through the contract may inhibit it, you
1928 have a workaround in which you could third party it?

1929 Dr. {Hamburg.} You know, I think that the union issue
1930 is really a non-issue here. We work closely with the union
1931 around the activities of union employees.

1932 Dr. {Cassidy.} Now, that is a little bit different than
1933 what we heard last time in which we were told that people had
1934 to volunteer, they could not be assigned, and that sort of
1935 thing.

1936 Dr. {Hamburg.} Well, we definitely seek volunteers for
1937 our foreign inspectional activities. We are addressing it in
1938 a number of ways. We do have a dedicated foreign

1939 inspectional cadre that really like to travel and have
1940 specifically volunteered.

1941 Dr. {Cassidy.} So just a pointed question, knowing that
1942 right now it is every 10 years or so overseas, if you had
1943 tomorrow to say listen, we haven't inspected them for 5
1944 years, you two are going and we expect an inspection report
1945 from you in however long it takes to do an inspection report,
1946 would you be able to do that?

1947 Dr. {Hamburg.} Well, we are dramatically ramping up our
1948 foreign inspections and we are doing it through both using
1949 domestically based inspectors who travel overseas. We are
1950 doing it through having foreign offices and inspectors who
1951 are based in country. We are doing it sharing inspectional
1952 information with our regulatory counterparts in other
1953 countries.

1954 Dr. {Cassidy.} Now, if I may interrupt, because I am
1955 almost out of time. I don't mean to be rude. But
1956 nonetheless, we are only doing it every 10 years. What do
1957 you project if we have this hearing 3 years from now that the
1958 frequency of inspection of an overseas plant will be by
1959 whatever mechanism we assign staff to do so?

1960 Dr. {Hamburg.} We are looking ultimately for parity
1961 between our domestic inspectional schedule and our foreign
1962 inspectional schedule. We want a level playing field, and it

1963 is interesting, we are not talking today so much about the
1964 generic user fee agreement but the foreign inspection are a
1965 particular issue around generic drugs and their manufacture
1966 and actually through leadership from the generic industry,
1967 you know, we have a first-time-ever user fee agreement that
1968 very much focuses on how can we strengthen the resources and
1969 programs to meet those demands of foreign inspections.

1970 Dr. {Cassidy.} Mr. Chairman, you have been very
1971 generous. Thank you. I yield back.

1972 Mr. {Pitts.} The chair thanks the gentleman. That
1973 concludes the questions from the members of the subcommittee.
1974 We will go to the rest of the members of the committee, and
1975 the chair recognizes Dr. Christensen from Virgin Islands for
1976 5 minutes for questions.

1977 Dr. {Christensen.} Thank you for the opportunity to sit
1978 in on this important hearing and to be able to ask questions.

1979 Most of the questions that I had around risk and benefit
1980 balancing and how it affects the time I think have already
1981 been asked several times and answered, so I am not going to
1982 ask that one. But I have a specific question on supply chain
1983 that relates to the territories, and I don't really expect
1984 you to answer it right this minute but maybe given me an
1985 opportunity to work with your staff on it. The medicines
1986 that come to the U.S. Virgin Islands are sometimes held by

1987 Food and Drug through Customs in Puerto Rico and almost
1988 always confiscated when they are being sent back to their
1989 supplier. We are outside of the Customs zone. That is part
1990 of the problem. But we are part of the United States. Our
1991 pharmacists are licensed, trained and licensed in the United
1992 States, and we are purchasing from U.S. companies. So what
1993 we would like to pursue is having a waiver or some special
1994 procedure to avoid this problem because it is a great burden
1995 to my hospitals and my pharmacies and of course, it had a
1996 deleterious impact on patients' access to clinically
1997 important drugs, and I am hoping that as you look through a
1998 new international regulatory system that we can find a way to
1999 fix that within that. So again, if you want to comment on
2000 it, fine, but I think it is--

2001 Dr. {Hamburg.} Well, only to say thank you for bringing
2002 this to our attention, and I think that we would like to work
2003 with you to better understand the nature of what is happening
2004 and why and what can be done to address it.

2005 Dr. {Christensen.} Right. And we have talked in the
2006 previous Administration about it, so some of your staff may
2007 know about it, but I know it is a fresh one for you.

2008 Could you tell me how the FDA's new Office of Minority
2009 Health works, for example, with the Office of Pediatric
2010 Therapeutics to ensure that racial and ethnic minority

2011 children are appropriately, ethically and adequately included
2012 in drug research on children and pediatric populations?

2013 Dr. {Hamburg.} Well, we are just standing up this new
2014 Office of Minority Health. It was actually something--the
2015 opportunity to put it in place was part of the health care
2016 reform act, and it is intended to sort of cut across the full
2017 range of activities within FDA but with a special focus on a
2018 set of important scientific, medical and public health issues
2019 including how can we assure the appropriate representation of
2020 racial and ethnic minorities in clinical studies and I think
2021 there are huge opportunities both to work with our Office of
2022 Women's Health and our pediatric offices but to work across,
2023 you know, all of the medical product areas so that we can
2024 really address these critical concerns.

2025 Dr. {Christensen.} On BPCA and PREA, often in children,
2026 the side effects of medicine or anything might not be seen
2027 for many years. Is there a requirement for the
2028 pharmaceutical industry to follow children for a certain
2029 period of time after they have been involved in clinical
2030 trials?

2031 Dr. {Hamburg.} You know, I am not sure that I can give
2032 you the complete response. We obviously have ongoing efforts
2033 to monitor adverse events, whether they are near term or long
2034 term, and our ability to do that in a meaningful way is

2035 enhanced by what we have been able to do in terms of
2036 strengthening our postmarket surveillance activities. In
2037 certain disease areas, there might be a particular concern
2038 anticipating possible longer-term risks or specific side
2039 effects in children and it might be part of the structuring
2040 of the clinical trial at the time of its initiation through
2041 PREA to put in place certain requirements and expectations
2042 about ongoing monitoring. But there may be some additional
2043 activities as well that I am not fully aware of.

2044 Dr. {Christensen.} Maybe we can follow up on some
2045 discussions with your office around that and see if there is
2046 something that needs to be done in terms of children and
2047 long-term impacts.

2048 Thank you, Mr. Chairman, I yield back the balance of my
2049 time.

2050 Mr. {Pitts.} The chair thanks the gentlelady and
2051 recognizes the gentleman from Virginia, Mr. Griffith, for 5
2052 minutes for questions.

2053 Mr. {Griffith.} Thank you, Mr. Chairman, and I know we
2054 have plowed through some of this territory but I think it is
2055 interesting. As a member of the committee but not of this
2056 subcommittee, it has been very educational and I do
2057 appreciate you being here, Mr. Chairman, and I appreciate you
2058 letting me participate.

2059 But you have heard from both sides of the aisle what I
2060 am about to say, and that is, we have all been contacted by
2061 constituents. That is why I am here today. I was contacted
2062 by a constituent who feels that the strong risk aversion at
2063 the FDA is creating at least the perception that it is
2064 slowing down or stopping the approval of new, innovative
2065 treatments for cancer and other life-threatening terminal
2066 diseases. And I like some of the others who have spoken here
2067 today, and I am not going to make you go through all the
2068 things you have already testified, are very concerned that if
2069 you are facing a certain death, you are willing to take more
2070 risk, and you are wondering why the government is getting in
2071 the way. So I would ask you first, you have already been
2072 over a number of things that the FDA is doing to try to make
2073 that process better, but have you given consideration to
2074 creating a waiver process where a consumer who is facing one
2075 of these diseases can waive liability and any concerns about
2076 a particular drug or biologic treatment or whatever in order
2077 to get that treatment when they are facing the consequences?
2078 Obviously, there has to be a disclaimer of all the either
2079 known or unknown risks involved, but have you all given
2080 consideration to doing something like that? Because thank
2081 God, I have never had to face that and hope I never do, but
2082 there are a lot of folks out there like the 41-year-old we

2083 heard about, and you have heard from both sides of the aisle,
2084 folks are willing to take those risks, particularly when they
2085 are younger and particularly if they have young children, as
2086 I do. You know, I would take those risks in a heartbeat if
2087 it was going to give me extra time with my kids.

2088 So I am just wondering, have you thought about creating
2089 some kind of a waiver--ok, this hasn't been approved but I am
2090 willing to take that risk? And if you haven't thought of
2091 that, would you? And then let me follow up with, and what
2092 other things is the FDA is doing that you have not already
2093 testified to, because I don't want you to have to be like a
2094 broken record and go over the things that you have already
2095 mentioned.

2096 Dr. {Hamburg.} Well, you know, obviously this is such
2097 an important point and it is something that goes to the very
2098 heart of what we do because, you know, our mission really is
2099 to try to get the best possible treatments to people who need
2100 them, and, you know, as we have already talked about, we are
2101 putting an increasing focus on how we think about benefits
2102 and risks and weigh them. We already do accept, you know--
2103 have a much higher tolerance for risk when you are talking
2104 about a disease that is serious, life threatening, has no
2105 other treatment. I don't believe that we have really
2106 explored the exact proposal that you put forward, and I think

2107 it would certainly require broader discussions than just
2108 within the FDA. And we do have some other programs.
2109 Compassionate use was mentioned for trying to get drugs to
2110 people that are in desperate, life-threatening situations but
2111 perhaps, you know, in the interest of time and completeness,
2112 you know, we could provide you with some additional
2113 information about the programs that we are undertaking, and
2114 we certainly can continue to think about other strategies
2115 including the one that you mentioned.

2116 Mr. {Griffith.} Well, and if you would, and, you know,
2117 this is one of those things where sometimes folks just
2118 sitting around the table brainstorming might come up with one
2119 of those eureka moments and have an epiphany.

2120 Let me shift a little bit to another question that has
2121 come up in my district. I represent a rural district. There
2122 are many recognized off-label uses for approved drugs but--I
2123 will pick up Dr. Cassidy's point. But I am told that the FDA
2124 severely restricts communications to doctors and patients
2125 about these uses. Representing a rural district, I have
2126 heard about doctors who find it difficult to get the
2127 information about off-label uses that could benefit many of
2128 their patients. So what can we do to better, both as the FDA
2129 and what can we do as Congress to help you better inform
2130 doctors, especially in rural communities so they know about

2131 potential effective off-label uses of approved treatments?

2132 Dr. {Hamburg.} Well, off-label use, as you know, you
2133 know, is an important part of many medical practices and FDA
2134 doesn't regulate the practice of medicine and off-label use
2135 is something that we recognize is happening and frequently I
2136 have talked with people within FDA about how can we really
2137 collect better information to understand off-label use so
2138 that it could inform the broader issues around the approved
2139 indications for the use of a drug, but I think that the big
2140 concern is when drug companies are actively marketing an
2141 unapproved drug for an off-label use and that is where the
2142 controversies have been really focused on.

2143 Mr. {Griffith.} Yes, ma'am. Thank you for your time. I
2144 yield back.

2145 Mr. {Pitts.} The chair thanks the gentleman and
2146 recognizes the gentlelady from California, Ms. Eshoo, for 5
2147 minutes for questions.

2148 Ms. {Eshoo.} Thank you, Mr. Chairman, for holding this
2149 hearing and also for extending both you and the ranking
2150 member a legislative courtesy to me to join this hearing
2151 today. It has always been a great source of pride to me to
2152 have served on this subcommittee for some 15 years, most of
2153 the years that I have been in the Congress, and I miss being
2154 here but I look forward to coming back and I am glad I am

2155 here today.

2156 I would like to ask unanimous consent that the lovely
2157 statement that I have be added to the record.

2158 Mr. {Pitts.} Without objection.

2159 [The information follows:]

2160 ***** COMMITTEE INSERT *****

|
2161 Ms. {Eshoo.} Commissioner Hamburg, it is wonderful to
2162 see you. I think that you know that I was the original
2163 author of both PREA and the BPCA, so I come here today with a
2164 great sense of pride and I welcome the comments and the
2165 questions that members have asked about both pieces of
2166 legislation that the Congress is preparing to reauthorize.

2167 As you know, PREA was created to ensure that drug
2168 companies were doing important clinical trials in children,
2169 an area which had been most frankly woefully underserved
2170 before the passage of the legislation. And without adequate
2171 pediatric labeling, doctors were left to guess what the
2172 appropriate dosages for children would be. I think there was
2173 maybe this assumption that was being made that children are
2174 little adults, and they are not; they are children. So I
2175 think that this has--we took a very important step with the
2176 passage of that legislation, and I think it is why it is
2177 crucial for companies to develop their pediatric plans as
2178 early in the drug development process as possible.

2179 Now, I understand that the FDA has draft guidance asking
2180 companies to submit their pediatric plans at the end of phase
2181 II but the PREA statute requires submission at the time of
2182 the new drug application. I think the sooner that companies
2183 focus on pediatric populations, the sooner kids will receive

2184 the drugs that they need in some cases to survive. So can
2185 you say with confidence that pediatric study discussions
2186 always start as early as the FDA recommends?

2187 Dr. {Hamburg.} Well, first, let me say thank you for
2188 your leadership, and before you walked into the room, I had
2189 actually made note of it in my opening remarks. But BPCA and
2190 PREA have been very important pieces of legislation and have
2191 enabled enormous progress in the pediatric therapeutics area.
2192 The question you raise, you know, is an important one. I
2193 know it has been under discussion within the agency and
2194 beyond, and I think it is sort of an ongoing discussion in
2195 terms of what is the most appropriate timing, and frankly,
2196 there probably is no one cookie cutter approach. It probably
2197 really does depend on the particular product in question and
2198 the types of trials required. But I think in general, my
2199 sense is that early engagement is always helpful and the
2200 ability--

2201 Ms. {Eshoo.} I ask because of how the statute reads.
2202 Do you have any idea what the percentage of pediatric plans
2203 are actually completed at the end of phase II? I mean, if
2204 you don't know, maybe you can get that to us.

2205 Dr. {Hamburg.} We can get that to you.

2206 Ms. {Eshoo.} Now, if a company does not submit its
2207 pediatric plan by the end of phase II, as the draft guidance

2208 recommends, does FDA have any enforcement mechanisms to
2209 address it?

2210 Dr. {Hamburg.} Now, you know, I want to make sure that
2211 I answer your question properly.

2212 Ms. {Eshoo.} I ask this because I think it would be
2213 helpful to have legislation to ensure that companies submit
2214 their pediatric plans at the end of phase II. In fact,
2215 Congressman Markey and I are working on this, and maybe I
2216 should just turn the question around. Would it helpful to
2217 you to have legislation that addresses what I just stated?

2218 Dr. {Hamburg.} Well, we do feel that at least as I
2219 understand it currently, you know, we have the tool of
2220 misbranding as a way of trying to respond to when the
2221 commitment is not met by the company with respect to
2222 completion of the pediatric studies, and that does seem like
2223 a bit--not quite the right regulatory or--

2224 Ms. {Eshoo.} I can sense it in your voice that there
2225 is--

2226 Dr. {Hamburg.} Yeah, it creates a situation--

2227 Ms. {Eshoo.} So you think legislation would be helpful?

2228 Dr. {Hamburg.} I think that looking at that and if
2229 there is an approach that could be more targeted and
2230 flexible, that that would be very useful in terms of pushing
2231 companies to complete this important work and doing it in a

2232 constructive way that ultimately benefits the patients.

2233 Ms. {Eshoo.} Thank you very much, and thank you for
2234 your work, Mr. Chairman, and our ranking member, thank you
2235 again for your legislative hospitality.

2236 Mr. {Pitts.} The chair thanks the gentlelady and
2237 recognizes the gentleman from California, Mr. Bilbray, for 5
2238 minutes for questions.

2239 Mr. {Bilbray.} Thank you very much for your courtesy,
2240 Mr. Chairman, and I just realized that at least on the other
2241 side of the aisle, there is a few that may remember the time
2242 I served on the committee for 6 years. A whole lot of new
2243 faces on this side.

2244 Doctor, we talk a lot about safety and regulation to
2245 protect it. We have an over-the-counter consumer product
2246 that is connected to over 500 deaths a year, and we continue
2247 to allow that to be sold over the counter. Do you want to
2248 explain to this committee why aspirin in its existing form is
2249 not more regulated or more restricted from consumer use even
2250 though there is what some people would call a very high death
2251 rate related to its use?

2252 Dr. {Hamburg.} Well, you know, aspirin obviously is a
2253 widely available product that we know has associated risks
2254 but also benefits. I don't think that I am prepared in this
2255 setting to discuss the whole context of the oversight and

2256 regulation of aspirin but I think it is an important reminder
2257 that even drugs that the average American would probably
2258 consider sort of safe and routine do have consequent risks
2259 and they need to be addressed in an ongoing way and that the
2260 FDA does in fact have a responsibility for the lifecycle of
2261 products, not just for approval but for monitoring, safety,
2262 efficacy and benefit, overall benefit to patients over the
2263 whole course of the product's use.

2264 Mr. {Bilbray.} Now, would it be fair to say, or if you
2265 can refer to your experts around you or whatever, would it be
2266 fair to say on the flip side of that issue that aspirin
2267 probably can be documented as being one of the most
2268 lifesaving drugs that have been readily available to the
2269 public in the last 30, 40, 50, 60 years?

2270 Dr. {Hamburg.} Aspirin has many benefits on different
2271 levels. That would be fair to say.

2272 Mr. {Bilbray.} Do you have any idea if there was any
2273 other drug out there that we could point to that probably has
2274 saved as many lives as aspirin has?

2275 Dr. {Hamburg.} You know, I am not really prepared to
2276 make those comparisons or have that--

2277 Mr. {Bilbray.} I would be very interested if you would
2278 take a look at the reality we have with aspirin, and I ask
2279 you to consider, and let us be very frank about it. If this

2280 product with its fatality problems came before the FDA today,
2281 could our existing system actually process it and get it out
2282 onto the market, or is it just one of those products that
2283 became so institutionalized before our regulatory oversight
2284 got where it is today? And my question is, do you think
2285 aspirin could get through the system today?

2286 Dr. {Hamburg.} Well, I wondered if that might be the
2287 ultimate question that you would be asking, and I guess that
2288 my answer in the form of a true bureaucrat is that I wouldn't
2289 be prepared to speculate without having really reviewed the
2290 information and the data, but I understand the issue that you
2291 are raising.

2292 Mr. {Bilbray.} I mean, my issue is the fact that if you
2293 only look at the negatives and if you focus, even if you look
2294 at the positives but if you focus on the negatives, in
2295 today's life, which usually happens, there are huge
2296 opportunities that may be denied, and my biggest concern is
2297 that I am looking at this and I don't see any way aspirin
2298 would be approved in our system, and how many people would
2299 die every year in this country and around the world if it
2300 wasn't available to the consumer? And I have to ask myself,
2301 do we know how many other drugs or treatments may be out
2302 there that have come later that cannot be accessible? So my
2303 big question is, has anybody ever challenged themselves to

2304 say do we have any idea how many deaths may be caused because
2305 we don't allow products like aspirin on the market today?

2306 Dr. {Hamburg.} Well, you know, as I was saying earlier
2307 in discussions, you know, we look in a very clear-eyed way at
2308 risks and benefits of the products that come before us, and I
2309 think we are striving now to deepen our strategies for
2310 addressing that and, you know, we do take a lot of risks.
2311 There is a sense that we are very risk-adverse.

2312 Mr. {Bilbray.} Doctor, I appreciate that and I am not
2313 blaming you. I am blaming the fact that the political side,
2314 we would raise holy hell, you would seeing us standing on the
2315 House Floor giving big speeches damning you for allowing this
2316 on the market, and I just want to sensitive that.

2317 Let me just say one thing. One of the great
2318 breakthroughs we did with AIDS in the 1990s when I was here
2319 was that we changed a lot of regulations, and multi-triaging
2320 was one of those things that we really moved the protocol for
2321 AIDS that hadn't been done for other research in other
2322 treatments. When it comes to cancer, it really appears that
2323 multi-triaging and a combination of drugs and uses may be one
2324 of those things we have learned from the AIDS success. Where
2325 we going now with FDA improving the ability for researchers
2326 and for pharmaceuticals to look at multiple drug use in the
2327 treatment of diseases such as AIDS and do we have an

2328 expedited process to try to move that process along?

2329 Dr. {Hamburg.} Well, I began my career in public
2330 service working on HIV/AIDS drug development and know exactly
2331 what you mean in terms of the importance of the
2332 breakthroughs, and it was really a combination of bringing
2333 the science together with the resources and commitment of
2334 industry, academia and the patient groups, and we were able
2335 to move very forward very swiftly and we were able to
2336 introduce, you know, some new regulatory approaches, etc. in
2337 the cancer arena and in other areas as well, other infectious
2338 diseases and other disease domains, we have a real
2339 opportunity as our science has deepened to do some of the
2340 kinds of things that you were just mentioning, and we
2341 actually just recently put out guidance to help industry
2342 think in some new ways about testing drugs in combination
2343 rather than doing one after another after another.

2344 Mr. {Bilbray.} And taking 20 years to do it.

2345 Dr. {Hamburg.} Yes.

2346 Mr. {Bilbray.} Mr. Chairman, I know my time is expired.
2347 To my colleagues, just to follow up on that, one of those
2348 other great successes that my colleagues will remember is
2349 that in the AIDS crisis, we could do blood tests and monitor
2350 virus levels to be able to see what cocktails were working
2351 rather than what we have now in cancer where you basically

2352 have to wait for the cancer to show up again. You have
2353 clinical trials in process right now on the East Coast for a
2354 blood test for lung and for breast cancer that is being
2355 looked at. Has anybody in your agency taken a look at the
2356 fact that this is not just a product that may be able to
2357 detect cancer for treatment but maybe one of those huge
2358 breakthroughs that cancer researchers are looking at to be
2359 able to more efficient in their research, much like they do
2360 with AIDS? Is anybody considering the connection between
2361 this blood test may not only be a good treatment but may be
2362 an essential part of research to address this issue?

2363 Dr. {Hamburg.} Yes, and let me just clarify that
2364 actually partly stemming from the work in HIV/AIDS, we do use
2365 surrogate markers including the kind of markers identified
2366 through blood tests in our approval process. That is really
2367 what accelerated approval is all about is identifying that
2368 can serve as surrogate endpoints for an early approval
2369 followed by additional clinical studies to confirm or not
2370 confirm the initial promise as indicated in those studies.
2371 So we take that very seriously. We use it in our decision
2372 making, and certainly what you were describing would fit
2373 within that framework of regulatory--

2374 Mr. {Bilbray.} Thank you for your courtesy, Mr.
2375 Chairman.

2376 Mr. {Pitts.} I thank the gentleman and recognize the
2377 gentleman from Massachusetts, Mr. Markey, for 5 minutes for
2378 questioning.

2379 Mr. {Markey.} Thank you, Mr. Chairman.

2380 The website clinicaltrials.gov was transformed into a
2381 mandatory registry that I created along with Representative
2382 Waxman in the 2007 FDA amendments. This website publishes
2383 information about the results of clinical trials designed to
2384 evaluate medical treatments but several problematic loopholes
2385 exist. For example, a drug company finds out from a clinical
2386 trial that a diabetes drug is not only ineffective but also
2387 causes severe side effects. As a result, the company
2388 abandons the drug's development, never seeks approval with
2389 the FDA and never publishes the results because there is no
2390 incentive to do so. Commissioner Hamburg, will the results
2391 of this trial ever have to be posted on the clinical trials
2392 database?

2393 Dr. {Hamburg.} As I understand it, currently, no. That
2394 is an important issue that you raise. I think it could be
2395 addressed but it is not included in--

2396 Mr. {Markey.} So if another researcher decided to
2397 pursue clinical trials of this same drug, they would have no
2398 idea about the dangers identified from the previous trial and
2399 would put more people at risk of the same adverse health

2400 effects that had already been identified so generally do you
2401 agree that it would be a good public health measure to ensure
2402 that results of all registered trials, regardless if the drug
2403 is approved or not, are posted on the database?

2404 Dr. {Hamburg.} I believe that NIH through its
2405 rulemaking process is currently looking at this question in
2406 terms of whether trials for drugs that aren't actually
2407 approved could be posted. I think you also raise a broader
2408 issue that certainly we are talking about with industry and
2409 others in terms of more transparency and the benefits, the
2410 common good of making more information about, you know, not
2411 just what works but what doesn't as well.

2412 Mr. {Markey.} Thank you. Now, some clinical trials
2413 that occur entirely overseas can be used to support a drug
2414 application with the FDA even though they are not subject to
2415 the disclosure requirements of the clinical trials database.
2416 Do you agree that any clinical trial regardless of where it
2417 takes place should be subject to the same transparency
2418 requirements if the trial is used as part of the company's
2419 approval application to the FDA?

2420 Dr. {Hamburg.} You know, yes, you know, in general we
2421 certainly agree that more transparency, more information is
2422 beneficial and we think that this is a bit of a disconnect
2423 and, you know, we would be interested in working with you

2424 further.

2425 Mr. {Markey.} So this is something that Ms. Eshoo and I
2426 are working on, this next subject, which is that the FDA data
2427 shows that since 2007, 78 percent of PREA's pediatric study
2428 requirements were not completed by their due dates, if at
2429 all. These are products that could benefit children but the
2430 studies needed to provide that information are not always
2431 being completed. Pediatric studies are especially
2432 challenging and companies may have a perfectly acceptable
2433 reason for asking FDA to extend their deadlines, but if the
2434 company does not meet its pediatric requirements and fails to
2435 provide a reasonable justification, what enforcement options
2436 does the FDA have?

2437 Dr. {Hamburg.} Well, we do, as I was discussing with
2438 Congresswoman Eshoo earlier, have, you know, a limited
2439 arsenal of tools and it really is an area where it is
2440 important, number one, to understand the reasons for the
2441 delays, and as you note, there are some reasons that are
2442 understandable, but these are studies that are important to
2443 get done. We need to support companies in getting them done
2444 and there should be expectations and accountability on the
2445 completion of those studies.

2446 Mr. {Markey.} Yes, it is my understanding that the
2447 FDA's only option for enforcement is misbranding the product

2448 if there is an enforcement action that you can take but that
2449 is an option very rarely, if ever, taken by the FDA. If the
2450 FDA were to deem a lifesaving treatment misbranded because
2451 the company failed to complete its pediatric requirements,
2452 children who were being prescribed the drug off-label would
2453 lose access to it. Adults would also lose access. Is that
2454 correct?

2455 Dr. {Hamburg.} That is correct, and that is why in some
2456 ways--I have heard it internally referred to as the nuclear
2457 option.

2458 Mr. {Markey.} So either FDA triggers the nuclear option
2459 of misbranding, costing everyone access to that drug, or they
2460 can do nothing, and that is very different from the way many
2461 other violations of the Food, Drug, and Cosmetic Act are
2462 handled, which can incur civil monetary penalties. Have
2463 civil monetary penalties been effective in other areas to
2464 ensure compliance?

2465 Dr. {Hamburg.} I think that they have been and they do
2466 give more flexibility and the ability to target the action to
2467 what needs to be done in a more effective way.

2468 Mr. {Markey.} And I see no reason, Ms. Eshoo and I
2469 agree on this, that companies failing to meet their
2470 obligations to children should enjoy those special
2471 protections. So we would like to work with you in giving you

2472 the flexibility to impose those penalties.

2473 And just finally, Ms. Schakowsky and Ms. Baldwin and I
2474 introduced a cosmetics bill last Congress. We reintroduced
2475 the same cosmetics bill in this Congress, and as you know,
2476 most people believe that the government makes sure that
2477 personal care products like shampoo and cosmetics are safe
2478 before they are sold. Does the FDA have statutory authority
2479 to require safety testing of cosmetic ingredients before they
2480 go on the market?

2481 Dr. {Hamburg.} We do not do premarket approval for
2482 cosmetics except in a very limited domain of color additives.

2483 Mr. {Markey.} And can you require a recall of any
2484 product in cosmetics?

2485 Dr. {Hamburg.} If there were serious safety issues
2486 raised with public health consequences, we would with the
2487 company to get them to voluntarily--

2488 Mr. {Markey.} But it is voluntary. You don't have a
2489 mandatory power.

2490 So Ms. Schakowsky and Ms. Baldwin and I are very
2491 interested again in pursuing that legislation and working
2492 with Mr. Pallone and working with the chairman towards the
2493 goal of finding a way of giving you the authority that you
2494 need to work on these issues. So if you would be willing to
2495 work with us, we are willing to work with you and with Mr.

2496 Pallone and others to see if we can do something
2497 legislatively in this area.

2498 Thank you, Mr. Chairman.

2499 Dr. {Hamburg.} Terrific. Thank you.

2500 Mr. {Pitts.} The chair thanks the gentleman. That
2501 concludes round one, and we will go to one follow-up on each
2502 side for round two. The chair recognizes Dr. Burgess for a
2503 follow-up question.

2504 Dr. {Burgess.} Dr. Hamburg, thank you for spending so
2505 much time with us here this morning. I just wanted to follow
2506 up on something that Mr. Ross from Arkansas brought up about
2507 the over-the-counter asthma inhalers, and while I recognize
2508 the problem actually originated in the EPA, not at the FDA,
2509 on the removal of CFCs as a propellant, you know, the fact of
2510 the matter remains, I spent New Year's Eve driving from
2511 pharmacy to pharmacy to make sure I had an adequate supply of
2512 Primatene because as he correctly points out, it is two vials
2513 for \$32, so it is a fairly reasonable price compared to the
2514 expensive price of the albuterol, which is a prescription
2515 device.

2516 My understanding is that the over-the-counter iteration
2517 that is non-CFC is currently in process with the HFA as a
2518 propellant and that FDA is evaluating that. I would just
2519 encourage you to do so with all great dispatch. These are

2520 things that have been around for a long time, and most people
2521 with asthma, as I do, experience times when the disease is
2522 much worse and times when it is not so bad, and those times
2523 when it is not so bad, I may get quite far away from having
2524 anything around the house that would be available to help me,
2525 and it was always comforting to know at 2 o'clock in the
2526 morning I could drive to a 24-hour pharmacy and purchase a
2527 Primatene inhaler. Now the only option is--and I am a
2528 doctor, I can write my own prescription, but for the vast
2529 majority of people, you have to go to the emergency room,
2530 likely going to get a breathing treatment and a pulse
2531 oximeter, maybe a blood gas, and you are going to spend
2532 \$1,500, \$2,500 for what could have been fixed, as Mr. Ross
2533 correctly points out, for a \$20 charge at an all-night
2534 pharmacy.

2535 So it is important to get the over-the-counter option
2536 back out there. Many people use these rescue inhalers not
2537 frequently but from time to time, and that is the part of the
2538 population that really would benefit from having these back
2539 and available again. Can we look to you to help us get
2540 those?

2541 Dr. {Hamburg.} We have indicated that, you know, we
2542 would welcome an application and we will work to expedite the
2543 review.

2544 Dr. {Burgess.} Because the active ingredient is not any
2545 different than what it has been for the last 100 years,
2546 right? And the difference is the propellant, and if it used
2547 in the albuterol inhalers, it can't possibly be harmful. I
2548 think it is as good as CFC. CFC gets you a much better
2549 dispersion. The HFA always ends up in the oropharynx and you
2550 have to relearn how to use it.

2551 But this is important to people, and every member of
2552 this committee, in fact, every Member of Congress is going to
2553 be hearing about this at some time during the year when their
2554 constituents run out of their existing supply of CFC inhalers
2555 and find that they cannot replace them.

2556 Thank you, Mr. Chairman.

2557 Mr. {Pitts.} The chair thanks the gentleman, and Mr.
2558 Pallone is recognized for 5 minutes for one follow-up.

2559 Mr. {Pallone.} Thank you, Mr. Chairman.

2560 Dr. Hamburg, some have suggested that FDA is insisting
2561 on too much clinical trial prior to approval and that it is
2562 resulting in an export of innovation and jobs abroad, and to
2563 help address this situation, some of the members have
2564 suggested that FDA's mission statement should be changed to
2565 include things like job creation and innovation. In fact,
2566 there is a bill, the Food and Drug Administration Mission
2567 Reform Act, that would accomplish this.

2568 Now, even assuming there is some truth to these reports,
2569 and I think that there is important evidence to suggest that
2570 there is not, revising FDA's mission statement seems like a
2571 drastic measure to me, and I just wanted you to comment on
2572 the implication of revising FDA's mission statement to
2573 include things like job creation. How would FDA even begin
2574 to assess whether certain agency actions would create jobs?

2575 Dr. {Hamburg.} Well, I think that it is very, very
2576 important that FDA as a science-based regulatory agency with
2577 a public health mission really focus our efforts on
2578 determining the safety, efficacy and quality of the products
2579 that come before us and that we do our work in the context
2580 that clearly understands that we need to make sure that we
2581 are bringing products to people in a timely way that they
2582 need and count on and that we do need to do everything we can
2583 to make sure we have the most modern and streamlined
2584 approaches and that we work closely with product sponsors in
2585 a way that is transparent, consistent and predictable to
2586 achieve our common goal of making important products
2587 available to people.

2588 I think that our safety and efficacy standards are very
2589 important to the success of industry as well as to improving
2590 and protecting the health of the public.

2591 Mr. {Pallone.} But what I am trying to find out is

2592 whether you would want to revise the FDA's mission statement
2593 to include things like job creation.

2594 Dr. {Hamburg.} Well, I was going to get to that and I
2595 think it would be very hard for us to factor in to this
2596 science-based decision making the question of how would
2597 approving or not approving this product impacts jobs and how
2598 would approving or not approving a product impact jobs of a
2599 competitor, and it would get very, very complicated, and
2600 frankly, I think it would be quite inappropriate and would
2601 ultimately not serve the American people well or serve
2602 industry well, and I think it is something that would be
2603 extremely hard to quantify, and I think that, you know, what
2604 is really important is that we make sure that operating
2605 within the ecosystem of biomedical innovation and product
2606 development that we ensure that we are doing our job as well
2607 as we can, which is to apply science-based, data-driven
2608 processes to our decision making, do it in as modern and
2609 streamlined a way as possible, and work as effectively with
2610 industry and other stakeholders to deliver the products that
2611 people need.

2612 Mr. {Pallone.} Thank you.

2613 Mr. {Pitts.} The chair thanks the gentleman. That
2614 concludes our questions for panel one. The chair thanks the
2615 panel, specifically Dr. Hamburg, for your excellent

2616 testimony. It is very important information you have shared
2617 with the committee.

2618 We will now excuse panel one and call panel two to the
2619 witness table, and while we change panels, we will take a 5-
2620 minute recess and reconvene at 12:45.

2621 [Recess.]

2622 Mr. {Pitts.} We will ask all of guests and witnesses to
2623 please take their seats, and would like to ask at this time
2624 unanimous consent to enter into the record a statement by
2625 NCPA, that is community pharmacists, and NACDS, National
2626 Association of Chain Drug Stores, into the record. It has
2627 been shared with the other side, so without objection, so
2628 ordered.

2629 [The information follows:]

2630 ***** COMMITTEE INSERT *****

|
2631 Mr. {Pitts.} I would like to now welcome panel two and
2632 thank all of you for agreeing to testify before the
2633 subcommittee today, and I would like to quickly introduce our
2634 expert panel.

2635 Mr. Geno Germano, President and General Manager of
2636 Specialty Care and Oncology at Pfizer, is our first guest.
2637 Dr. David Gollaher, President and CEO of California
2638 Healthcare Institute. Mr. Richard Pops, Chairman and CEO of
2639 Alkermes. Mr. Pops is testifying on behalf of the
2640 Biotechnology Industry Organization. Mr. Allan Coukell,
2641 Director of Medical Programs for the Pew Health Group; Ms.
2642 Diane Dorman, Vice President of Public Policy at the National
2643 Organization of Rare Disorders; Dr. David Wheadon, the Senior
2644 Vice President for Scientific and Regulatory Affairs at
2645 PhRMA; and Dr. Daniel Frattarelli, Chair of the American
2646 Academy of Pediatrics, Committee on Drugs.

2647 So we will go in that order. Again, thank you all for
2648 coming. We have your prepared statements, and we will ask
2649 each of you to summarize in 5 minutes your opening
2650 statements.

2651 Mr. Germano, we will begin with you. You are recognized
2652 for 5 minutes.

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2653 ^STATEMENTS OF GENO GERMANO, PRESIDENT AND GENERAL MANAGER,
2654 SPECIALTY CARE AND ONCOLOGY, PFIZER, INC.; DAVID GOLLAHER,
2655 PH.D., PRESIDENT AND CEO, CALIFORNIA HEALTHCARE INSTITUTE;
2656 RICHARD POPS, CHAIRMAN AND CEO, ALKERMES, ON BEHALF OF
2657 BIOTECHNOLOGY INDUSTRY ORGANIZATION; DAVID E. WHEADON, M.D.,
2658 SENIOR VICE PRESIDENT, SCIENTIFIC AND REGULATORY AFFAIRS,
2659 PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA; ALLAN
2660 COUKELL, DIRECTOR OF MEDICAL PROGRAMS, PEW HEALTH GROUP, THE
2661 PEW CHARITABLE TRUSTS; DIANE EDQUIST DORMAN, VICE PRESIDENT,
2662 PUBLIC POLICY, NATIONAL ORGANIZATION FOR RARE DISORDERS; AND
2663 DANIEL A.C. FRATTARELLI, M.D., F.A.A.P., CHAIR OF PEDIATRICS,
2664 OAKWOOD HOSPITAL AND MEDICAL CENTER, AND CHAIR, AMERICAN
2665 ACADEMY OF PEDIATRICS, COMMITTEE ON DRUGS

|
2666 ^STATEMENT OF GENO GERMANO

2667 } Mr. {Germano.} Thank you, Chairman Pitts and members of
2668 the subcommittee. My name is Geno Germano. I am President
2669 and General Manager of Specialty Care and Oncology at Pfizer.
2670 Founded in 1849 in New York City, we have grown to become the
2671 world's largest biopharmaceutical company, providing
2672 treatments for a myriad of diseases that afflict people
2673 around the world. I appreciate this opportunity to testify

2674 on behalf of Pfizer and our 40,000 U.S. colleagues to
2675 unequivocally support the reauthorization of the Prescription
2676 Drug User Fee Act.

2677 Behind the acronym PDUFA is another acronym: R&D,
2678 research and development. Research and development is the
2679 lifeblood of Pfizer. It is the lifeblood of our industry and
2680 it is the lifeblood of great American innovation. Today it
2681 takes on average more than a billion dollars and 12 to 15
2682 years to research and develop a new medicine. Approximately
2683 one in 10,000 compounds that enter the drug discovery phase
2684 is every approved by the Food and Drug Administration and
2685 made available to patients. Our R&D is ultimately codified
2686 in our patents. Patents represent our license to move
2687 forward and are a fundamental legal basis for our existence.

2688 It is important to remember, we file our patents on
2689 compounds in the very early stages of development, often a
2690 decade or more before the review process begins at the FDA.
2691 Therefore, by the time we had submitted an application to
2692 FDA, the patent life is already eroded to a meaningful
2693 extent, making an effective and efficient process with FDA
2694 imperative for our firm.

2695 Biopharmaceutical companies like Pfizer typically have
2696 at most between 10 and 14 years to recoup our investment
2697 before generic competition enters the market. However, the

2698 public value, the public health value of our investment
2699 continues for generations to come.

2700 It is through this foundational work in R&D and
2701 manufacturing that the biopharmaceutical industry supports
2702 more than 3 million U.S. jobs and nearly \$300 billion in
2703 total output to GDP. PDUFA will help keep R&D and new
2704 medicine introductions in the United States.

2705 The financial commitment and significant time and
2706 resources required to develop a drug reflect the
2707 uncertainties inherent in our business. The scientific
2708 uncertainties are ultimately reduced to the core question:
2709 does the benefit of the drug outweigh the risk? And this is
2710 a question we and FDA seek to answer, and it will vary
2711 depending upon the treatment and the intended patient
2712 population. Regulatory uncertainties can complicate this
2713 dynamic if the review process at FDA is ambiguous and
2714 inefficient. This is why a strong partnership and
2715 communication with the FDA are essential.

2716 As the head of the specialty care business, I am
2717 intimately engaged in the development of our medicines. My
2718 business focus is on developing therapies for complex and
2719 rare diseases, many forms of cancer, and vaccines for the
2720 prevention of life-threatening infections.

2721 Pevnar 13, a vaccine for the prevention of pneumococcal

2722 disease, is a great example of an important medical
2723 advancement. In December of last year, Prevnar 13 received
2724 approval from FDA for adults 50 years of age and older under
2725 the accelerated review process, a pathway specifically
2726 intended to speed new medicines to market for significant
2727 unmet health needs. Then last Friday, FDA approved our new
2728 cancer medicine, Enlighta, that we developed for patients
2729 with advanced renal cell cancer whose disease continues to
2730 progress after first-line therapy fails. The development
2731 pathway for critical medicines and vaccines like these are
2732 not cookie cutter in nature, and it is essential to have a
2733 strong, functional regulatory agency for advancements like
2734 these to continue.

2735 In my full statement, I discuss the major provisions of
2736 the new PDUFA agreement. I would like to highlight one of
2737 these, the review enhancements for new molecular entities, or
2738 NMEs, which will have an immediate impact on Pfizer and
2739 medicines in our pipeline. A good example of the benefit of
2740 an effective NME review process is Xalkori, which was
2741 approved by FDA last August. Xalkori is an NME and is the
2742 first lung cancer drug approved by the FDA in more than 6
2743 years. This scientific innovation is also one of the first
2744 personalized medicines targeting a genetic abnormality shared
2745 by only 3 to 5 percent of the 200,000 lung cancer patients

2746 diagnosed in the United States each year. Xalkori was a
2747 fast-track product that was given priority review by FDA.
2748 The goal was to review in 6 months. FDA reviewed it in 4
2749 months. While Xalkori's approval is an example of getting it
2750 right, the challenge we have is making sure that situations
2751 like Xalkori are the rule and not the exception. The NME
2752 review process enhancements will help achieve that goal.
2753 These enhancements embody what we consider to be the
2754 foundation of a successful review: communication and
2755 transparency.

2756 The improved process will encourage better issue
2757 identification and resolution at the fine stages of the
2758 review cycle. Further, these enhancements will have a direct
2759 impact on the dozens of NMEs at various stages of development
2760 in our pipeline. These are potential new treatments and
2761 therapeutic areas such as oncology, pain, cardiovascular
2762 disease and vaccines.

2763 The ability of Pfizer to do its job depends on the
2764 ability of FDA to do its job, and PDUFA provides a framework
2765 and resources for that to happen. PDUFA is must-pass
2766 legislation. It is must-pass for Pfizer and the
2767 biopharmaceutical industry. It is must-pass for FDA, but
2768 most importantly, it is must-pass for patients and society as
2769 a whole.

2770 Thank you for this opportunity to testify. I look
2771 forward to answering any questions you may have and hearing
2772 your views.

2773 [The prepared statement of Mr. Germano follows:]

2774 ***** INSERT 2 *****

|
2775 Mr. {Pitts.} The chair thanks the gentleman and
2776 recognizes the gentleman, Dr. Gollaher, for 5 minutes for an
2777 opening statement.

|
2778 ^STATEMENT OF DAVID L. GOLLAHER

2779 } Mr. {Gollaher.} Thank you, Chairman Pitts and Ranking
2780 Member Pallone. My name is David Gollaher, and I am
2781 President and CEO of the California Healthcare Institute.
2782 California has by far the largest cluster of innovative
2783 research institutions and biotechnology companies in the
2784 world. Today there are about 270,000 jobs directly connected
2785 to biomedical R&D in California.

2786 My purpose today is first to support the reauthorization
2787 of PDUFA, then to explain why PDUFA is critical to drug
2788 innovation, and then briefly to review work that CHI, our
2789 institute, has been conducting with the Boston Consulting
2790 Group, BCG, together and analyzed data that accurately
2791 reflect FDA performance.

2792 I know there has been a lot of criticism of the FDA, but
2793 all of us agree that a strong, efficient FDA is important to
2794 our industry and to patients, an agency that performs well,
2795 encourages medical innovation and a regulatory system that
2796 has clear rules, that operates transparently, builds
2797 confidence among investors, and confidence is key because
2798 patients need to be confident that their drugs meet the
2799 highest standards of safety and effectiveness while industry

2800 needs to be confident that the FDA is abreast of the latest
2801 science and is applying it reasonably to innovative products.

2802 The first point I would like to make is about the
2803 relationship of advanced science to regulation. We live in
2804 an unprecedented age of biological sciences. After the human
2805 genome project was completed in 2003, our ability to
2806 understand diseases at the level of genes and cells is racing
2807 head. Still, though, if we compare the past several years to
2808 the period during the 1980s and 1990s when there was so many
2809 pioneering biotech drugs along with breakthrough drugs for
2810 HIV/AIDS, we can see that today drug development has lagged.
2811 It hasn't kept up with science.

2812 The reasons for this are complicated. For one thing,
2813 our bodies are the most complex organisms in nature, and
2814 developing drugs that have powerful effects on disease
2815 without harming healthy cells and tissue turns out to be
2816 extremely difficult, so difficult, in fact, that developing a
2817 new medicine now costs well over a billion dollars.

2818 In trying to become more efficient and reduce
2819 development costs, the drug industry is searching for the
2820 optimum model for R&D but the most productive model and scale
2821 for biotech research remains a quest in progress.

2822 The problem is that we continue to see high failure
2823 rates for drugs that enter the regulatory pipeline. Only 5

2824 to 8 percent of new molecular entities that start out as drug
2825 candidates make it all the way to the market. Commissioner
2826 Hamburg has pointed out that we are investing between
2827 industry and academia about \$100 billion in research today
2828 and not getting our fair share of new medicines, but this
2829 isn't true across the board. In 2011, the FDA issued a
2830 report citing 35 innovative treatments for hepatitis C,
2831 prostate cancer, lupus, pneumonia and other serious
2832 disorders. This report showed how the FDA used expedited
2833 approval authority, flexible clinical study requirements, and
2834 resources collected under PDUFA to improve the rate of
2835 approvals. Oncology, for instance, emerged as a particularly
2836 bright spot, and our recent work with BCG found that cancer
2837 drugs experience rapid review on the order of 10 to 15
2838 months. But there were other areas--cardiovascular, central
2839 nervous system, gastrointestinal--that stretched almost twice
2840 as long.

2841 The point is, there are major differences in timelines
2842 depending on a drug's therapeutic area, and in our view, this
2843 suggests an opportunity, namely, for the FDA to learn from
2844 its own best practices and then replicate those practices
2845 across the agency. To accomplish this, though, will require
2846 more data than we have had in the past but timely, accurate
2847 data would prove equally valuable for internal FDA

2848 benchmarking and for industry management.

2849 It is hard to overstate the importance of good data. A
2850 time-honored principle of management is that what gets
2851 measured gets done. Our work with BCG over the past 2 years,
2852 mining the agency phone data in order to gain a better
2853 understanding of how it operates, suggests a few things to
2854 us. First, that we meet regularly together and analyze the
2855 best possible data and that there is an opportunity to
2856 provide longitudinal data over the next PDUFA cycle so that 5
2857 years from now FDA, industry and Congress can share the
2858 understanding of real trends over time. It is ironic that
2859 for an agency that regulates more than 20 percent of U.S. GDP
2860 and relies increasingly on industry user fees that there has
2861 been so little in the way of consistent tracking.

2862 In addition, better data may help the agency, Congress
2863 and industry to develop a better understanding of benefits
2864 versus risks. Virtually all medicine carry some capacity for
2865 harm, and a zero-risk mentality would shut down development
2866 of beneficial drugs altogether. But more attention needs to
2867 be devoted to how the FDA's policies and operations encourage
2868 or discourage investment in different therapeutic areas. In
2869 other words, how should we measure risk if the agency's
2870 demands for data become so intense that investors avoid that
2871 therapeutic area altogether. This is happening today in

2872 areas like diabetes and obesity.

2873 I would like to conclude by observing that PDUFA has
2874 been a remarkable success. For this legislation to move
2875 science forward, it needs to remain highly focused on
2876 enabling the agency to promote innovation, on encouraging it
2877 to address areas of inefficiency, on balancing its mission to
2878 protect public health with the importance of attracting
2879 robust private sector investment into new drugs and
2880 biologics. Ultimately, public health and economic
2881 competitiveness are two sides of the same coin. Without
2882 investment, the next generation of breakthroughs will never
2883 materialize nor will the jobs to manufacture them.
2884 Commissioner Hamburg wrote an op-ed last year calling FDA
2885 America's innovation agency. I think this is more an
2886 aspiration than a historical fact, but it is an aspiration
2887 that we all share, and PDUFA V is an important step toward
2888 accomplishing it.

2889 Thank you, and I would be happy to answer any questions.

2890 [The prepared statement of Mr. Gollaher follows:]

2891 ***** INSERT 3 *****

|
2892 Mr. {Pitts.} The chair thanks the gentleman and
2893 recognizes Mr. Pops for 5 minutes for an opening statement.

|
2894 ^STATEMENT OF RICHARD F. POFS

2895 } Mr. {Pops.} Thank you, Chairman Pitts and Ranking
2896 Member Pallone. I appreciate the opportunity to be here
2897 today. I am Richard Pops, Chairman and CEO of Alkermes, and
2898 I am here testifying on behalf of the Biotechnology Industry
2899 Organization, or BIO. I coordinated BIO's engagement on the
2900 PDUFA V discussions with FDA, and I have got more than 20
2901 years of experience in managing biotechnology companies and
2902 successfully developing new therapies for patients. So I
2903 know firsthand the impact that PDUFA has had on patients and
2904 on medical innovation.

2905 BIO, in summary, supports a swift enactment of PDUFA V
2906 recommendations that improve this regulatory process and
2907 provide patients and doctors with earlier access to
2908 breakthrough therapies that we focus our lives on developing.
2909 So at Alkermes, our company, we are in a very exciting phase
2910 of growth with a diversified portfolio of commercial products
2911 that have already made it through the FDA process, and we
2912 have had that experience, but also new medications in
2913 development where we are in the midst of the regulatory
2914 process addressing central nervous system disorders such as
2915 addiction, schizophrenia and depression.

2916 We began as a raw startup in labs next to MIT up in
2917 Massachusetts, and today we employ over 1,200 individuals in
2918 Massachusetts, Georgia, Ohio and worldwide, and we operate
2919 large manufacturing facilities in both Ohio and in Georgia as
2920 well.

2921 The key to our success and I think the success of the
2922 industry in general is a reliable and predictable FDA, and
2923 the PDUFA program is an incredibly important part of it.

2924 The PDUFA V recommendations are based on the principles
2925 that a science-based transparent and well-managed review
2926 process that appropriately balances benefit and risk can
2927 enhance the public trust and increase patient access to new
2928 medicines. Industry and FDA agreed upon a set of
2929 enhancements under PDUFA V designed to reinforce FDA's review
2930 performance and get back to basics for patients. These
2931 proposals have also been informed by an unprecedented level
2932 of public input, which has further strengthened the technical
2933 agreement. These enhancement include a new molecular entity,
2934 or NME, review program that we hope will lead to further
2935 review cycles and earlier patient access to needed
2936 treatments, enhanced communication during drug development,
2937 regulatory science modernization and robust safety and
2938 postmarket surveillance capacities.

2939 While BIO, of course, supports the entirety of the

2940 technology agreement, today I would like to focus primarily
2941 on the enhanced communication in PDUFA V. This initiative is
2942 based on the philosophy that timely interaction communication
2943 with biotechnology and life science companies during drug
2944 development should be a core agency activity. While many
2945 biotechnology companies operate on the cutting edge of
2946 biomedical science and develop new therapies, science is a
2947 collaborative process. It doesn't occur in a vacuum. And it
2948 is critical to promote interactive scientist-to-scientist
2949 communications between FDA and sponsors.

2950 In the course of drug development, we often have simple
2951 clarifying questions, the responses of which could have a
2952 significant impact on the development program but are not
2953 extensive enough to warrant formal meetings with FDA. To
2954 obtain timely responses to such questions, we currently often
2955 have to engage in lengthy exchange of multiple formal letters
2956 with FDA, which is an inefficient and cumbersome use of both
2957 FDA's and sponsors' time. For small biotechnology companies
2958 reliant on limited venture capital funding sources, these
2959 delays can create significant impediments to development
2960 programs and therefore innovation.

2961 So as part of the enhanced communication program, FDA
2962 will establish best practices for this type of interactive
2963 dialog and train staff on communication. Independent reports

2964 commissioned by FDA have demonstrated that enhanced
2965 communication during drug development ultimately results in
2966 higher quality applications which can improve efficiency for
2967 FDA reviewers. This proposal was a top BIO priority and we
2968 are pleased that it was included in the agreement.

2969 In addition to the enhanced communication features, the
2970 PDUFA V agreement makes new resources available to modernize
2971 regulatory science in the areas of personalized medicine and
2972 rare disease drug research. Modern approaches to drug
2973 development and evaluation will introduce new efficiencies in
2974 the drug development process and provide FDA with additional
2975 tools to evaluate the benefits and the risks of
2976 pharmaceutical products. These proposals will also integrate
2977 more structured and systematic approaches to addressing
2978 benefits and risks and allow FDA to conduct outreach to
2979 patients and hold workshops to better understand patient
2980 perspectives on disease severity and unmet medical need.

2981 BIO looks forward to working with the committee and the
2982 FDA to implement PDUFA V, and I want to thank you again for
2983 having us here today.

2984 [The prepared statement of Mr. Pops follows:]

2985 ***** INSERT 4 *****

|
2986 Mr. {Pitts.} The chair thanks the gentleman and
2987 recognizes Dr. Wheadon for 5 minutes for an opening
2988 statement.

|
2989 ^STATEMENT OF DAVID E. WHEADON

2990 } Dr. {Wheadon.} Thank you. Chairman Pitts Ranking
2991 Member Pallone and members of the subcommittee, good
2992 afternoon. I am David Wheadon, Senior Vice President of
2993 Scientific and Regulatory Affairs at the Pharmaceutical
2994 Research and Manufacturers of America, better known as PhRMA.
2995 PhRMA appreciates this opportunity to testify today and share
2996 our views on the fifth reauthorization of the Prescription
2997 Drug User Fee Act, PDUFA, and the reauthorization of the Best
2998 Pharmaceuticals for Children Act, BPCA, and the Pediatric
2999 Research Equity Act, PREA.

3000 PhRMA and its member companies, the country's leading
3001 pharmaceutical research and biotechnology companies, strongly
3002 support the original goals of PDUFA, namely to provide
3003 patients with faster access to innovative medicines, to
3004 preserve and strengthen FDA's high standards for safety,
3005 efficacy and quality, and to advance the scientific basis for
3006 the agency's regulatory oversight. PDUFA has advanced public
3007 health by accelerating the availability of innovative
3008 medicines to patients while helping to ensure patient safety.

3009 Furthermore, PDUFA has helped to improve America's
3010 competitiveness around the world. Since the passage of the

3011 original Prescription Drug User Fee Act in 1992, the United
3012 States has become the world leader in bringing new medicines
3013 to patients first. Ensuring that the United States maintains
3014 a policy and regulatory environment that encourages an
3015 efficient, consistent and predictable drug review process is
3016 key to keeping America competitive in today's global economy.

3017 PhRMA strongly endorses the recommendation of PDUFA V
3018 performance goals letter, which was created with
3019 unprecedented transparency and input from diverse
3020 stakeholders. This agreement will provide FDA with the
3021 resources and the tools required to further enhance the
3022 timeliness, completeness and efficiency of the drug review
3023 process including provisions to advance regulatory science
3024 and modernize drug development, to improve benefit-risk
3025 decision making, and to further strengthen FDA's focus on
3026 patient safety.

3027 I would like to focus for a moment on one specific
3028 provision in the PDUFA V agreement. PDUFA V will improve the
3029 review process for new molecular entity, NME, drug and
3030 biologic applications which will be particularly significant
3031 for patients because NMEs are novel compounds that have the
3032 potential to address unmet medical needs and advance patient
3033 care. Specifically, it is anticipated that earlier and more
3034 comprehensive communication between the agency and drug

3035 sponsors as required in this enhanced review program will
3036 improve the rate of on-time first-cycle successes. The
3037 success of the new review program and of the agency's ability
3038 to achieve its drug review goals will be independently
3039 assessed and reported in 2015 and 2017. PDUFA V will
3040 continue to provide FDA with the resources and tools that are
3041 essential to support patient safety and promote medical
3042 innovation through enhanced timeliness, completeness and
3043 efficiency of the drug review process.

3044 PhRMA encourages Congress to reauthorize PDUFA in a
3045 timely manner based on the negotiated PDUFA V performance
3046 goals and to minimize the inclusion of additional provisions
3047 that may have the unintended consequence of distracting from
3048 the act's original intent.

3049 The Best Pharmaceuticals for Children Act and the
3050 Pediatric Research Equity Act have been extraordinarily
3051 successful in improving medical care for children by driving
3052 research to create innovative medicines for use in pediatric
3053 patients. According to the FDA, the current pediatric
3054 exclusivity program has done more to spur research and
3055 generate critical information about the use of medicines in
3056 pediatric patients than any other government initiative.
3057 Ensuring that the pediatric exclusivity incentive is
3058 preserved is key to continued innovation and improvement in

3059 pediatric medical care in the face of rising research costs.
3060 Since their initial enactment and subsequent
3061 reauthorizations, BPCA and PREA have been subject to a sunset
3062 clause under which their provisions expire after 5 years
3063 unless reauthorized by Congress. To build upon the
3064 tremendous success of BPCA and PREA in improving medical care
3065 for children, Congress should permanently reauthorize BPCA
3066 and PREA.

3067 In closing, I would like to use this opportunity to
3068 briefly discuss the issue of pharmaceutical supply chain
3069 integrity. PhRMA supports granting FDA discretion to set
3070 routine inspection intervals for foreign and domestic
3071 facilities according to risk. We support providing FDA with
3072 the flexibility to prioritize inspections of foreign
3073 establishments based on the risk they present and believe
3074 relying on set criteria such as compliance history, time
3075 since last inspection, and volume of type of products
3076 produced will enhance the FDA's ability to target its
3077 inspection resources efficiently and effectively. A more
3078 detailed description of additional recommendations on how to
3079 strengthen the integrity of the supply chain can be found in
3080 PhRMA's written testimony. We look forward to continuing to
3081 work with this committee, FDA and other stakeholders on these
3082 important issues.

3083 Chairman Pitts and members of the subcommittee, thank
3084 you for the opportunity to testify. I am happy to answer any
3085 questions.

3086 [The prepared statement of Dr. Wheadon follows:]

3087 ***** INSERT 5 *****

|
3088 Mr. {Pitts.} The chair thanks the gentleman and
3089 recognizes Mr. Coukell for 5 minutes for an opening
3090 statement.

|
3091 ^STATEMENT OF ALLAN COUKELL

3092 } Mr. {Coukell.} Chairman Pitts, Ranking Member Pallone
3093 and committee members, thank you for the opportunity to be
3094 here today.

3095 My name is Allan Coukell. I am the Director of Medical
3096 Programs with the Pew Health Group, which seeks to improve
3097 the health and wellbeing of Americans by supporting policies
3098 that foster innovation and reduce risks to consumers. I am
3099 here today to talk about the safety of the U.S. drug supply.
3100 Pew has focused on this for the last 4 years as has this
3101 committee.

3102 In recent years, pharmaceutical manufacturing has been
3103 transformed. What was once a domestic industry is now
3104 global. Forty percent of our finished drugs and 80 percent
3105 of the active ingredients now originate outside our borders.
3106 Much of the supply is purchased in India and China. The
3107 number of non-U.S. plants that supply the United States has
3108 doubled in just the past decade. Yet the Food, Drug, and
3109 Cosmetic Act remains overwhelmingly domestically focused.
3110 This puts consumers at risk and American manufacturers on an
3111 uneven playing field. While the leading companies are
3112 already doing thorough assessments of their supply chains, we

3113 have to make sure that there is no incentive for the weaker
3114 actors to gain a competitive advantage by cutting corners.

3115 Just 4 years ago, hundreds of American patients were
3116 sickened and some died after they received a blood-thinning
3117 drug, heparin, that had been adulterated during manufacture
3118 in China. This was a U.S. company that was reliant on an
3119 upstream network of suppliers that it didn't know and
3120 couldn't control. Since that tragedy, this committee has
3121 held nine hearings and heard from more than 60 witnesses.
3122 You have conducted a careful and thorough investigation that
3123 has identified serious gaps in the system. We don't know who
3124 adulterated that heparin from China but we certainly know how
3125 to reduce the risk that someone else will adulterate some
3126 other imported drug in the future.

3127 Congress needs to act to protect Americans. We need a
3128 system that reduces risks, that rewards companies that have
3129 proper quality systems in place, promotes an even playing
3130 field, and uses taxpayer dollars efficiently. Pew's ``After
3131 Heparin'' report identifies the risks and suggests some
3132 pragmatic solutions. Let me make three key points.

3133 First, inspections. Not that far from here is one of
3134 the U.S.'s largest pharmaceutical manufacturing facilities.
3135 It is a Mylan facility in West Virginia that employs a lot of
3136 people, and like any other domestic manufacturing facility,

3137 it can expect an FDA inspection about every 2 years. That
3138 company's competitors in India and China also making drugs
3139 for the U.S. market face nowhere near that level of scrutiny.
3140 A plant outside the United States knows that FDA may visit
3141 only once before the product is first approved and then may
3142 never return, and that reduces the incentive to make ongoing
3143 investments in quality. The FDA should inspect plants both
3144 domestic and overseas based on risk, and no company should go
3145 uninspected for more than 4 years. We support the call by
3146 Mylan and others in industry for a level playing field to
3147 ensure safety regardless of where the drugs come from.

3148 Inspections are one part of the solution. Let me talk
3149 for a moment about supplier quality. Pfizer, represented
3150 here today on this panel, has invested heavily in supply
3151 chain integrity from production and ingredient sourcing to
3152 distribution security. Let me quote from previous testimony
3153 by Pfizer. They said ``Companies in emerging markets are
3154 operating in a development regulatory environment with a
3155 novice inspector. Many have rudimentary quality systems, or
3156 none at all. Before a U.S. pharmaceutical firm can
3157 considering sourcing from these suppliers, it is imperative
3158 that the firm work with suppliers to upgrade their quality
3159 systems and standards.''

3160 The Pew report outlines well-documented cases of

3161 suppliers concealing the actual sources of drug ingredients,
3162 in some cases bringing in chemical materials that were not
3163 intended for pharmaceutical use. We call for modernizing
3164 current regulations to ensure that every company has
3165 appropriate measures in place to ensure quality standards at
3166 their suppliers.

3167 And finally, we need to make sure that the FDA has the
3168 tools that are appropriate for today's global paradigm. For
3169 example, companies with high quality systems and an
3170 established track record shouldn't face delays at the border.
3171 Companies that don't have those things should face heightened
3172 scrutiny. We need to make sure that the FDA has the clear
3173 authority at the border to refuse products when the plant
3174 that made them has denied an FDA inspection.

3175 The proposed generic user fee agreement will provide FDA
3176 with new resources for increased inspections of overseas
3177 generic manufacturing. It is an important step, and the
3178 PDUFA reauthorization is the opportunity to bringing the FDA
3179 into the 21st century to give Americans a greater assurance
3180 of safety.

3181 Let me conclude with something that we heard often over
3182 the course of our research. If there are feasible practical
3183 steps that we don't take, it is not a question of if there is
3184 another tragedy, it is a question of when.

3185 Thank you, and I welcome any questions.

3186 [The prepared statement of Mr. Coukell follows:]

3187 ***** INSERT 6 *****

|
3188 Mr. {Pitts.} The chair thanks the gentleman and
3189 recognizes Ms. Dorman for 5 minutes for an opening statement.

|
3190 ^STATEMENT OF DIANE EDQUIST DORMAN

3191 } Ms. {Dorman.} Thank you, Mr. Chairman. Thank you,
3192 Ranking Member Pallone. Thank you for the opportunity to
3193 testify before you today. I am Diane Dorman, Vice President
3194 for Public Policy for NORD, the National Organization for
3195 Rare Disorders.

3196 Since 1983, NORD has served as a leading voice and
3197 advocate for the approximately 30 million men, women and
3198 children with rare diseases in the United States. NORD's
3199 mission is to foster a social, political and financial
3200 culture of innovation that supports the basic and
3201 translational research necessary to develop new diagnostic
3202 tests and therapies for all rare disorders. This requires a
3203 regulatory environment that encourages the development and
3204 timely approval of new, safe and effective treatments for
3205 rare disorders.

3206 Reauthorizing PDUFA presents an opportunity for Congress
3207 to achieve that goal. Greater clarity and predictability for
3208 the review of novel therapies for rare disorders can be
3209 achieved by allocating some of the PDUFA resources to support
3210 the enhancement of regulatory science. Of special
3211 significance in the draft agreement is the rare disease

3212 initiative that will enhance development of drugs and
3213 biologics for the treatment of rare conditions. We support
3214 these efforts and look forward to the opportunity to work
3215 with the agency and with Congress to guarantee the success of
3216 this initiative.

3217 The rare disease community was heartened recently when
3218 the drug approval summary for 2011 was announced. Of the 35
3219 innovative drugs approved in 2011, ten were orphan drugs. We
3220 hope and expect that further investment in orphan products
3221 will lead to continued development of therapies that address
3222 the unmet medical needs of patients. We are encouraged that
3223 the Orphan Drug Act has brought about such successful
3224 innovation in the market for rare disease therapies.

3225 The reality is that we have barely started the journey.
3226 There is still approximately 6,800 rare diseases that lack an
3227 FDA-approved therapy. The reauthorization of PDUFA offers
3228 hope that we may build on previous successes by strengthening
3229 the review process still further and by creating an
3230 environment that encourages innovation and investment. We
3231 believe that the rare disease program will enhance the
3232 regulatory science needed to accelerate development of new
3233 therapies. This initiative allocates a small fraction of
3234 user fees to support the existing rare disease program and
3235 CDER. The agreement completes the current staffing and

3236 implementation plan and establishes a rare disease liaison
3237 within the Center for Biologics.

3238 Last October, NORD released a landmark study that looked
3239 at all drugs for diseases other than cancer approved as
3240 orphans since 1983 to identify whether and when FDA exercised
3241 flexibility in the review process. Of the 135 drug approvals
3242 studied, NORD concluded that the FDA demonstrated flexibility
3243 in the review of effectiveness data on orphan drug therapies
3244 for two out of every three orphan drugs approved. FDA
3245 clearly has demonstrated in its actions on orphan products
3246 over the past three decades that it recognizes the importance
3247 of therapies for people with rare disorders. NORD believes
3248 it would be helpful for such flexibility to be recognized in
3249 a formal FDA policy and for officials to incorporate
3250 flexibility in a systematic way in their evaluations of each
3251 new therapy.

3252 While the statutory standard for safety and efficacy
3253 should be the same for all medical products, enhancement of
3254 the rare disease program will allow FDA to provide greater
3255 clarity in how it applies the standards for safety and
3256 effectiveness to orphan products. A formal policy setting
3257 forth the agency's view of flexibility in conducting orphan
3258 product review is likely to provide more certainty to
3259 innovators seeking to develop rare disease therapies.

3260 Further, we would like to see the proposed public meeting and
3261 staff training implementation dates moved forward to occur no
3262 later than 2013.

3263 PDUFA V will provide FDA with the resources needed to
3264 maintain a strong professional staff that is necessary for
3265 the development of clear guidelines and the expedited review
3266 of innovative therapies.

3267 In addition to the rare disease program, there are two
3268 other policy considerations that we feel are worthy of your
3269 consideration: current conflict-of-interest provisions and
3270 patient participation in risk assessment. First, during
3271 FDAAA negotiations, NORD argued that because patient
3272 populations are very small and the number of researchers who
3273 study a particular rare disease is limited, identifying
3274 experts not financially conflicted to sit on an advisory
3275 committee would be difficult, if not impossible. Those
3276 concerns were realized in 2008 when it took the FDA nearly 6
3277 months to identify an expert to review a life-saving therapy
3278 to treat infantile spasms. While conflict-of-interest
3279 considerations are clearly necessary, our view is that the
3280 existing provisions in the Federal Advisory Committee Act and
3281 the Ethnics in Government Act of 1978 are adequate to
3282 safeguard against conflicts of interest. A separate standard
3283 is not needed.

3284 Second, NORD, working with like-minded patient
3285 organizations, has developed a proposal submitted to the FDA
3286 to allow the patient community to communicate on a more
3287 frequent and periodic basis with medical reviewers and other
3288 relevant FDA staff to make risk tolerance and other
3289 decisions. We advocate that more systematic processes be
3290 established at FDA to enable contributions from the patient
3291 community at the time that critical decisions on risk
3292 tolerance are being made. We do not seek to create a
3293 burdensome or time-consuming process; rather, we want to be
3294 sure that patients have the opportunity to share their views.

3295 In closing, I want to thank the committee again for
3296 giving NORD the opportunity to testify today regarding the
3297 reauthorization of PDUFA. The rare disease community
3298 believes that engaging Congress and FDA officials in the
3299 process has and will continue to lead to practical, detailed
3300 improvements to the regulatory process that will accelerate
3301 the development of orphan products from concept to access.

3302 Thank you very much.

3303 [The prepared statement of Ms. Dorman follows:]

3304 ***** INSERT 7 *****

|
3305 Mr. {Pitts.} The chair thanks the gentlelady and
3306 recognizes Dr. Frattarelli for 5 minutes for an opening
3307 statement.

|
3308 ^STATEMENT OF DANIEL A.C. FRATTERELLI

3309 } Dr. {Frattarelli.} Thank you. Mr. Chairman, members of
3310 the subcommittee, my name is Dr. Daniel Frattarelli. I am a
3311 practicing pediatrician and Chair of Pediatrics at Oakwood
3312 Hospital in beautiful Dearborn, Michigan. I am here today
3313 representing the American Academy of Pediatrics in my
3314 official capacity as Chair of the AAP's Committee on Drugs.

3315 The testimony I give you today is supported and endorsed
3316 by the Elizabeth Glazer Pediatric AIDS Foundation, and I am
3317 here today to discuss the Best Pharmaceuticals for Children
3318 Act and the Pediatric Research Equity Act, and I would like
3319 to begin just by amplifying something that Dr. Wheadon said.
3320 When we are looking at BPCA and PREA, we can really say
3321 unequivocally that these two laws have added more pediatric-
3322 specific information to the labels of drugs and biologics
3323 than we have been able to in the 70 years prior to their
3324 enactment, and it is vitally important for infants, children
3325 and adolescents that these laws be reauthorized.

3326 I wish to extend the academy's sincerest thanks to
3327 Representative Anna Eshoo for her longstanding support and
3328 for championing these important laws for children, and
3329 although not the subject of today's hearing, the academy also

3330 wishes to acknowledge and thank Representatives Mike Rogers
3331 and Ed Markey, who together authored the Pediatric Medical
3332 Device Safety and Improvement Act of 2007.

3333 Now, as a pediatrician, I see firsthand the need for all
3334 children to have medicines that are studied for their use,
3335 and thankfully, we have gone from a time back when I trained
3336 when about 80 percent of the drugs that we used didn't have
3337 any specific pediatric labeling, to today, where that number
3338 is down to about 50 percent, and this success is a direct
3339 result of BPCA and PREA. Since 1997, 426 labels have been
3340 updated with new pediatric information, and in many cases,
3341 studies have altered the dosages or formulation we give our
3342 patients, and in others, drugs that were previously thought
3343 to be safe or effective in children have proved not to be.

3344 The 2007 reauthorization led to several improvements in
3345 the function of these laws. All BPCA and PREA studies now
3346 result in label changes, and the number of times companies
3347 have declined BPCA studies has gone down tremendously while
3348 the number of products studied under BPCA and PREA has gone
3349 up, and the consistency and quality of pediatric studies has
3350 improved significantly, largely through the hard work of the
3351 FDA's internal pediatric review committee.

3352 Based on what we have learned about these laws since
3353 1997, the academy offers five recommendations for

3354 improvements to BPCA and PREA in 2012. The first of these is
3355 to do pediatric study plans earlier. Now, PREA is a
3356 premarket requirement for safety and effectiveness. However,
3357 the law does not require the submission of a plan for
3358 pediatric studies until a company submits its drug
3359 application to the FDA. Submission of this plan so late in
3360 the process can lead to insufficient planning and potentially
3361 avoidable delays in getting important pediatric data. The
3362 AAP therefore recommends amending PREA to require the
3363 submission of a pediatric study plan by the end of phase II.

3364 The second recommendation is to improve accountability.
3365 We heard this already also that 78 percent of PREA studies
3366 due after September 27, 2007, are currently late or were
3367 completed late. While many of these studies might be delayed
3368 for good reason such as difficulty recruiting patients, FDA's
3369 publicly available data do not distinguish between the
3370 reasonable and the unreasonable delays. We feel the FDA
3371 should have the authority to grant extensions when there is a
3372 good cause, but in cases where there isn't a good cause, FDA
3373 should have added enforcement tools comparable to those it
3374 has for postmarketing commitments involving adults.

3375 Third recommendation is to promote studies in younger
3376 age groups. Now, the neonatologists, the people who take
3377 care of babies from birth to age one month, report that

3378 almost 90 percent of the drugs that they use routinely have
3379 never been labeled for this population, and neonatal drug
3380 research faces some unique hurdles. The AAP believes that
3381 the FDA should be required to ensure that BPCA and PREA
3382 written requests includes neonates whenever possible, and if
3383 they are not, explain the rationale why. PREA should be
3384 triggered when a company decides to expand to a new age group
3385 so that pediatricians will have data for an age group that is
3386 as young as the FDA determines necessary. The GAO also
3387 identified a lack of neonatal expertise at the FDA, and we
3388 feel that a dedicated neonatologists added at FDA would
3389 assist in reviewing divisions in thinking through these
3390 neonatal drug studies.

3391 Fourth recommendation is to increase transparency. As
3392 we learned in the 2007 amendments, increased transparency
3393 benefits policymakers and researchers. Building on this, the
3394 AAP also recommends that new written requests under BPCA be
3395 made public at the time they are accepted or declined.

3396 And our fifth recommendation is to make PREA permanent.
3397 We call upon Congress to make PREA permanent in 2012. The
3398 FDA currently has permanent authority to ensure the safety
3399 and efficacy of drugs used in adults, and children deserve
3400 the same. As part of this legislation, Congress should also
3401 reauthorize the important program at the National Institutes

3402 of Health to fund the study of older drugs no longer subject
3403 to BPCA and PREA.

3404 I would like to thank the committee again for allowing
3405 me the opportunity to share with you the strong support of
3406 the American Academy of Pediatrics for the reauthorization of
3407 BPCA and PREA, and would be happy to answer any questions
3408 that you have.

3409 [The prepared statement of Dr. Frattarelli follows:]

3410 ***** INSERT 8 *****

|
3411 Mr. {Pitts.} The chair thanks the gentleman, and I will
3412 now begin questioning and recognize myself for 5 minutes for
3413 that purpose.

3414 Mr. Germano, will you explain how the PDUFA agreement
3415 will help improve predictability and transparency of the drug
3416 review process, why this is important to American patients
3417 and jobs?

3418 Mr. {Germano.} I think that the measure that I spoke of
3419 in my testimony was a measure that is particularly important.
3420 The PDUFA provisions allow for a review process that has a
3421 number of important enhancements. Most notably, as the
3422 number of interactions that now would be mandatory for
3423 communication and transparency between the agency and the
3424 sponsor companies, I think very often issues that arise
3425 during the review process are not clearly understood or not
3426 consistently understood between the agency and the sponsor
3427 company, and I think that this enhanced level of
3428 communication and transparency is likely to result in a
3429 greater level of understanding and issue resolution and
3430 consistency in the review process leading to, you know,
3431 review times that likely could be shortened, and, you know, a
3432 clarity on expectations between the two parties. If we can
3433 get through the process more efficiently, we can bring new

3434 products to the market more quickly and benefit patients, and
3435 it is good all around for the FDA, for the company and for
3436 physicians and patients who need our medicines.

3437 Mr. {Pitts.} Thank you.

3438 I will just down the line. Dr. Gollaher, in your
3439 testimony you make a connection between differences in FDA
3440 review times across therapeutic areas and how that affects
3441 development decisions by investors and companies, and can you
3442 speak to that issue a little further? You also mentioned the
3443 adage that you can't manage what you don't measure, and PDUFA
3444 has long required the agency to report on numerous
3445 performance measurements. You suggest that performance would
3446 benefit from some more granular reporting at the review
3447 division level. Can you elaborate on that?

3448 Mr. {Gollaher.} Sure. I think those two are related.
3449 Investors in large companies like Pfizer but even more
3450 venture capitalists who are looking at funding new ventures
3451 consider the time to market for their inventions, for their
3452 investments, and as we have seen, for example, in diabetes
3453 and in cardiovascular, venture investment has almost
3454 completely dried up because the time for review and the cost
3455 of clinical studies is so great. So the FDA exists in an
3456 ecosystem. It exists in a market in which it sends signals
3457 about its standards, about times and so forth, and those

3458 signals are extraordinarily important for the amount of
3459 investment that flows into new inventions and innovative
3460 products.

3461 On the data question, you know, we just heard the
3462 Commissioner talking about moving to electronic submissions
3463 and basically taking the FDA from the analog era that it has
3464 inhabited to the digital age, and that is really important,
3465 but at bottom, FDA is really a data management agency. I
3466 mean, it collects data from industry, it analyzes the data
3467 and makes decisions. The opportunity for a better assessment
3468 of some of the metrics that people have been talking about,
3469 for example, transparency, communication and so forth, and
3470 how the agency is performing against those can be measured
3471 and I think should be part of the ongoing assessment of
3472 agency performance.

3473 Mr. {Pitts.} Thank you.

3474 Mr. Germano, you had mentioned in your testimony that
3475 one of your vaccines got approved through the accelerated
3476 approval pathway. Can you give us background on the
3477 importance of the accelerated approval pathway, why it is
3478 important to get the vaccine to patients as soon as possible?

3479 Mr. {Germano.} Yes. Just last December, our vaccine
3480 Prevnar 13 was approved for prevention of pneumococcal
3481 disease in individuals 50 years of age and older under this

3482 accelerated review process, and the accelerated review
3483 process is a measure that the FDA can use when they deem a
3484 medicine or, in this case, a vaccine to be appropriate to
3485 satisfy a significant unmet medical need for a serious
3486 disease or a serious condition, and in this case, just to
3487 give you some understanding of the seriousness of
3488 pneumococcal disease, pneumococcal pneumonia accounts for
3489 over 300,000 hospitalizations a year in the United States and
3490 over 25,000 deaths, so it is a very significant disease state
3491 and a high burden of both disease and high burden of cost for
3492 society. So the FDA utilized the accelerated review process
3493 to review and approve this medicine and now really that there
3494 is only one other hurdle to get through to bring this vaccine
3495 to patients or to society really and that is a CDC
3496 recommendation for usage, and we are hopeful that we will get
3497 a CDC recommendation later this month when their advisory
3498 council on immunization practices meets, and then we will be
3499 able to bring the vaccine to the American public.

3500 Mr. {Pitts.} Thank you.

3501 I think we are going to have to do a second round. My
3502 time is up. I will recognize the ranking member, Mr.
3503 Pallone, for 5 minutes for questions.

3504 Mr. {Pallone.} Thank you, Mr. Chairman.

3505 I wanted to ask this question, I guess of Mr. Germano

3506 and I guess Mr. Pops and Dr. Wheadon, the three of you could
3507 answer. We heard from Dr. Hamburg this morning that the FDA
3508 rarely, if ever, meets the waiver caps related to the number
3509 of persons with a conflict of interest that can serve on an
3510 FDA advisory panel. At the same time, we know there are
3511 concerns from the public about FDA panelists having conflicts
3512 of interest related to the issues they are reviewing. About
3513 3 weeks ago, the Wall Street Journal published an article
3514 highlighting the conflict of interest three panelists had one
3515 panel had in relation to a product they were reviewing. You
3516 know, I know it is a concern, I mean, we are concerned
3517 because we want to have the best experts possible on the
3518 panels but we need to help the FDA get such experts and get
3519 them in a timely manner.

3520 But I am having difficulty seeing how removing the
3521 waiver caps will solve anything when FDA is not meeting these
3522 caps, and my question is, given that the waiver caps are not
3523 routinely reached, can you explain how removing the caps
3524 would improve the current situation, if you believe it would,
3525 and are there any other fixes you would suggest in addition
3526 to or instead of removing the waiver caps? Let us start with
3527 Mr. Germano.

3528 Mr. {Germano.} Okay. I will start. And I think this
3529 is a particularly important area for Pfizer. As I mentioned

3530 in my testimony, we are focused on bringing new medicines in
3531 the rare disease and orphan disease area, and this is an area
3532 where oftentimes there are a small number of highly expert
3533 opinion leaders and physicians.

3534 Mr. {Pallone.} I don't have a lot of time, so what do
3535 you think? I mean, should we be removing them?

3536 Mr. {Germano.} Well, I think that we--you know, our
3537 view is that there is a need to improve the process of the
3538 advisory committees, particularly in areas where there is a
3539 paucity of experts, and I don't know if it is additional
3540 waivers or better utilization of the waivers that exist. I
3541 am not familiar enough with the issues, but there is a need
3542 for improvement.

3543 Mr. {Pallone.} Would either of the other two of you
3544 like to answer?

3545 Mr. {Pops.} Just being directly responsive to your
3546 question, I don't think removal of the waivers does a whole
3547 lot for the reasons you cited. I think FDA has different
3548 standards than other agencies of the government with respect
3549 to conflict. My own view is that I think they are too
3550 restrictive. And coming at it from the innovators' point of
3551 view, the most important thing for us when we convene a panel
3552 is that the people sitting at the panel are expert in the
3553 disease because they are the best suited to make the decision

3554 between risk and benefit that are so critical for patients.

3555 Mr. {Pallone.} Okay. Dr. Wheadon?

3556 Dr. {Wheadon.} Thank you, Representative Pallone. I

3557 think in addition to what Mr. Pops just added--

3558 Mr. {Pitts.} Is your mic on?

3559 Dr. {Wheadon.} I think it is. Can you hear me?

3560 Mr. {Pallone.} Yes, I can hear you. Maybe talk closer

3561 to it.

3562 Dr. {Wheadon.} I think it is also important for us to

3563 consider broadening the question and looking at it from

3564 perhaps a different perspective from just waiver caps, and

3565 that might be recognizing that both FDA and industry have a

3566 vested interest in working with the best expertise. Should

3567 there be a penalty for FDA because industry has engaged that

3568 expertise and helping it develop its plan for investigation

3569 and research and vice versa, should industry not be allowed

3570 to engage that expertise because FDA may be planning to use

3571 that individual in an advisory committee. And in the case of

3572 rare diseases, it is even more of a particular issue because

3573 there could be so few experts for both industry and FDA to

3574 engage.

3575 Mr. {Pallone.} All right. Thanks.

3576 Let me get a second question in here. We talked about

3577 how in today's world drug manufacturing is a global affair

3578 and outsourcing is common, and robust supply chain management
3579 is best practice for industry including supplier
3580 qualification and assessment. So I wanted to ask Mr. Germano
3581 again, Pfizer has underscored in previous testimony the
3582 importance of ensuring the quality of suppliers, particularly
3583 those in emerging economies. Can you tell me what Pfizer is
3584 doing to ensure supplier quality? Do you believe that every
3585 company knows their suppliers and knows the quality system in
3586 place?

3587 Mr. {Germano.} Well, I mean, you know, product supply
3588 quality is the highest interest to Pfizer and I think that we
3589 have put a number of important measures in place to ensure
3590 the integrity of our supply, and you know, some of those
3591 measures include risk assessments of potential suppliers, you
3592 know, contractual measures to ensure the effectiveness and
3593 quality of those suppliers. We go into some of the suppliers
3594 and work with them to upgrade their systems. We have audits
3595 on a routine basis. So we employ quite an array of measures
3596 to ensure the quality and integrity of our suppliers.

3597 Mr. {Pallone.} I was going to ask Mr. Coukell but I
3598 guess I am out of time, Mr. Chairman. Thanks.

3599 Mr. {Pitts.} The chair thanks the gentleman and
3600 recognizes Dr. Burgess for 5 minutes for questioning.

3601 Dr. {Burgess.} Thank you, Mr. Chairman.

3602 Ms. Dorman, let us stay on the issue of the conflicts
3603 because you referenced that in your prepared testimony, and I
3604 do believe it is extremely important. In fact, when this
3605 reauthorization occurred in 2007, I was way down at the kids'
3606 table on the minority side and wasn't really able to make the
3607 point as effectively as it needed to be made, but we have got
3608 vacancies on the advisory panels. Now, we have got waivers
3609 that can be applied and there are caps on the waivers. Do
3610 you think the system itself creates an environment where
3611 otherwise qualified people say you know what, I don't need
3612 that, I'm not going to go through that. So have we created a
3613 hostile environment to the researchers and the people who
3614 might be knowledgeable about these products because of the
3615 restrictions placed on the advisory panels in the 2007
3616 reauthorization?

3617 Ms. {Dorman.} I don't know if I would say that there is
3618 a hostile environment per se but some of the restrictions,
3619 especially related to, you know, their finances and their
3620 investments and things like that, could be a deterrent to
3621 some people to expose themselves to that type of level of
3622 scrutiny. I will say, there is something that really does
3623 need to be done. A colleague of mine is president of the
3624 Friedrich's Ataxia Research Association, and he was asked by
3625 the FDA to apply to sit on an advisory committee, and he was

3626 turned down because of perceived conflicts, and this is a man
3627 whose child died of Friedrich's ataxia, so there are real
3628 concerns that really need to be looked at, and we feel as if
3629 it should be--FDA should not held to an even higher standard
3630 than all other federal agencies.

3631 Dr. {Burgess.} Well, as I recall, during the
3632 discussion, the reference to the Institute of Medicine said
3633 no more than 40 percent of the advisory panel should be made
3634 up of people who potentially had a conflict, and I thought
3635 that was an okay number. That means you still have--as you
3636 correctly alluded to, the universe of people who have an
3637 understanding of the diseases and the treatments proposed is
3638 vanishingly small with some of these, and if you exclude even
3639 one individual, that may be a significant percentage of the
3640 population, the scientific population that actually
3641 understands the studies at hand.

3642 Ms. {Dorman.} That is correct. I mean, the patient
3643 population--the rare disease community is very, very small.
3644 Patient organizations work with researchers. They work with
3645 companies to encourage the development of these orphan
3646 products. So yes, in the rare disease community, basically
3647 everyone is pretty conflicted.

3648 Dr. {Burgess.} Well, are all conflicts equal? In the
3649 real world, are all conflicts equal?

3650 Ms. {Dorman.} No, I don't think so.

3651 Dr. {Burgess.} Yes, I don't either.

3652 Let me ask you this. Do you think we have actually--
3653 that the advisory conflict policy has hindered bringing new
3654 products to market?

3655 Ms. {Dorman.} No. It may have delayed like in the case
3656 of Savril but I don't think it has, in my opinion.

3657 Dr. {Burgess.} In my opinion, hindered and delayed
3658 would be identical, but I will accept your answer.

3659 Well, would you support loosening some of these
3660 restrictions?

3661 Ms. {Dorman.} Excuse me?

3662 Dr. {Burgess.} Would you support the loosening of some
3663 of these restrictions that were placed in the 2007
3664 reauthorization?

3665 Ms. {Dorman.} Yes, we would.

3666 Dr. {Burgess.} In the interest of full disclosure, I
3667 have a bill out there, 3206, which attempts to undo some of
3668 these restrictions. Have you had an opportunity to look at
3669 that legislation?

3670 Ms. {Dorman.} Yes, I have, and I have spoken with your
3671 staff.

3672 Dr. {Burgess.} And Dr. Hamburg implied that she didn't
3673 need a legislative fix, but in your estimation, would a

3674 legislative fix expedite the solution to this problem in your
3675 world?

3676 Ms. {Dorman.} That has been our position, yes.

3677 Dr. {Burgess.} And no great surprise, my position too.

3678 Dr. Wheadon, let me ask you a question. Dr. Hamburg
3679 referenced coming into the electronic age for some of the
3680 applications for the premarket approval process, and I guess
3681 I am surprised that that is not farther along. Do you have a
3682 sense as to what is the volume of new product applications,
3683 new drug applications that are sitting on paper applications
3684 in boxes in the basement of someone's warehouse?

3685 Dr. {Wheadon.} Well, I think we may be talking about
3686 two different things. Most sponsors, if not all, certainly
3687 the member companies that we represent now submit what is
3688 called an electronic document. So everything is electronic.
3689 It is no longer boxes in U-Haul trucks as it used to be 20
3690 years ago.

3691 I think what Dr. Hamburg was referring to and what we
3692 reference in the PDUFA agreement is an attempt to have more
3693 of a common template such that that electronic data is
3694 collected in a common format regardless of who the sponsor
3695 may be. The ultimate benefit of that is, when the agency
3696 needs to look across products, across sponsors, the data is
3697 collected in a similar way. It is much easier to collate,

3698 much easier to do analyses and come to some robust
3699 conclusions. Right now, it is all over the place and it
3700 makes it much more difficult for the agency to do that type
3701 of analysis. So I don't think Dr. Hamburg was intending to
3702 imply that they are still collecting data on a paper format.
3703 That is not the case. It is just doing it more physically
3704 such that the agency can carry out its job much more
3705 effectively.

3706 Dr. {Burgess.} Thank you.

3707 Thank you, Mr. Chairman. I will yield back the time.

3708 Mr. {Pitts.} The chair thanks the gentleman and
3709 recognizes the ranking member emeritus, Mr. Dingell, for 5
3710 minutes for questions.

3711 Mr. {Dingell.} Mr. Chairman, I thank you for your
3712 courtesy.

3713 First, welcome to Dr. Daniel Frattarelli. He is a
3714 constituent of mine from Oakwood Hospital and from Dearborn
3715 Medical Center in Dearborn, Michigan, my hometown. Doctor,
3716 it is a pleasure to welcome you. Thank you for being here.

3717 Dr. {Frattarelli.} Thank you.

3718 Mr. {Dingell.} As members of the committee well know, I
3719 have long believed that the FDA does not have the people, the
3720 funding or the authorities it needs to properly oversee an
3721 increasingly global drug supply chain. That has been

3722 supported by testimony and evidence submitted in hearings
3723 before this committee for a number of years. So in support
3724 of that posture, I would like to direct my questions to you,
3725 Mr. Germano of Pfizer, and please answer to the following
3726 questions yes or no. Do you agree that both FDA and industry
3727 have a responsibility to ensure the security of our drug
3728 supply chain? Yes or no.

3729 Mr. {Germano.} Yes.

3730 Mr. {Dingell.} Do you agree that the knowledge of your
3731 suppliers is important? Yes or no.

3732 Mr. {Germano.} I am sorry. The knowledge about
3733 suppliers?

3734 Mr. {Dingell.} Yes, your knowledge and experience with
3735 them as to their behavior and the quality of the goods that
3736 they are delivering you. Yes or no.

3737 Mr. {Germano.} Yes.

3738 Mr. {Dingell.} Thank you. There are no traps here.

3739 Mr. {Germano.} I just want to make sure I understand
3740 the question.

3741 Mr. {Dingell.} Just give the answers and you will be
3742 satisfied and so will I.

3743 Mr. {Germano.} Okay.

3744 Mr. {Dingell.} Does Pfizer have systems in place so
3745 that they can know and understand their suppliers and monitor

3746 the manufacturing quality of these suppliers? Yes or no.

3747 Mr. {Germano.} Yes.

3748 Mr. {Dingell.} Should all companies making drugs in the
3749 United States know their suppliers and have quality systems
3750 in place there to assure that they are getting safe supplies
3751 from their suppliers? Yes or no.

3752 Mr. {Germano.} Yes.

3753 Mr. {Dingell.} Now, I must assume, however, though,
3754 that there would be some instances where additional help
3755 would be needed by American suppliers, i.e., in the heparin
3756 case where raw materials or components for the heparin were
3757 clearly not safe and the result was American manufacturers
3758 were put at risk. Should FDA have additional authorities to
3759 provide that kind of support for American manufacturers? Yes
3760 or no.

3761 Mr. {Germano.} Yes.

3762 Mr. {Dingell.} No traps here. I want you to be
3763 comfortable.

3764 Should the companies be using risk analysis to target
3765 safety risks? Yes or no.

3766 Mr. {Germano.} Yes.

3767 Mr. {Dingell.} And that is not a standalone basis.
3768 Obviously they would have to use other things.

3769 Now, these are for Dr. Wheadon of PhRMA. Doctor, I want

3770 you to be comfortable with these, and I am not trying to lay
3771 any traps for anybody here. I want to focus on inspections.
3772 Do you agree that requiring FDA to conduct comparable
3773 inspections of domestic and foreign drug facilities is
3774 important to ensuring a level playing field for our drug
3775 manufacturers? Yes or no.

3776 Dr. {Wheadon.} Certainly, the answer is yes based on--

3777 Mr. {Dingell.} Sorry?

3778 Dr. {Wheadon.} I am sorry. Certainly, the answer is
3779 yes based on the ability to assess risk.

3780 Mr. {Dingell.} Good. I have very limited time, Doctor,
3781 and I beg your cooperation here.

3782 Dr. {Wheadon.} I understand.

3783 Mr. {Dingell.} Do you agree that conducting comparable
3784 inspections of domestic and foreign facilities is important
3785 to public health? Yes or no.

3786 Dr. {Wheadon.} That is a yes.

3787 Mr. {Dingell.} And of course, it is important to the
3788 fairness with which we treat our manufacturers. Is that not
3789 so?

3790 Dr. {Wheadon.} I think it is important to be fair
3791 across the board.

3792 Mr. {Dingell.} Now, do you agree that FDA needs
3793 adequate resources to conduct comparable inspections of

3794 domestic and foreign drug manufacturers? Yes or no.

3795 Dr. {Wheadon.} I believe the agency should have
3796 adequate resources.

3797 Mr. {Dingell.} Now, if FDA does not treat manufacturers
3798 alike, it is very liable to be unfair to U.S. manufacturers
3799 because of its inability to impose equal burdens upon both
3800 domestic and foreign manufacturers who are outside of our
3801 borders and outside the capabilities of FDA to reach them.
3802 Isn't that so?

3803 Dr. {Wheadon.} I think FDA has ability to impact
3804 foreign manufacturers if they are importing drugs into the
3805 United States.

3806 Mr. {Dingell.} But you would advocate that FDA do have
3807 such authority?

3808 Dr. {Wheadon.} I think FDA has that ability to impact
3809 those manufacturers--

3810 Mr. {Dingell.} Please answer my question.

3811 Dr. {Wheadon.} And they should, yes, sir.

3812 Mr. {Dingell.} Okay. Does the prescription drug user
3813 fee agreement currently provide resources for preapproval
3814 inspection? Yes or no.

3815 Dr. {Wheadon.} Yes, it does.

3816 Mr. {Dingell.} Does the prescription drug user fee
3817 agreement currently provide resources for any inspections

3818 beyond the preapproval inspection? Yes or no.

3819 Dr. {Wheadon.} That is a qualified yes, it does.

3820 Mr. {Dingell.} Qualified? But it should be ``yes'',
3821 shouldn't it? Because FDA should have that authority, should
3822 they not?

3823 Dr. {Wheadon.} FDA has the ability to inspect
3824 facilities with resources--

3825 Mr. {Dingell.} That is one of the questions we are
3826 going to be going into, Doctor.

3827 The generic drug user fee agreement provides additional
3828 resources for FDA to conduct GMP inspections of both domestic
3829 and foreign drug facilities. Would you support providing
3830 similar resources to FDA for inspections of facilities
3831 manufacturing innovator drugs? Yes or no.

3832 Dr. {Wheadon.} No.

3833 Mr. {Dingell.} Do you agree that a risk-based
3834 inspection schedule for domestic and foreign drugs facilities
3835 based, for example, on compliance history, time since last
3836 inspection, volume and type of product would allow the FDA to
3837 better target the use of their resources? Yes or no.

3838 Dr. {Wheadon.} Yes.

3839 Mr. {Dingell.} One obstacle to ensuring comparable
3840 inspections of domestic and foreign facilities is the lack of
3841 complete and adequate information that FDA has on drug

3842 manufacturing establishments. Do you support requiring
3843 domestic and foreign drug manufacturing facilities to
3844 register with FDA to provide a unique facility identifier and
3845 to list their products? Yes or no.

3846 Dr. {Wheadon.} I think that is one I would have to come
3847 back to you with further comment on. I am not prepared to
3848 give a specific yes or no on that one.

3849 Mr. {Dingell.} Very good. One question then. Why is
3850 it that PhRMA does not support additional resources for GMP
3851 inspections?

3852 Dr. {Wheadon.} Well, this is more than a yes or no,
3853 right?

3854 Mr. {Dingell.} It is a fairly simple question. I know
3855 you have a fairly easy to understand answer.

3856 Dr. {Wheadon.} Right. So as you correctly point out,
3857 Representative Dingell, the PDUFA fees that the innovative
3858 industry presently pays goes towards preapproval inspections.
3859 When an inspector goes into a facility, be it domestic or
3860 foreign, they don't only look at the product that is under
3861 consideration for approval, they look at the system of that
3862 manufacturing establishment. So a GMP inspection is carried
3863 out in the context of preapproval inspections.

3864 Mr. {Dingell.} Am I somewhat dense in not understanding
3865 why we would want to see to it that FDA has the authority

3866 that it needs to carry out its responsibilities in the best
3867 way possible?

3868 Dr. {Wheadon.} We certainly agree that FDA should have
3869 the resources to carry out their responsibilities very
3870 efficiently.

3871 Mr. {Dingell.} I note, Mr. Chairman, I have exceeded my
3872 time by 3 minutes and 5 seconds. You have my thanks and my
3873 apologies.

3874 Mr. {Pitts.} The chair thanks the gentleman and yields
3875 to the gentleman from Illinois, Mr. Shimkus, for 5 minutes
3876 for questions.

3877 Mr. {Shimkus.} Thank you, Mr. Chairman, and I apologize
3878 for missing the first part. I have a lot of questions about
3879 nuclear waste I could offer to you, but it is good to be here
3880 on the health panel.

3881 I would also like to go to Ms. Dorman, and can you just
3882 elaborate on how the FDA's risk-based, current risk-based
3883 analysis is affecting patients?

3884 Ms. {Dorman.} Well, it is the feeling of many patient
3885 organizations that the FDA has become far more risk averse
3886 than it should be, and so we want some way that patients can
3887 communicate directly with the reviewers. We have had
3888 conversations with the FDA leadership but the reviewers
3889 actually looking at the data don't normally hear from the

3890 patients or their families.

3891 Mr. {Shimkus.} And what would the patients and the
3892 families tell them if they were listening?

3893 Ms. {Dorman.} It depends on the disease, I suppose, or
3894 the condition, but just let them know what their quality of
3895 life is, to know more about the disease, what the risks of
3896 the disease are, what the progression of the disease is. I
3897 think those are some of the things that the reviewers would
3898 like to hear, and I would like to point out to the committee
3899 that Mr. Shimkus was the sponsor of the rare diseases back in
3900 2002. Thank you.

3901 Mr. {Shimkus.} No, thank you, and that is not why I
3902 went to you but I appreciate that.

3903 So I think you kind of answered this. How would you
3904 improve that risk-based system? What would you want us to do
3905 in a public policy arena to try to fix that?

3906 Ms. {Dorman.} What we have proposed directly with the
3907 FDA, we are working internally with the officials there, what
3908 we have proposed, which isn't really written in stone, would
3909 allow patients in an unburdensome way, maybe through a portal
3910 there on their website that would communicate some of those
3911 things. We don't want it to be a burdensome process for the
3912 agency at all. But to empower patients in some way, shape or
3913 form to feel as if they have more control over approval of a

3914 product.

3915 Mr. {Shimkus.} And technologically, that shouldn't be
3916 real difficult, should it?

3917 Ms. {Dorman.} I am a real techno dweeb but I would say
3918 it is probably not all that difficult to do.

3919 Mr. {Shimkus.} I would also agree with you.

3920 Let me stay with you and ask about the FDA's vacancies
3921 on their advisory committees. Do you know how many there
3922 are, and what does that mean in this discussion that we are
3923 having?

3924 Ms. {Dorman.} I really don't know what the numbers
3925 might be.

3926 Mr. {Shimkus.} And what is the problem with vacancies?

3927 Ms. {Dorman.} Well, the problem is that it can delay
3928 consideration of products if they are unable to find someone
3929 who is expert, especially in the rare disease world where,
3930 you know, there are not of people expert in their conditions.
3931 Usually the patients know more about their conditions than
3932 their doctors do, so--

3933 Mr. {Shimkus.} Say that again. I mean, just reiterate
3934 that point.

3935 Ms. {Dorman.} I am speaking just from NORD's
3936 perspective. I mean, many patients have more knowledge about
3937 their condition, about the progression of their disease than

3938 some of the physicians do. So it is very important to have
3939 their input, and they are anxious to do so.

3940 Mr. {Shimkus.} And I would agree with you there. I
3941 mean, they are anxious because either they are suffering
3942 themselves or having the life experience. They are also very
3943 passionate to try to make the system better for the future,
3944 and by being involved in the process, helpful. That gives
3945 them a role in this that they would like to be involved in.

3946 Ms. {Dorman.} Yes, and it is helping our organizations
3947 understand the regulatory process more. So many of them are
3948 focused entirely on research at NIH and know very little
3949 about the FDA process. But on March 1, they are having a
3950 one-day advocacy meeting with patient organizations and over
3951 180 organizations have signed on, so they will give them an
3952 opportunity to learn about the FDA and the FDA to learn about
3953 their condition.

3954 Mr. {Shimkus.} Great. Thank you.

3955 And just briefly, Mr. Gollaher, I have been very
3956 concerned about capital research fleeing the United States
3957 because of the FDA's slowness. We have also heard a lot of
3958 testimony about venture capitalism. Is that true, if we have
3959 research and development, venture capital moving overseas?
3960 Where are they going and what does this mean for U.S. jobs?

3961 Mr. {Gollaher.} To some degree, and this is less true

3962 in the drug industry than the medical device industry, there
3963 has been a shift of first in human trials and of middle-stage
3964 and late-stage research to Europe and the device field has a
3965 faster and more user-friendly regulatory system. And we have
3966 certainly seen in California, we have seen across the country
3967 that most venture capitalists will not look at a business
3968 plan for a device company that doesn't have a European
3969 strategy. That is a tremendous change in the last 10 years.

3970 Mr. {Shimkus.} And that would really affect jobs and
3971 the economy. I mean, if they get the approval in Europe,
3972 they are most likely going to start there.

3973 Mr. {Gollaher.} Well, no, that is right, and there are
3974 also a number of sequelae. So for example, if you introduce
3975 a product in Germany before here, the doctors learn to use
3976 it. Some of the factors that are involved in early-stage
3977 manufacturing may go there as well. And you also teach your
3978 competition how to make the product. So it is a real issue.

3979 Mr. {Shimkus.} Thank you very much. I yield back my
3980 time, Mr. Chairman.

3981 Mr. {Pitts.} The chair thanks the gentleman and
3982 recognizes the gentleman from California, Mr. Waxman, for 5
3983 minutes for questions.

3984 Mr. {Waxman.} Thank you, Mr. Chairman.

3985 Dr. Frattarelli, in your testimony you provide

3986 compelling evidence of the benefits to children that the Best
3987 Pharmaceuticals for Children Act provides. As you know,
3988 because of studies conducted in response to BPCA and the
3989 Pediatric Research Equity Act, we learned invaluable
3990 information about the use of drugs in children. However,
3991 despite how well it has worked, you point out that the AAP
3992 believes that Congress should not remove the BPCA 5-year
3993 sunset provision because it provides Congress the opportunity
3994 to assess whether the BPCA continues to strike the right
3995 balance between achieving critical pediatric information and
3996 providing an appropriate incentive. Can you briefly expand
3997 on our testimony regarding why Congress should retain that 5-
3998 year sunset provision?

3999 Dr. {Frattarelli.} Sure. One of the big issues here is
4000 that it is kind of a moving target that we are talking about.
4001 The cost that this is going to incur by varying the period of
4002 exclusivity these drugs obtain will change over time, and
4003 that cost is going to be borne by a lot of groups, private
4004 insurance companies and the government as well. So there is
4005 a financial side to this, but the other part is, every 5
4006 years having the opportunity to look at these again, revise
4007 them, gives us some real benefits. If we go through, you
4008 know, what happened last time we went and reauthorized these,
4009 we had some changes made so that, for example, now all the

4010 information that we get from these studies results in a label
4011 change and the information is more publicly available. Those
4012 are two real meaningful and important things to have, and
4013 they came about because we had this opportunity to
4014 reevaluate.

4015 Mr. {Waxman.} That is a very good argument. The other,
4016 of course, is that when we have a 6-month exclusivity, that
4017 is a lot of money, and that cost, as you point out, is being
4018 carried by the people who pay for these drugs, whether it is
4019 government, insurance or private individuals. If you have a
4020 6-month exclusivity, especially if it is a drug like Lipitor
4021 where the annual sales are over \$5 billion, that just can be
4022 a huge amount that is being passed on to others.

4023 And so we need to maintain a balance between providing
4024 adequate incentives for developing new indications for
4025 pediatric populations and not unduly burdening patients and
4026 payers with high drug costs for any longer than is necessary.

4027 During the 2007 reauthorization, we put forward a
4028 proposal to trim that 6 months of exclusivity for drugs with
4029 very high profit margins, so-called blockbuster drugs. I
4030 thought that made sense, but we didn't prevail in including
4031 it. I agree, it is critical to retain that sunset provision
4032 so we have an opportunity to evaluate these questions, both
4033 the balance and the research questions as well.

4034 Ms. Dorman, we have heard concerns from several parties
4035 about the development of drugs for rare diseases. I talked
4036 in my opening statement about a proposal under consideration
4037 that would make changes to FDA's fast-track approval system
4038 for orphan drug, the ULTRA Act. Specifically, it would
4039 require the FDA to use whatever data was available to
4040 evaluate and approve surrogate endpoints for review of these
4041 drugs and would prevent FDA from requiring additional
4042 clinical data even when FDA considers such additional data
4043 necessary to enable it to make an approval decision based on
4044 that endpoint. That is a concern to me. My understanding is
4045 that under current law, FDA has a great deal of discretion to
4046 identify and require appropriate scientific evidence.

4047 NORD recently did a study looking at whether FDA is
4048 flexible in its requirements for the approval of orphan
4049 drugs. Can you describe the conclusions of this study in
4050 more detail? What is NORD's view on the need for legislative
4051 changes to FDA's fast-track approval program for orphan
4052 drugs, specifically on the ULTRA Act?

4053 Ms. {Dorman.} We feel as if ULTRA would require the FDA
4054 to rely on surrogate endpoints based on little or no clinical
4055 evidence, and it could expose patients to unnecessary risk
4056 and in our opinion would lower the approval standards of the
4057 FDA, and that is our concern. That study is really a

4058 landmark study. Of the 130, you know, products that were
4059 reviewed by a former chair, many of them, 90 of the 135, were
4060 approved based on administrative flexibility or case-by-case
4061 flexibility, and I think the example that Dr. Hamburg gave
4062 this morning in her testimony regarding the new therapy for
4063 cystic fibrosis, it was approved in 3 months, so they do use
4064 that flexibility when something that important comes forward.

4065 Mr. {Waxman.} Well, we all want these drugs on the
4066 market as fast as possible but I would be concerned about any
4067 proposal to remove FDA's ability to require clinical data
4068 when FDA thinks it is essential to assure that these drugs
4069 are safe and effective, so I certainly agree with the
4070 position NORD has been taking.

4071 Ms. {Dorman.} Thank you.

4072 Mr. {Waxman.} Thank you, Mr. Chairman.

4073 Mr. {Pitts.} The chair thanks the gentleman and
4074 recognizes the gentleman from New Jersey, Mr. Lance, for 5
4075 minutes for questions.

4076 Mr. {Lance.} Thank you, Mr. Chairman.

4077 To Mr. Germano, very nice to see you again. In your
4078 testimony, you noted that Pfizer's enhanced focus on rare
4079 diseases, specifically allocating the majority of your
4080 research and development efforts to the areas that represent
4081 the intersection between unmet medical needs and your

4082 strength in biology and chemistry, given that, could you
4083 comment on how the enhancements in regulatory science
4084 contained in the goals letter will support the development of
4085 products for rare diseases?

4086 Mr. {Germano.} Yes, I think that there are a number of
4087 elements of the proposed PDUFA V that will help in the
4088 advancement and review and development of medicines for rare
4089 diseases. I think the NME review process that I spoke of
4090 before will help bring, you know, clarity to the review
4091 process, which I think will be helpful. I think that some of
4092 the provisions in the, you know, enhancements in regulatory
4093 science, you know, specifically for rare diseases, biomarker
4094 identification and, you know, other measures that are in the
4095 PDUFA V I think are all intended to elevate the capability of
4096 the FDA and the potential for better transparency and problem
4097 solving and decision making between the company and the FDA.

4098 Mr. {Lance.} Thank you. Are there any other changes
4099 that you could see that would incentivize innovative
4100 biopharmaceutical companies into developing more products for
4101 unmet needs?

4102 Mr. {Germano.} Well, I think overall, you know,
4103 confidence in the development pathway is a very big part of
4104 providing an incentive for a company to take on a project in
4105 the development of a new molecular entity in particular. So

4106 some of these provisions relate directly to improving
4107 confidence in the pathway and agreements that exist between
4108 the agency and the sponsor company. Beyond that, I think,
4109 you know, intellectual property and exclusivity assurance
4110 will give greater confidence to the sponsor to make the
4111 investments necessary to bring these kinds of medicines
4112 forward.

4113 Mr. {Lance.} Thank you very much.

4114 To Mr. Pops, I think it is critical that we ensure a
4115 consistent and transparent evaluation of benefit-risk during
4116 FDA's review of new drugs. Unfortunately, from my
4117 perspective, this evaluation has on occasion kept life-
4118 improving, life-saving drugs from patients, and in your
4119 opinion, what do we need to do in order to rebalance the
4120 analysis?

4121 Mr. {Pops.} The was one of the real questions that was
4122 brought up during the PDUFA V technical negotiations, and I
4123 think that what we--

4124 Mr. {Lance.} Which I know you were involved.

4125 Mr. {Pops.} Is that in PDUFA V, and I think the
4126 Commissioner mentioned earlier, there is this patient-centric
4127 and more formalized risk-benefit evaluation that we are
4128 seeking to implement through PDUFA V. I think we have a long
4129 way to go but I think the agency has an interest in bringing

4130 more rigor and formalization to the risk-benefit analysis.

4131 Mr. {Lance.} Thank you.

4132 Is there anyone else on the panel who would like to

4133 comment on that? Very good. Thank you very much.

4134 I yield back the balance of my time, Mr. Chairman.

4135 Mr. {Pitts.} The chair thanks the gentleman and

4136 recognizes the gentleman from New York, Mr. Towns, for 5

4137 minutes for questions.

4138 Mr. {Towns.} Thank you very much, Mr. Chairman.

4139 Let me begin by thanking you, Ms. Dorman, for working

4140 with my staff and Mr. Stearns on ULTRA. This bill is still a

4141 work in progress, and we look forward to receiving NORD's

4142 recommendations for changes to the text as your group has

4143 promised my staff within the next few weeks. We look forward

4144 to continued working with you on that.

4145 Let me go to you, Mr. Germano. Last year, the FDA

4146 approved the Pfizer drug under priority review in 4 months.

4147 In your experience, is this common for orphan drug review,

4148 and what made this one so exceptional?

4149 Mr. {Germano.} This was--I think you are referring to

4150 our drug crizotinib, and the brand name is Xalkori. It is a

4151 drug for--

4152 Mr. {Towns.} That is correct.

4153 Mr. {Germano.} --a specific subset of patients with

4154 non-small-cell lung cancer, and in this case, there is a
4155 genetic marker to identify patients who are most likely to
4156 respond to the medication. So we were able to--once the
4157 identification of the genetic marker occurred, we were able
4158 to work with our partners at Abbott Laboratories to develop a
4159 companion diagnostic and complete a clinical trial that
4160 demonstrated, you know, fairly clearly the benefit-risk
4161 profile of this medicine for this particular patient
4162 population. So it is a great example of the benefit of
4163 personalized medicine or precision medicine approach to drug
4164 development. You know, the more we are able to do this, you
4165 know, the more efficient the development process is, the more
4166 efficient the review process is and the more quickly we can
4167 get new medicines to patients.

4168 So, you know, I can't say it is commonplace. I think we
4169 are all working harder and harder to find, you know, genetic
4170 markers and biomarkers of activity, whether it is efficacy or
4171 safety signals that we are after to help bring more clarity
4172 to the benefit-risk profile of our medicines and make it
4173 easier for us to develop them and for the agency to review
4174 them.

4175 Mr. {Towns.} Let me just say that I really appreciate
4176 Pfizer's strong commitment to finding treatments for rare
4177 diseases. To the best of your knowledge, have any of

4178 Pfizer's recently offered drug approvals been approved under
4179 the accelerated approval pathway at FDA?

4180 Mr. {Germano.} Well, this one that we are speaking of,
4181 crizotinib, was approved under the accelerated review
4182 process.

4183 Mr. {Towns.} Any others?

4184 Mr. {Germano.} We have another drug for a rare disease,
4185 a rare polyneuropathy that we have recently filed with the
4186 FDA and we are seeking accelerated review of that product as
4187 well.

4188 Mr. {Towns.} Do you have any ideas or suggestions as to
4189 how we might be able to improve the accelerated process? Do
4190 you have any ideas or suggestions that you might want to
4191 offer?

4192 Mr. {Germano.} Well, I think that some of the
4193 provisions of PDUFA V are likely to be helpful. Again, I
4194 think the greater amount of required interaction between the
4195 agency and the sponsor, the focus that the agency will put
4196 on, you know, risk-benefit framework, biomarker understanding
4197 and, you know, rare and orphan disease issues that are
4198 components of the PDUFA V should be helpful in improving our
4199 ability to bring these kinds of medicines to the market.

4200 Mr. {Towns.} I want to go to a very quick yes or no. I
4201 am very committed to supporting the FDA in their timely

4202 approval of safe, effective treatment options, particularly
4203 for rare diseases. For this reason, I am proud to be working
4204 with my colleague from Florida, Congressman Stearns, on an
4205 initiative that I hope will encourage the development of
4206 innovative, safe drugs in this space. The goal is to improve
4207 access to the FDA's existing accelerated approval pathway for
4208 drugs designed to treat patient with life-threatening rare
4209 diseases, and this would be a yes or no. Let me ask you, Mr.
4210 Germano, and of course Mr. Pops and Ms. Dorman, do you
4211 support this goal?

4212 Mr. {Germano.} To--

4213 Mr. {Towns.} Do you support the goal?

4214 Mr. {Germano.} I am sorry?

4215 Mr. {Towns.} Congressman Stearns and I are working on
4216 this initiative that I hope will encourage the development of
4217 innovative, safe drugs in this space. The goal is to improve
4218 access to FDA's existing accelerated approval pathways for
4219 drugs designated to treat patients with life-threatening rare
4220 diseases. Do you support that?

4221 Mr. {Germano.} Yes, I would support that.

4222 Mr. {Towns.} Okay. Ms. Dorman?

4223 Ms. {Dorman.} Yes.

4224 Mr. {Towns.} Thank you very much, and I would note, Mr.
4225 Chairman, I don't have anything to yield back, but I yield

4226 back.

4227 Mr. {Pitts.} The chair thanks the gentleman and
4228 recognizes Mr. Guthrie for 5 minutes for questions.

4229 Mr. {Guthrie.} I think the previous two kind of went
4230 down the path I was going to go with Ms. Dorman. I think
4231 that we do need to make sure that we have a good accelerated
4232 program for people with risk, and I have a friend caught up
4233 in another situation, and the argument, I always say this. I
4234 have bad allergies. I don't want something put out to keep
4235 me from sniffing that is going to have adverse effects to
4236 me. But when you have a friend who has Lou Gehrig's disease,
4237 or ALS, and there is some opportunities for them to go
4238 forward, as long as the patient knows the risk and what could
4239 be there, I think that we should have a process for them to
4240 go forward. So I agree with Mr. Stearns and Mr. Towns and I
4241 would like to work with you on that because I think that is
4242 important to do.

4243 On the venture capital, which is more medical devices, I
4244 gather, a lot of times they are encouraged to go to Europe
4245 just because they get approved. If they get approved in the
4246 home country where they manufacture, they also get--I think
4247 China recognizes it. So the President talked about
4248 manufacturing, which is my background, we are in a situation
4249 where we have American manufacturers having to locate in

4250 Europe because of our regulatory process, which we are not
4251 comparing to a country that doesn't have substantial safety
4252 concerns. I mean, we are talking about the European Union
4253 that we are not competitive with in our approval process.

4254 But I want to get to Mr. Coukell. On this panel, a lot
4255 of people say ``as a doctor.'' I don't get to say that, but
4256 as a quality control engineer--that was my background before
4257 in manufacturing--Pew has done some research on drug
4258 pedigree, and just if you can talk about that and
4259 particularly I would like the safety of the supply chain,
4260 particularly foreign supply chains dealing with third parties
4261 or foreign regulators. I mean, if you could talk about what
4262 your research has been in the drug pedigree world?

4263 Mr. {Coukell.} Thank you for that question, sir. It is
4264 an area that I didn't touch on my testimony, but we looked at
4265 as drugs move from the manufacturer through distributors to
4266 the pharmacy and ultimately to the patients, what is the
4267 pedigree system or the absence of. So if I could share one
4268 short story. A couple of years ago, there was a tractor-
4269 trailer load of insulin that was stolen in North Carolina and
4270 disappeared for a while. Insulin is a drug that should be
4271 refrigerated. And then it showed up back in pharmacies of a
4272 major chain grocery store in a couple of different States.
4273 And between there is passed through a couple of different

4274 wholesalers. And so the question is, is there a system by
4275 which the pharmacy at the end use could have recognized that
4276 as stolen product, flagged it, do we have a system that lets
4277 you track the product through the system, do we have a unique
4278 serial number on the drugs, and the answer is we don't have
4279 that. California has law which is scheduled to come into
4280 effect in 2015. Our view is that a national standard would
4281 be much more preferable.

4282 Mr. {Guthrie.} What about your looking into
4283 ingredients, foreign ingredients and the integrity and
4284 dealing with foreign regulators or third parties? I think
4285 you looked into that in your report as well. And what are
4286 solutions? I mean, you said unique serial numbers. Are
4287 there other things like working with foreign regulators or
4288 third-party groups?

4289 Mr. {Coukell.} So let me make two points that I think
4290 are important. One is, a manufacturer absolutely has to have
4291 confidence that they know who is in their upstream supply
4292 chain and that they know what quality standards are in place
4293 and that there isn't a risk of sub standard product coming in
4294 through the backdoor and making its way into the supply
4295 chain.

4296 Mr. {Guthrie.} Did you find that manufacturers didn't
4297 know that or didn't have systems in place for that?

4298 Mr. {Coukell.} We absolutely found a whole spectrum,
4299 and there are great manufacturers in every country, but there
4300 are also risks. In our report, there is a photograph from a
4301 manufacturing facility in China with a whole wall of 50-
4302 gallon drums stacked up about one deep, and the inspectors
4303 went in there and said, you know, what is behind those drums;
4304 well, nothing. So they climbed over and found behind the
4305 drums a whole warehouse full of uncertified active
4306 pharmaceutical ingredient that was destined for, in that
4307 case, a European supply chain. So it does occur.

4308 On the question of foreign regulators, I think we
4309 acknowledged that the FDA is moving in the right direction on
4310 this, which is no one country can inspect the whole world,
4311 and so we have to deploy limited resources in a rational way.
4312 We do duplicate inspections and rely on other trusted
4313 regulators wherever possible.

4314 Mr. {Guthrie.} In automotive manufacturer, you actually
4315 hire people to come in and certify and audit your plant, and
4316 Ford or GM or Chrysler would accept that. Using third-party
4317 auditors that are reputable, that you can--the trick to it
4318 was or the issue was that you actually paid them to come to
4319 your plant to certify you to Ford's standard, but they had a
4320 reputation to uphold as well, and so--

4321 Mr. {Coukell.} Absolutely, and I think Congress did

4322 some of that for food in the Food Safety Modernization Act a
4323 couple of years ago. You know, one of the real leaders in
4324 industry on quality, a vice president of quality for one of
4325 the big companies has said every supplier and sub-supplier
4326 should be audited by somebody, but at the same time, if there
4327 is one company that is making, you know, an inactive
4328 ingredient like talc or something for tablets and they are
4329 supplying 30 companies, you don't need 30 audits.

4330 Mr. {Guthrie.} Right. Common sense.

4331 Thanks. I yield back.

4332 Mr. {Pitts.} The chair thanks the gentleman.

4333 That concludes the questioning, and I would like to
4334 thank the witnesses and members for participating in today's
4335 hearing. We have had a lot of very important information
4336 come before the committee, and I remind members that they
4337 have 10 business days to submit questions for the record. I
4338 will ask the witnesses to please respond promptly to those
4339 questions. Members should submit their questions by the
4340 close of business on Wednesday, February 15th.

4341 With that, without objection, the subcommittee is
4342 adjourned.

4343 [Whereupon, at 2:24 p.m., the Subcommittee was
4344 adjourned.]