

1 {York Stenographic Services, Inc.}

2 HIF160.140

3 HEARING ON ``PROMOTING THE DEVELOPMENT OF ANTIBIOTICS AND  
4 ENSURING JUDICIOUS USE IN HUMANS''

5 WEDNESDAY, JUNE 9, 2010

6 House of Representatives,

7 Subcommittee on Health

8 Committee on Energy and Commerce

9 Washington, D.C.

10 The subcommittee met, pursuant to call, at 10:09 a.m.,  
11 in Room 2123 of the Rayburn House Office Building, Hon. Frank  
12 Pallone, Jr. [Chairman of the Subcommittee] presiding.

13 Members present: Representatives Pallone, Dingell,  
14 Eshoo, Green, DeGette, Capps, Matheson, Barrow, Christensen,  
15 Sarbanes, Waxman (ex officio), Shimkus, Whitfield, Murphy of  
16 Pennsylvania, Burgess, Blackburn, Gingrey and Barton (ex  
17 officio).

18 Staff present: Sarah Despres, Counsel; Ruth Katz,

19 Public Health Counsel; Stephen Cha, Professional Staff; Eric  
20 Flamm, Professional Staff; Rachel Sher, Counsel; Alvin Banks,  
21 Special Assistant; Ryan Long, Minority Legislative Analyst;  
22 and Aarti Shah, Minority Professional Staff.

|  
23 Mr. {Pallone.} The subcommittee will come to order.

24 Today we are having a hearing on antibiotic resistance  
25 and the threat to public health, and I will recognize myself  
26 initially for an opening statement.

27 Today we are going to examine how we can best safeguard  
28 the effectiveness of antibiotics once they are on the market.  
29 We will also explore how we can ensure the adequate  
30 development of new safe and effective antibiotics. Later  
31 this year we expect to have a final hearing, essentially this  
32 is the second of three hearings, and the third or final  
33 hearing will be on antibiotic use in animal agriculture.

34 As we discussed in our first hearing, antibiotics are  
35 among the most significant medical innovations of the 20th  
36 century. The CDC lists control over infectious disease as  
37 one of its top 10 great public health achievements of the  
38 last century and mentions antimicrobials as crucial to that  
39 accomplishment.

40 Unfortunately, the potential of antimicrobials continues  
41 to be compromised. It is estimated that over 2 million  
42 people acquire bacterial infections in U.S. hospitals each  
43 year and 90,000 die as a result of these infections. We  
44 should all be alarmed that at least 70 percent of these  
45 infections are resistant to at least one drug and more and

46 more bacteria are proving to be resistant to the antibiotics  
47 currently on the market. Unfortunately, these resistant  
48 diseases are among the most predominant illnesses in the  
49 population including respiratory diseases such as pneumonia,  
50 food-related diseases including E. coli and salmonella, and  
51 hospital-acquired infections commonly known as MRSA.

52         As a matter of public health, it is imperative that we  
53 adopt a multi-pronged strategy to address antibiotic  
54 resistance. Today we will examine how we can best safeguard  
55 the effectiveness of antibiotics once they are on the market.  
56 We probably all heard stories of physicians that have  
57 overprescribed antibiotics to people who may have viral  
58 instead of bacterial infections, and while they may do this  
59 to safeguard against infection just in case, the overuse  
60 actually puts us all at risk. Patients also share blame.  
61 How many of us know someone that stopped taking their  
62 antibiotics once they felt better, even if they didn't finish  
63 the treatment.

64         Our experts will also explore how we can ensure the  
65 adequate development of new safe and effective antibiotics on  
66 the market. It is a challenging situation because unlike  
67 some pharmaceuticals which are used to treat chronic  
68 illnesses, there is not a clear return on investment for  
69 antibiotics. Antibiotics are unique because not only are

70 they used for short periods of time per illness, but the more  
71 they are used, the less effective they become. So in order  
72 to preserve their effectiveness, we as a society should all  
73 share the goal that they be used as rarely as possible. This  
74 is obviously not the business model that companies dream of,  
75 however, and I would like to welcome all of our witnesses  
76 today including government representatives from the FDA and  
77 BARDA and also our private witnesses from the Infectious  
78 Disease Society of America, the American Medical Association,  
79 the American Academy of Pediatrics, and Cubist  
80 Pharmaceuticals. The witnesses will undoubtedly share key  
81 information related to our mutual goal of protecting the  
82 public from antibiotic resistance.

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

84 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
85           Mr. {Pallone.} I would like to now recognize our  
86 ranking member, Mr. Shimkus, and also thank you for your  
87 cooperation in putting this together today. I know it has  
88 not been easy for the last 24 hours, but thank you.

89           Mr. {Shimkus.} Thank you, Mr. Chairman, and we want to  
90 welcome our witnesses both in this panel and the next, and  
91 this is an important issue. This is the second in a series  
92 that we also feel is very important.

93           Antimicrobial drugs have provided tremendous benefit for  
94 the public health over the last half century. In order to  
95 ensure it remains so, we must continue to promote appropriate  
96 and effective use and the uses we already have. Overuse and  
97 misuse can limit the effectiveness and make outright  
98 resistance grow even faster. The other half of the equation  
99 is research and development and product development which are  
100 mainly concerned over the prospect of new drugs coming  
101 online. We know the cupboard is almost bare, and of the  
102 limited drugs in development, most of them, if not all, will  
103 never see approval. Any investment in antibiotics is not  
104 likely to match that of traditional drug development and  
105 there remains an uncertain approval process when it comes to  
106 FDA. The FDA must continue to work on providing confidence  
107 and clarity so we can encourage the development of new

108 antibiotics.

109           And as I talked before the hearing, we all have great  
110 respect for the work that the FDA does and it is the gold  
111 standard in the world but many of us are concerned that we  
112 are asking them to do too much with limited resources. Those  
113 of us who aren't in the business of increasing resources  
114 would want to help you make the job more efficient and  
115 directive. That is why I have always been a risk-based  
116 person, that that is where our money should go, and we will  
117 continue to work in that direction, but we do appreciate you  
118 being here.

119           Mr. Chairman, I will be brief but I will also just raise  
120 my issue of the concern that we need a hearing on the new  
121 health care law. The President used yesterday his bully  
122 pulpit to talk about the benefits of the law. We still have  
123 yet to have a hearing on it, and I think it is probably time.  
124 If there are things the President thinks are important and is  
125 willing to go out to the American public to profess the  
126 benefits, we ought to be able to talk about those benefits  
127 here. We also should talk about some of the challenges. We  
128 did have our Republican health solutions group meet, as I  
129 discussed in the last hearing, and during that hearing Dr.  
130 Todd Williamson testified on behalf of the Coalition of State  
131 Medical National Specialty Societies representing more than

132 80,000 physicians from across the country, and his testimony  
133 said, ``The most significant cost of the new health care law  
134 will be to our patients. They will suffer decreased access  
135 to the doctors and care they need. My sickest and most  
136 vulnerable patients will suffer the most because of a  
137 depleted pool of physicians while the government continues to  
138 expand eligibility for its underfunded programs.'' In the  
139 State of Texas, 300 physicians have already stopped seeing  
140 Medicare patients over the last 2 years. Is Texas a snapshot  
141 of what is to come for the rest of the Nation when 15 percent  
142 cuts go into effect? And when it comes to Medicaid, we know  
143 the situation is even worse for physicians, in some cases,  
144 paying them 50 percent of what private insurance does. But  
145 the health reform law sets out to force millions of more  
146 Americans into Medicaid. We will face similar results when  
147 it comes to access and quality of care for patients. The  
148 State of Illinois is \$12.8 billion in debt, and Medicaid  
149 already consumes one-third of the spending for the increased  
150 cost of these new Medicaid populations.

151       Just yesterday, we had in the papers talked about N  
152 Health, which sells HSA high deductibles to employers  
153 recently announced it will terminate all its customers by  
154 December 31, 2010, because it cannot survive the health care  
155 law mandates and regulations. Then there is American

156 National Insurance Company, which similarly announced two  
157 subsidiaries, American National Life Insurance Company of  
158 Texas and Standard Life, an accident insurance company, won't  
159 sell health insurance to people in the individual market  
160 after June 30, 2010, because of the health reform law. Can  
161 we really tell these people this if you like what you have  
162 you can keep it when these companies go out of the business  
163 as the President promised to the American people. And it is  
164 only June of 2010. The full effects of this law won't go  
165 into effect until 2014. Are these problems only the tip of  
166 the iceberg?

167         So once again, Chairman, I certainly have an  
168 appreciation for our hearing today but we will continue to  
169 raise the health reform law and call on you for formal  
170 hearings to discuss the many issues both positive as the  
171 President promoted yesterday and negative, these health  
172 insurance companies leaving the market, what is working and  
173 what needs to be address before it is fully implemented.

174         Thank you, Mr. Chairman. I yield back my time.

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

176 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
177 Mr. {Pallone.} Thank you, Mr. Shimkus.

178 Our chairman of the full committee, Mr. Waxman.

179 The {Chairman.} Thank you very much, Chairman Pallone,  
180 for calling this second of a series of hearings that we are  
181 having on antibiotic resistance, which is a growing and  
182 dangerous threat to the public health and it is an issue that  
183 deserves the full and complete attention of this committee.

184 At our first hearing, we learned about the impact of  
185 antibiotic resistance on human health, and today we will  
186 continue that discussion, but also focus on two important and  
187 directly related issues: the preservation of effective  
188 medicines that already make up our antibiotics drug arsenal,  
189 and the development of new antibiotics to fight resistant  
190 bugs.

191 By definition, this is an inherently difficult goal to  
192 achieve. After all, the very use of antibiotics leads to the  
193 development of pathogens that can no longer be treated by  
194 those antibiotics. In this case, rather than use it or lose  
195 it, with antibiotics it is use it and lose it. Already  
196 untold numbers of Americans die or are infected each year by  
197 antibiotic-resistant microbes. We pay a high price in other  
198 ways as well--additional hospital stays, hospital readmission  
199 and increased doctor visits. These will add unnecessarily to

200 the Nation's annual health care bill.

201       Our hearing in May made clear that it will take a multi-  
202 pronged approach to overcome this very serious and very  
203 present problem. Today we will focus on two such strategies,  
204 a reduction in the inappropriate use of antibiotics and the  
205 expansion of the antibiotic product line and market. I  
206 believe that we must pursue both lines of attack. We simply  
207 must find ways to cut back on both the overuse and misuse of  
208 these drugs.

209       At the same time, we need to ensure the existence of a  
210 market environment that encourages the development and  
211 commercialization of new safe and effective antibiotics to  
212 treat those pathogens resistant to existing antibiotics.  
213 Such an environment does not appear to appear to be in place  
214 today.

215       As we consider possibilities for market incentives, we  
216 must not lose sight of the potential impact those incentives  
217 may have on patients, especially if new antibiotics are more  
218 expensive than the patients can afford to buy.

219       The written testimony we have already received lays out  
220 a variety of approaches to meet these objectives. I look  
221 forward to hearing more about them from our witnesses today.  
222 As we do, I hope we can continue to work on a bipartisan  
223 basis towards a public-private plan of action to address the

224 overall and pressing antibiotic resistance problem that we  
225 now face.

226 I thank the witnesses for their testimony and look  
227 forward to hearing from them. Thank you, Mr. Chairman.

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

229 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
230 Mr. {Pallone.} Thank you, Chairman Waxman.

231 The gentleman from Kentucky, Mr. Whitfield.

232 Mr. {Whitfield.} Thank you, Mr. Chairman, and I also  
233 want to thank the witnesses for being with us today on this  
234 very important subject. Certainly the American people are  
235 very much focused today on access to health care, quality of  
236 health care as well as cost of health care, and the subject  
237 matter that we are going to discuss today is one very  
238 important component of that.

239 It has already been stated that 2 million people roughly  
240 acquire infections in hospitals and about 90,000 of those die  
241 each year. Seventy percent of the hospital-acquired  
242 infections are caused by bacteria that are resistant to  
243 particular drugs most commonly used.

244 We certainly understands that the process for developing  
245 clinical trials at the FDA is extremely complex and we look  
246 forward to the testimony today to explore opportunities to  
247 make it less complex but also ensuring safety. I know it is  
248 my understanding that there about 15 antibiotics that are in  
249 the pipeline today at FDA for approval, and I am not sure how  
250 I know this but evidently we don't think there is much chance  
251 that many of those are going to be approved, but we do need  
252 to explore ways to provide incentives for pharmaceutical

253 companies as well as trying to make the system less complex  
254 but also ensuring safety, and I am delighted we are having  
255 this hearing and look forward to the testimony of all our  
256 witnesses.

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

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

|  
259 Mr. {Pallone.} Thank you, Mr. Whitfield.

260 The {Chairman.} Mr. Chairman, before you recognize--

261 Mr. {Pallone.} Yes?

262 The {Chairman.} I just want to make a unanimous consent  
263 request, which I should have made. It is to put into the  
264 record a statement by Dr. Michael T. Flavin, chairman and  
265 chief executive officer of Advanced Life Sciences prepared  
266 for the record for this committee.

267 [The information follows:]

268 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
269 Mr. {Pallone.} Without objection, so ordered. Thank  
270 you, Mr. Chairman.

271 And next is our chairman emeritus, Mr. Dingell.

272 Mr. {Dingell.} Mr. Chairman, thank you for holding  
273 today's hearing on what is a growing and real public health  
274 crisis.

275 Two months ago, we had a hearing on the basics of  
276 antibiotic resistance during which one of our witnesses, Dr.  
277 Thomas Frieden, director of the Centers for Disease Control,  
278 stated that we are moving into a post-antibiotic world. He  
279 warned that there may be soon no clinical treatments for some  
280 infections. This is a very real and frightening crisis.

281 Today, 19,000 people die a year of multi-drug-resistant  
282 MRSA. Our soldiers are coming home from Afghanistan and Iraq  
283 with acinetobacter, which is often resistant to at least  
284 three classes of antibiotics, and hospital-acquired  
285 antibiotic-resistant infections cost our health care system  
286 up to \$34 billion a year. Imagine what we are going to have  
287 to do when we find that we cannot deal with serious diseases  
288 the way we can now with antibiotics.

289 I want to thank our witnesses today for joining us, and  
290 I hope that from our witnesses we can begin to get this  
291 country on a track where we practice sound evidence-based

292 public policy that can make us better stewards of antibiotic  
293 use and of our future and how we can assist all of the  
294 stakeholders in this public health issue. More specifically,  
295 we need to learn, amongst other things, how do we prevent the  
296 spread of infections that require antibiotic treatments? How  
297 do we best educate patients and doctors about judicious and  
298 prudent use of antibiotics? And finally, how do we improve  
299 upon the current incentives and regulatory structures that  
300 bring new antibiotics and diagnostic tests into the  
301 marketplace?

302         The growing number of bacteria resistant to antibiotics  
303 is frightening and will become more so. Even more  
304 frightening is the thought that our health providers and  
305 general public have not realized the magnitude of the problem  
306 that we face with resistant bacteria. Less-effective  
307 treatments for bacterial infections mean longer-lasting  
308 illnesses, more doctor visits, extended hospital stays, the  
309 need for more-expensive and toxic medications, and in a  
310 growing number of cases, death of the patient. Our children  
311 are at a greater risk because they have the highest rates of  
312 antibiotic use. We have to be smart about our approach in  
313 addressing this issue, and today's hearing should provide  
314 great insight and direction, and it is time that we recognize  
315 the urgency of this situation.

316 I thank you, Mr. Chairman, and I yield back the balance  
317 of my time.

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

319 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
320 Mr. {Pallone.} Thank you, Chairman Dingell.

321 Next is our ranking member of the full committee, Mr.  
322 Barton.

323 Mr. {Barton.} Thank you, Mr. Chairman. It is always  
324 good to have a hearing looking to the future. We look  
325 forward to the testimony today of the individuals who are  
326 going to testify about our antibiotics and what we are doing  
327 to make sure that the next generation of antibiotics  
328 continues to be as effective as the current generation is.

329 We also look forward, Mr. Chairman, to having you and  
330 the full committee chairman at some point in time schedule  
331 some hearings on the new health care law. We find daily  
332 evidence that it is not what it appears to be. HHS has  
333 already missed numerous deadlines. We have had the CBO and  
334 other budget agencies come out that instead of saving money  
335 it is going to cost hundreds of billions, perhaps a trillion  
336 dollars more than estimated. The President must think it is  
337 in some trouble. He had a campaign-style rally this week  
338 trying to drum up support. We need to do due diligence, and  
339 if there are things in the law that need to be changed, the  
340 sooner we get about changing them, the better it will be for  
341 the American people. So I hope that that happens sooner  
342 rather than later.

343           But in terms of today's hearing, we do look forward to  
344 the testimony from our witnesses because this is an issue  
345 that does deserve some attention and we appreciate you giving  
346 it to us.

347           With that, I yield back, Mr. Chairman.

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

349 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
350 Mr. {Pallone.} Thank you, Mr. Barton.

351 The gentlewoman from California, Ms. Eshoo.

352 Ms. {Eshoo.} Thank you, Chairman Pallone, for holding  
353 this hearing on antibiotic resistance, which is a growing  
354 concern for scientists, for the medical community, for  
355 patients and certainly for policymakers. I want to extend a  
356 warm welcome to both Drs. Woodcock and Robinson and thank you  
357 for the work, the important work that you do.

358 The discovery of antibiotics transformed medical care in  
359 the 20th century. Many bacterial infections which were once  
360 deadly are now treatable illnesses. People no longer die  
361 from minor cuts, from ear infections or pneumonia.  
362 Antibiotics treat infections on the battlefield, after  
363 surgeries and in doctors' office across the country.

364 But antibiotics are not the universal remedy to all  
365 illnesses. The widespread and inappropriate use of  
366 antibiotics leads to dangerous antibiotic-resistant bacteria,  
367 and due to the relatively low side effects of antibiotic use,  
368 physicians often prescribe them for maladies such as flu or  
369 the common cold. Antibiotics cannot treat these illnesses  
370 and their misuse leads to the rise of antibiotic-resistant  
371 strains of illnesses, and as these strains appear, some  
372 patients may have nowhere to turn when they have exhausted

373 their antibiotic options.

374           Attempts to reduce antibiotic resistance must be  
375 comprehensive. We should curb the overuse of them and at the  
376 same time encourage the development of new antibiotics to  
377 keep pace with new strains of resistant infection.  
378 Antibiotic resistance has the potential to become a  
379 significant public health crisis. I am especially interested  
380 to learn about what role BARDA and Project BioShield may play  
381 in promoting the development of new antibiotics.

382           So my thanks to the FDA for not only testifying today  
383 but for your ongoing, I think extraordinary work, and I look  
384 forward to working with all the members of the committee to  
385 address the issue of antibiotic resistance.

386           I yield back, Mr. Chairman.

387           [The prepared statement of Ms. Eshoo follows:]

388 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
389 Mr. {Pallone.} Thank you.

390 Next is the gentleman from Texas, Mr. Burgess.

391 Dr. {Burgess.} Thank you, Mr. Chairman. It is an  
392 important hearing, important witnesses. I am going to submit  
393 my statement for the record and reserve time for questions.

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

395 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
396 Mr. {Pallone.} Thank you.

397 Our vice chair, the gentlewoman from California, Ms.

398 Capps.

399 Mrs. {Capps.} Thank you, Mr. Chairman. Thank you for  
400 holding this hearing, and welcome to our witnesses in both  
401 panels.

402 A few weeks ago, as others have recalled, we held an  
403 informative hearing on the subject of antibiotic resistance.  
404 I think this hearing is a logical follow-up to the many  
405 questions that arose at that time. Most importantly, how do  
406 we balance the simultaneous need to halt the development of  
407 antibiotic resistance while incentivizing the development of  
408 effective antibiotics and ensuring patient compliance? I  
409 think we will learn from our witnesses today that the  
410 solution lies in a multifaceted approach that relies on, one,  
411 improving our basic research capabilities; two, incentivizing  
412 the private sector to invest in the necessary research and  
413 development; three, better educating health professionals on  
414 the most effective prescription of antibiotics and the ways  
415 to do this; and last, and I am sure there are more, making  
416 our public more aware of the ways they minimize risk of  
417 infection, prevention, in other words.

418 So I look forward to hearing from our witnesses on their

419 suggestions for achieving these objectives and how we can  
420 develop the most appropriate policies to implement them, and  
421 I yield back the balance of my time.

422 [The prepared statement of Mrs. Capps follows:]

423 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
424 Mr. {Pallone.} Thank you.

425 Next is the gentleman from Georgia, Mr. Gingrey.

426 Dr. {Gingrey.} Thank you, Mr. Chairman.

427 Antibiotics are a critical treatment for many bacterial  
428 infections and oftentimes their usage saves lives.

429 Unfortunately, overutilization of antibiotics makes it more  
430 likely that bacterial resistance to antibiotic therapy will  
431 develop. Staying ahead of bacterial resistance to  
432 antibiotics is vital to our health care system. We can do  
433 that in part by educating medical providers on the proper use  
434 of these drugs. Many illnesses can be treated by proper  
435 diagnosis and over-the-counter remedies rather than relying  
436 on prescribing antibiotics. In many instances, it is  
437 appropriate and does not require much time or cost to take a  
438 culture in order to properly identify a patient's condition.  
439 If we are to combat bacterial infections, taking the  
440 necessary steps to identify appropriate cases for antibiotics  
441 is an important first step.

442 Mr. Chairman, we must also be aware that patient demand  
443 plays a big part in the overutilization of antibiotics. In  
444 many instances, patients will request an antibiotic from  
445 their provider because they are convinced it will cure common  
446 infections faster than over-the-counter treatment, and that

447 is certainly not always the case. Having spent time in  
448 general practice during my 30-year medical career, I  
449 understand how patient demands can influence provider  
450 decision. Therefore, any education efforts should include  
451 those aimed at informing patients of the dangers of overusage  
452 of antibiotics.

453         Unfortunately, no amount of education is going to stop  
454 antibiotic resistance. New forms of antibiotics must be  
455 available if we are to effectively deal with this emerging  
456 problem. Today the high cost of drug development and short  
457 treatment courses have caused a decreasing number of  
458 companies to pursue antibiotic development. In other words,  
459 their success has led to the fact that there is a shortage  
460 now of antibiotics. Any solution geared towards addressing  
461 future bacterial infections must ensure that proper  
462 incentives are identified and supported that will encourage  
463 greater antibiotic development. This committee should not  
464 shy away from reviewing the pathway of drug development, from  
465 drug discovery all the way through to licensing. My hope is  
466 that a balanced and thorough review of the antibiotic market  
467 will help ensure that we properly identify any disincentives  
468 that may exist with regard to the production of new  
469 antibiotics and are better prepared to promote incentives  
470 that may reverse this current trend. I believe this problem

471 is one that can best be solved by encouraging industry and  
472 government to work together to find the solutions that our  
473 future health needs require.

474         Mr. Chairman, with these thoughts in mind, I would like  
475 to thank you for holding today's hearing on this important  
476 and growing issue. I look forward to hearing the expert  
477 testimony from our distinguished panel of witnesses, and I  
478 yield back the balance of my time.

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

480 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
481 Mr. {Pallone.} Thank you.

482 The gentleman from Utah, Mr. Matheson.

483 Mr. {Matheson.} Thank you, Mr. Chairman, for holding  
484 this hearing today, and thanks to the witnesses as well.

485 As you are aware, I have reintroduced legislation in  
486 this Congress, H.R. 2400, the Strategies to Address the  
487 Antimicrobial Resistance Act, or the STAR Act, as the acronym  
488 is, which I believe is a comprehensive piece of legislation  
489 to strengthen our Nation's response to pathogens that are  
490 increasingly resistant to antibiotics. Senators Sherrod  
491 Brown and Orrin Hatch introduced the companion bill in the  
492 110th Congress. Over 25 health care stakeholders support  
493 this legislation, a number of which will testify today in  
494 this hearing. H.R. 2400 provides strategies and authorizes  
495 critically needed funding to strengthen federal antimicrobial  
496 resistance surveillance, prevention and control and research  
497 efforts. It also strengthens coordination within the  
498 Department of Health and Human Services' agencies as well as  
499 across other federal departments that are important to  
500 addressing antimicrobial resistance and considers  
501 opportunities to address this issue globally.

502 The STAR Act provides a rare opportunity to bring many  
503 partners together to protect public health. This legislation

504 was developed with input from infectious disease experts and  
505 leaders in public health and provides authority for the  
506 federal government to combat antimicrobial resistance in four  
507 ways. Number one: It reauthorizes the antimicrobial  
508 resistance task force, establishing an advisory board of  
509 outside experts and an antimicrobial resistance office  
510 reporting to the Secretary of Health and Human Services,  
511 whose director will coordinate government efforts to combat  
512 antimicrobial resistance. Number two, it creates an  
513 antimicrobial resistance strategic research plan as well as  
514 establish the antimicrobial resistance surveillance and  
515 research network. Number three, the bill calls for  
516 collecting available and relevant data to allow government to  
517 better address the antimicrobial resistance problem, and  
518 fourth, it establishes demonstration projects to encourage  
519 more appropriate use of existing antibiotics.

520 Mr. Chairman, as you are aware, our committee has had a  
521 critical role in establishing the foundation of work for this  
522 issue. Our chairman emeritus, Mr. Dingell, requested a  
523 report on the impact of antibiotic-resistant bacteria in the  
524 103rd Congress. In the 106th Congress, Chairman Stupak  
525 introduced legislation to direct the Secretary of HHS to  
526 establish the antimicrobial resistance task force. In the  
527 10th Congress, several members of this committee joined

528 Senator Sherrod Brown, who at that point was a member of this  
529 committee, to introduce legislation to provide funding for  
530 the top priority action items of the public health action  
531 plan.

532 I provided this brief snapshot of this history for my  
533 colleagues to show that while some work has been  
534 accomplished, the war against resistance to infection looms  
535 large for our Nation's public health, and to be clear for my  
536 colleagues on both sides of the aisle, this is a public  
537 health emergency that in the year 2007 alone infected more  
538 than 94,000 people and its estimated cost to our health care  
539 system was millions of dollars.

540 I look forward to the hearing today and hearing from our  
541 witnesses and look forward to doing whatever we can to work  
542 with this committee to help move this legislation forward. I  
543 yield back my time.

544 [The prepared statement of Mr. Matheson follows:]

545 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
546 Mr. {Pallone.} Thank you, Mr. Matheson.

547 The gentleman from Pennsylvania, Mr. Murphy.

548 Mr. {Murphy of Pennsylvania.} Thank you, Mr. Chairman.

549 Two million people will acquire infections in hospitals  
550 this year. Between 90,000 and 100,000 will die. The costs  
551 will be about \$50 billion to treat them. And by those  
552 numbers, so far today this year, 44,133 people have died from  
553 a hospital-acquired infection.

554 Although today we are talking about the overprescribing  
555 of antibiotics, let us understand the most effective  
556 antibiotic is the one you do not have to prescribe.  
557 Prevention does work. Hospitals that vigorously gather data  
558 on infection rates and enforce infection controls see decline  
559 in infection rates but many doctors, families, hospital staff  
560 do not do this, and that is the root of one of our problems  
561 that we have to address.

562 Over time, I have introduced over repeated Congresses  
563 legislation to require hospitals and clinic to report their  
564 infection data. Unfortunately, we have not moved it forward  
565 at all in committee and has not moved anywhere in the House.  
566 This means that hospitals are not required to gather  
567 information nor report their infection rates, and as such, a  
568 lot of people are dying because we are not paying attention

569 to it.

570           The solutions don't require great science or approval  
571 from the FDA. It means that people that come near a patient  
572 have to wash their hands, use sterile equipment, wear clean  
573 clothes such as gowns or gloves or masks, clean up before and  
574 after procedures, use antibiotics before and after surgery,  
575 and have close monitoring of infection rates and quick  
576 reaction time when infections occur.

577           So I have reintroduced this bill once again, H.R. 3104.  
578 I hope that in addition to dealing with bacteria that are  
579 resistant to antibiotics, we also begin to deal with  
580 resistance by caregivers to passing legislation that requires  
581 them report infection rates. To me, it is incomprehensible  
582 that the very providers who are out there saying we need to  
583 reduce infection rates are the ones opposed to finding out  
584 what those infection rates are. It is reprehensible that on  
585 one side of our mouth we are saying we want people to live  
586 and out of the other side of the mouth we are saying people  
587 don't tell anybody that we are not doing a very good job  
588 about it. I hope that sometime this committee will consider  
589 this legislation, require hospitals and clinics to begin to  
590 look at these rates and report them, and in so doing, I might  
591 add, when hospitals do this, they save lives. It is  
592 repeatedly demonstrated. And once again, the most effective

593 antibiotic is the one you don't have to use. I yield back.

594 [The prepared statement of Mr. Murphy of Pennsylvania

595 follows:]

596 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
597 Mr. {Pallone.} Thank you.

598 The gentlewoman from the Virgin Islands, Ms.

599 Christensen.

600 Mrs. {Christensen.} Thank you, Chairman Pallone. Good  
601 morning.

602 As I read the testimonies last night and reflected on  
603 the first hearing with Drs. Frieden and Fauci, I kept  
604 thinking that we are supposed to leave a better world for our  
605 children than we have and there are many events that bring  
606 this into question and the issue of the antibiotic resistance  
607 which threatens to set the treatment of infectious diseases  
608 back into the Dark Ages is one of them. Dr. Frieden's and  
609 Dr. Fauci's testimony were very informative, and the  
610 witnesses we will hear from today will add to our  
611 understanding of the issue and to their recommendations.

612 As a family physician like my colleague over here, who  
613 practiced for over 20 years, I know the pressure that doctors  
614 are under to prescribe antibiotics and how difficult it is to  
615 have a patient continue on their regimen once they start to  
616 feel better, and those are but two of our challenges. The  
617 fact that only five out of several hundred drugs in the  
618 pipeline are antibiotics speaks volumes about the level of  
619 the crisis and the need to incentivize the pharmaceutical

620 industry, something I recall not doing very well initially  
621 with BioShield but greatly improving on in 2006 with BARDA.

622         This is a multifaceted problem in which everyone from  
623 the patient to the provider and all the health care workers,  
624 the Department and Congress have an important role to play.  
625 We have several agencies and pieces of legislation with which  
626 we begin to address the crisis and I look forward to what our  
627 witnesses have to say about them.

628         I want to thank you, Chairman Pallone and Ranking Member  
629 Shimkus for this hearing and the witnesses for their presence  
630 and for their very informative testimonies. Thanks.

631         [The prepared statement of Mrs. Christensen follows:]

632 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

633 Mr. {Pallone.} Thank you, Ms. Christensen.

634 I just wanted to yield briefly to our ranking member,  
635 Mr. Barton, for a personal point.

636 Mr. {Barton.} I want to make a point of personal  
637 privilege, Mr. Chairman. Congresswoman Blackburn, whose  
638 birthday was yesterday, is smiling amongst us and she has had  
639 the great foresight to hire my stepdaughter or employ my  
640 stepdaughter as one of her interns, Lindsay Taylor, who is a  
641 junior at the University of Texas majoring, I believe, in  
642 business with a minor in marketing, and she did some of the  
643 work to prepare for the hearing today. So I want to  
644 introduce Marsha's intern and my stepdaughter Lindsay Taylor  
645 to the committee. Wave.

646 Mr. {Pallone.} Thank you, and welcome.

647 Mr. {Barton.} Thank you, Mr. Chairman.

648 Mr. {Pallone.} Thank you. Welcome. And happy birthday  
649 to you also, Marsha.

650 Next is--actually next is the gentlewoman from  
651 Tennessee, Ms. Blackburn.

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

653 Welcome to those that are here today and thank you for  
654 the work that you have done in preparation for coming to us.  
655 Mr. Chairman, I thank you for the hearing today.

656           An interesting little tidbit as we prepared for this.  
657   According to the Tennessee Department of Health, the  
658   antibiotic resistant rates in Tennessee are among the highest  
659   in the Nation, and we know that this has come from overuse  
660   and misuse of antibiotics and it has contributed to this.  
661   This is something we have been fighting in our State for a  
662   long time as prescription use was higher than it should be.  
663   We know that it is a looming public health crisis, and it is  
664   of concern to us when we look at the rising incidence of  
665   drug-resistant bacteria, and we are concerned about the  
666   stagnant R&D of new therapies to treat some of these new  
667   infections.

668           It is alarming that medical professionals have very few  
669   resources to treat some of these patients as demand far  
670   outpaces supply of the antimicrobials. While prevention is  
671   key, not every infection is preventable, and we understand  
672   that but there is a growing concern about R&D, and it  
673   concerns me that there are only a few small private companies  
674   that are investing in R&D and putting their money into that  
675   and developing the new therapies that are needed, and we know  
676   it is difficult to hit a moving target, and as the  
677   antimicrobial pathogens constantly mutate, resulting in long-  
678   term R&D investment needs, and also realizing that for many  
679   of these there is a short-term usage.

680           And the other thing we are concerned about and that we  
681 hear from our medical community about is uncertainty from the  
682 FDA. So as we go through the hearing today, those are points  
683 that we are going to want to cover with you, the concern  
684 about R&D, the concern about uncertainty with the FDA, and  
685 then also just the antibiotic resistance rates that we see in  
686 our State.

687           I thank you, and I yield back.

688           [The prepared statement of Mrs. Blackburn follows:]

689           \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
690 Mr. {Pallone.} Thank you, Ms. Blackburn.

691 And I guess last, although I am not sure, is the  
692 gentlewoman from Colorado, Ms. DeGette.

693 Ms. {DeGette.} Thank you very much, Mr. Chairman. At  
694 least you didn't say I was last and least. I will submit my  
695 opening statement for the record.

696 I just want to point out a couple of facts that are even  
697 more disturbing than some of the facts we have heard from the  
698 members. One-third of the world's population is infected  
699 with TB, and in 2008 multidrug-resistant TB accounted for 5  
700 percent of all tuberculosis cases, which is the highest  
701 percentage recorded to date, and even more frightening is the  
702 emergence of extensively drug-resistant tuberculosis that is  
703 resistant to all major TB drugs available. In the United  
704 States, 70 percent of the 2 million who die from hospital-  
705 acquired infections were infected with strains resistant to  
706 at least one antibiotic, and according to the CDC, \$1.1  
707 billion is spent annually on unnecessary antibiotic  
708 prescriptions for adult upper respiratory infections. Those  
709 billions of dollars could be spent on developing new  
710 antimicrobials, not needlessly encouraging antibiotic  
711 resistance.

712 Unfortunately, antibiotic resistance will never go away

713 because bacteria have an incredible capacity to evolve and  
714 multiply. Bacteria have existed on earth a thousand times  
715 longer than we have and can undergo 500,000 generations in  
716 the time it takes humans to undergo one generation. And so  
717 really, all the members today agree that we need to  
718 proactively confront antibiotic resistance. We can't  
719 eliminate it but what we can do is significantly reduce the  
720 rate and spread of antibiotic-resistant pathogens.

721         So everybody has noted it is important that we use  
722 antibiotics prudently, but prudent use alone is not enough.  
723 We need a multi-pronged approach that has regulation,  
724 surveillance, research and obviously new discoveries must  
725 rigorously be pursued in parallel. In addition, while it is  
726 not the topic of the hearing today, we need to look very  
727 closely at overuse of antibiotics in agriculture because that  
728 is another big problem that we face.

729         So it is a multi-pronged problem. I am glad, Mr.  
730 Chairman, you are looking at it in a multiple series of  
731 hearings, and since I am the last member, I am going to yield  
732 back the balance of my time so we can hear from our  
733 distinguished witnesses. Thank you.

734         [The prepared statement of Ms. DeGette follows:]

735 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
736           Mr. {Pallone.} Thank you, Ms. DeGette.

737           So that does conclude the opening statements by our  
738 members and we will turn to our first panel, who are already  
739 seated. I want to welcome you. On our first panel to our  
740 left, or to my left, I should say, is Dr. Janet Woodcock, who  
741 is director of the Center for Drug Evaluation and Research at  
742 the FDA, and next to her is Dr. Robin Robinson, who is  
743 director of Biomedical Advanced Research and Development  
744 Authority with the Department of Health and Human Services.  
745 You know the drill, 5-minute opening statements. They become  
746 part of the record, and you can submit additional written  
747 statements in writing for inclusion in the record after, if  
748 you like.

749           So I will begin with Dr. Woodcock. Thank you.

|  
750 ^STATEMENTS OF JANET WOODCOCK, MD, CENTER FOR DRUG EVALUATION  
751 AND RESEARCH, FOOD AND DRUG ADMINISTRATION; AND ROBIN  
752 ROBINSON, MD, DIRECTOR, BIOMEDICAL ADVANCED RESEARCH AND  
753 DEVELOPMENT AUTHORITY, DEPARTMENT OF HEALTH AND HUMAN  
754 SERVICES

|  
755 ^STATEMENT OF JANET WOODCOCK

756 } Dr. {Woodcock.} Mr. Chairman and members of the  
757 subcommittee, I am Janet Woodcock. I am the director of the  
758 Center for Drug Evaluation and Research at the FDA, and I  
759 thank you for the opportunity to testify on this important  
760 topic.

761 Maintaining access to lifesaving antibiotics and  
762 combating antimicrobial resistance are critically important  
763 to the FDA. As a rheumatologist, I can attest both to the  
764 power of these drugs as they save the lives of many of my  
765 immunocompromised patients and to the tragedy when they were  
766 really not enough to combat the infection and I lost young  
767 patients, some of the most difficult episodes of my  
768 professional career.

769 Antimicrobial therapy is really one of the triumphs of  
770 modern medicine. Louis Thomas, who is one of our

771 distinguished American physicians, clinician and scientists,  
772 witnessed the dawn of the antibiotic era when he was a  
773 medical trainee, and he describes a transformation from  
774 helplessness in the face of almost certain death of a patient  
775 to intervention that could rapidly restore a patient to  
776 health. We can't go back to this helplessness, and I think  
777 that is what drives the concern about antibiotic resistance.  
778 These were truly wonder drugs at that time.

779         But what was not known at the time is that these  
780 medicines came with an expiration date. The use of  
781 antimicrobials, especially indiscriminate use, will affect  
782 the timing of that expiration date but every antibiotic will  
783 get to the end of its usefulness as the members have already  
784 said because the microbes have many strategies to elude our  
785 chemical attacks and so we must use our intelligence, our  
786 science and our technology to stay ahead of the microbes. We  
787 must use antimicrobials carefully to prolong their  
788 effectiveness but we must also have new interventions in the  
789 pipeline.

790         Over the last half century, biomedicine has relied upon  
791 the private sector to fill this pipeline fueled by  
792 government-supposed basic science. This arrangement has  
793 produced a vast array of active antimicrobials. However,  
794 over the last two decades a combination of economic and

795 scientific factors has decreased this productivity. The  
796 pipeline is diminished at a time when the need could not be  
797 greater.

798 I would like to provide some insight into the scientific  
799 problems that we face. Our success in developing  
800 antimicrobials means that most common infections are  
801 adequately treated with existing therapy. This change in the  
802 history of infections makes it more difficult to study new  
803 treatments. For critically ill individuals, though, time is  
804 of the essence in getting treatment and delays to obtain  
805 consent and to complete study enrollment are often not  
806 acceptable and limit enrollment of very ill patients into  
807 studies of new treatments and the historical widespread  
808 antibiotic use has resulted in a patchwork of resistance  
809 problems that have already been alluded to.

810 In the absence of rapid diagnostic tests for the  
811 identity and resistance patterns of the infecting organisms,  
812 doctors don't know what they are facing when they are  
813 treating an individual patient. These factors create the  
814 need for new scientific methods to study antimicrobial drugs.  
815 FDA has been working with the scientific community to develop  
816 these methods. This is an example of regulatory science, the  
817 kind that has been advanced by Dr. Peggy Hamburg, our FDA  
818 commissioner. FDA plans to publish additional guidance on

819 these methods within the next 6 months to help establish new  
820 scientific standards for evaluation of antimicrobial drugs.

821 In closing, I would like to add a note of optimism to  
822 this picture. The filings for new studies of experimental  
823 antibiotics in people, which are called INDs, the first test  
824 of a new therapy in humans, has been in a steep decline since  
825 1987, and every year we have seen fewer and fewer new  
826 compounds come into the clinic for testing, but in the last 3  
827 years we have seen a reversal of this trend with a sharp  
828 upward move. We have seen more small companies and startups  
829 involved in the field and interest in medically important  
830 infectious conditions that lack good treatment. This may be  
831 good news for our patients. But to bring this into the hands  
832 of doctors, to bring these new innovations into the hands of  
833 doctors requires concerted effort on the part of academia,  
834 government and the private sector, and we hope to contribute  
835 to that. Thank you.

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

837 \*\*\*\*\* INSERT 1 \*\*\*\*\*

|

838 Mr. {Pallone.} Thank you, Dr. Woodcock.

839 Dr. Robinson.

|  
840 ^STATEMENT OF ROBIN ROBINSON

841 } Dr. {Robinson.} Good morning, Chairman Pallone, Ranking  
842 Member Shimkus, Chairmen Waxman and Dingell and other  
843 distinguished members of the subcommittee, I am Robin  
844 Robinson, director of Biomedical Advanced Research and  
845 Development Authority, known to most of you as BARDA, at HHS.

846 Antimicrobial resistance is a major concern to you, to  
847 the Nation and also to BARDA, and we appreciate the  
848 opportunity to talk to you about how we are going to move  
849 forward in combating this problem.

850 As has been stated, antimicrobials are our primary  
851 weapons in the fight against old and new infectious diseases.  
852 The discovery and development of antibiotics in the mid-20th  
853 century is among the greatest advances in the history of  
854 medicine and public health and they remain a mainstay in our  
855 treatment and use of medicine.

856 In addition to antibiotic resistance being a problem in  
857 community-acquired diseases, antibiotic resistance provides  
858 an additional concern to BARDA as resistance to current  
859 antimicrobials could be intentionally introduced by genetic  
860 manipulation and to otherwise susceptible bacteria including  
861 bioterrorism bacterial agents producing a biological

862 superweapon that would render our stockpiles of antibiotics  
863 obsolete during an attack. Further, naturally occurring  
864 drug-resistant isolates of several biodefense pathogens  
865 including plague have been detected by environmental and  
866 clinical surveillance, making the availability of antibiotic-  
867 resistant bioterrorism pathogens even more feasible. Thus,  
868 the increasing prevalence of antimicrobial-resistant bacteria  
869 is not only a matter of concern for public health but of  
870 national security.

871       Antibiotic resistance is further exacerbated by the  
872 dearth of antibiotic candidates that are coming through the  
873 development pipeline with a little bit of glimmer coming from  
874 what Dr. Woodcock has just said. The consequences of the  
875 limited antibiotic development pipeline are obvious and seen  
876 every day among medical practitioners and public health  
877 officers with tragic outcomes for growing number of patients  
878 and using drugs that are becoming obsolete. The public  
879 health and biodefense repercussions of antibiotic resistance  
880 call for greater public-private partnerships between the  
881 federal government and industry to provide the necessary  
882 support, core clinical development and manufacturing services  
883 and incentives to make a robust development pipeline of new  
884 classes of antibiotics and other products.

885       Into this setting of escalating antibiotic resistance,

886 what can BARDA do? BARDA was established by the Pandemic and  
887 All-Hazards Preparedness Act of 2006 to ensure the United  
888 States has sufficient supply of vaccine and drugs to respond  
889 to public health emergencies caused by pandemic influenza,  
890 chemical, biological, radiological and nuclear threats, and  
891 emerging infectious diseases. BARDA uniquely bridges a  
892 critical gap referred to as the Valley of Death in the public  
893 health, medical and biodefense infrastructure that is  
894 facilitating the advanced development and manufacturing  
895 acquisitions of medical countermeasures that have little or  
896 no commercial markets by forcing public and private  
897 partnerships. In its short history, BARDA has taken a multi-  
898 pronged approach to pandemic influenza and biodefense medical  
899 countermeasure programs to stimulate drug and vaccine  
900 development and manufacturing capabilities.

901 Similarly, we have proposed that we move forward with  
902 this multi-pronged approach for antibiotic resistance. This  
903 approach and the authorities provided by the Pandemic and  
904 All-Hazards Preparedness Act would allow BARDA to develop new  
905 classes of antibiotics as well as other medicines including  
906 vaccines and diagnostics that are authorized under PAHPA for  
907 BARDA to address in this fight against antibiotic resistance.

908 So what would our strategy be for combating antibiotic  
909 resistance? First, to continue our development of new

910 classes of broad-spectrum antimicrobials not only for  
911 biodefense but for public health. Secondly, vaccines for  
912 high-priority bacterial pathogens, and these vaccines would  
913 be, say, for Staph aureus that would combat MRSA. And  
914 lastly, point-of-care diagnostics for high-priority bacterial  
915 pathogens which would actually change the way that medicine  
916 could be practiced by actually having point-of-care  
917 diagnostics that a physician could provide the appropriate  
918 care for patients. Together these actually have a ripple  
919 effect not only on antimicrobial resistance but also in the  
920 pipeline for other drugs by using multi-utilization platform  
921 technologies and moving forward with these together we think  
922 that we can make a big difference going forward.

923         So I look forward to being able to answer questions for  
924 you in BARDA's section of the pie as we go forward. Thank  
925 you.

926         [The prepared statement of Dr. Robinson follows:]

927 \*\*\*\*\* INSERT 2 \*\*\*\*\*

|  
928           Mr. {Pallone.} Thank you, Dr. Robinson, and we will  
929 move right to questions, and I will recognize myself  
930 initially.

931           I wanted to ask Dr. Woodcock a question. A couple of  
932 the witnesses on the second panel, which we haven't heard  
933 from but we have their testimony, they cite regulatory  
934 uncertainty as one of the factors contributing to why there  
935 are so few effective antibiotics on the market today and that  
936 this uncertainty compounds the other economic disincentives  
937 that confront companies considering investing in the  
938 development of new antibiotics. An example of this  
939 regulatory uncertainty, according to one of the witnesses,  
940 they cite the FDA's failure to finalize certain documents  
941 that would provide guidance to industry on how to satisfy  
942 FDA's requirements for pre-market clinical trials of  
943 specified antibiotics. Now, your testimony, Dr. Woodcock,  
944 describes some of the difficult questions and issues  
945 surrounding these clinical trials on new antibiotics and I  
946 recognize that the stakes here are high, but on the one hand  
947 you are faced with what we all recognize as a dangerous lack  
948 of new safe and effective antibiotics. On the other hand,  
949 FDA doesn't want to approve new antibiotics that not only may  
950 not work but could also contribute to the resistance problem.

951 So formulating these guidelines is obviously not easy but I  
952 wanted you to tell some more about the difficulties you faced  
953 in developing and completing these guidelines, if you will.

954 Dr. {Woodcock.} Well, first of all, let me say that the  
955 regulatory path is pretty clear for an obviously superior  
956 treatment so if a treatment were developed that could beat  
957 other antibiotics or treat resistant therapy where no other  
958 antibiotic is effective, that regulatory path is very clear.  
959 The problem is for treatment areas where there is a lot of  
960 satisfactory therapy and those are typically the targets for  
961 commercial development because, as some of the members  
962 already alluded to, those are very widespread in the  
963 community, sinusitis and so forth. Where there is very  
964 effective therapy out there, it is difficult to tell whether  
965 a new treatment is actually equivalent to the existing  
966 treatments and we don't want to run the risk of successively  
967 approving more inferior treatments to the point where at some  
968 point we have approved therapies that aren't actually  
969 effective.

970 Mr. {Pallone.} Okay.

971 Dr. {Woodcock.} So we are developing new scientific  
972 methods to evaluate these conditions in a time where there is  
973 adequate antibiotic therapy out there and it is more  
974 difficult to do that. However, companies that wish to pursue

975 other types of infections that are currently not very well  
976 treated, that is a clearer path but that is not as  
977 commercially desirable a path to get onto the market.

978         Mr. {Pallone.} Now, what about the timelines? Can you  
979 tell us the anticipated timelines for completing the draft  
980 guidelines you listed in your testimony, and then what would  
981 companies or what should companies do now before they are  
982 completed? Can they rely on the draft guidances or wait  
983 until they are finalized?

984         Dr. {Woodcock.} Companies may come to the FDA and  
985 obtain advice on an individual basis, development plan basis,  
986 and that's what companies can do right now is talk to the  
987 FDA, but in an era, in a time of some scientific uncertainty,  
988 there is more risk to development, but I would reiterate that  
989 this is for these common infections, many of them that have  
990 currently satisfactory treatment. We do expect to move to  
991 finalize many of our guidances that we have published in  
992 draft. We are going to publish in the next 6 months several  
993 additional drafts of versions because there has been a great  
994 deal of scientific controversy about these evaluation methods  
995 and what methods would rely result in effective antibiotics  
996 being approved by the FDA, which is what we all, I think,  
997 want.

998         Mr. {Pallone.} You are still talking about drafts,

999       though.   What about the final documents?

1000           Dr. {Woodcock.}   Yes, we will move to finalize these  
1001 documents as rapidly as possible.   We are moving to finalize  
1002 some of the documents.

1003           Mr. {Pallone.}   Okay.   I mean, it seems like these are  
1004 very difficult scientific issues but at the same time it is  
1005 important to get them right, but I just wanted to stress how  
1006 important it is to resolve these issues and get these  
1007 guidelines finalized as soon as possible.   I know you are not  
1008 giving me specific timeliness but it is really important to  
1009 get it moving.

1010           Dr. {Woodcock.}   We agree with that, and we have  
1011 recently entered into a collaboration to do what we call  
1012 qualification work, which people might call validation work.  
1013 We are looking at these new end points in clinical trials and  
1014 see how they perform, and that is the kind of regulatory  
1015 science work that really can move this ahead and provide  
1016 everyone with the confidence that these new scientific  
1017 methods are the right methods to test these new products and  
1018 move them efficiently through the pipeline.   So we agree but  
1019 unfortunately there was some scientific work that had to be  
1020 done to get these into final.

1021           Mr. {Pallone.}   Thank you.

1022           Mr. Shimkus.

1023           Mr. {Shimkus.} Thank you, Mr. Chairman. I think I am  
1024 going to follow your line, but first, Dr. Woodcock, the  
1025 chairman had the benefit of receiving testimony from the  
1026 second panel to read what they said to ask you questions.  
1027 FDA submitted your testimony at 9:20 p.m. last night, or at  
1028 least the minority staff got it at 9:20 p.m., which is way  
1029 from the 48 hours. So we just want to raise that issue to  
1030 ensure that we get timely submissions so we can do our due  
1031 diligence on our side just as the chairman did, and that does  
1032 help to have a heads-up of what the second panel is going to  
1033 do.

1034           Following into my questioning, I am going to follow this  
1035 line of thought on the antibiotic development and regulatory  
1036 uncertainty, which you were already alluding to. What we  
1037 have heard is that there is not certainty or it is unclear  
1038 the type of clinical trials that are needed, and when  
1039 companies have invested a lot of capital in the trials, only  
1040 then to be told that their clinical trials were insufficient,  
1041 what can you do from a regulatory perspective to help clear  
1042 up this regulatory uncertainty?

1043           Dr. {Woodcock.} There is no doubt that predictability  
1044 is one of the most important things for incentivizing  
1045 commercial development in a specific indication area. So  
1046 those who have to invest money need to know that if they dot

1047 all the i's and cross all the t's that they can get their--  
1048 and the drug works and is safe they can get it across the  
1049 finish line. We recognize that and we do everything possible  
1050 to provide that predictability of development path. However,  
1051 as science changes, we have to--and the history of the  
1052 diseases have changed based on the availability of all these  
1053 other effective antibiotics, we have had to change the  
1054 evaluation methods. That created a transition period that  
1055 was very uncomfortable. We hope we are ending, reaching the  
1056 end of that transition period so that we have new designs  
1057 that are very clear and we have predictable development  
1058 paths. But I will say I think that the time when companies  
1059 seek to get sort of blockbuster antibiotics to treat otitis  
1060 media or respiratory conditions and so forth and get those on  
1061 the market, that is not exactly what you are talking about  
1062 here, I think, in getting a new pipeline moving through. You  
1063 are talking about getting new, effective antibiotics--

1064       Mr. {Shimkus.} Right. My follow-up will be on the  
1065 pipeline, so I mean, your analysis is correct. But it seems  
1066 to me that what you are saying is, you don't need any  
1067 additional authority to bring this certainty, you just need  
1068 to make a decision for new antibiotic regime of what is then  
1069 going to be considered a safe clinical trial, right? You  
1070 have the authority to do this?

1071 Dr. {Woodcock.} Yes, we have the authority. We need an  
1072 evaluation method that we can rely upon, so if you test the  
1073 antibiotic with that method you can reliably say that  
1074 antibiotic works because that is what we are assuring the  
1075 physicians and the patients is, you take this, this is an  
1076 effective antibiotic.

1077 Mr. {Shimkus.} Right. Then following up on what you  
1078 mentioned before, is the pipeline there?

1079 Dr. {Woodcock.} We are seeing--yes, the pipeline is  
1080 diminished and has been for many years. What we are seeing  
1081 in the very early stages of clinical development is a  
1082 remarkable upturn. We can't--

1083 Mr. {Shimkus.} And that is in your testimony. You  
1084 talked about the decline, but then some new submissions by  
1085 smaller companies in your testimony. Do you need to  
1086 encourage more people to now get involved so that the  
1087 pipeline is not there? Do you need any more additional  
1088 authority?

1089 Dr. {Woodcock.} I don't think it is FDA authority. Our  
1090 role is to make sure these treatments are safe and effective  
1091 and that there is a clear development path for these. It is  
1092 clear, I think, to everyone that more incentives of some type  
1093 or some type of encouragement of investors and companies and  
1094 scientists and so forth to enter into this area is needed.

1095 Mr. {Shimkus.} Thank you. Let me move quickly to Dr.  
1096 Robinson. What is your role in fostering new antibiotic  
1097 development?

1098 Dr. {Robinson.} As I said in my testimony, we are  
1099 responsible for antimicrobials for biotreats as part of our  
1100 Project BioShield mandate but we are also responsible for  
1101 emerging infectious disease as mandated by PAHPA, and we are  
1102 reaching out further with dual-purpose antibiotics not only  
1103 for plague, tularemia and so forth but also we will be going  
1104 forward with community diseases including those that are  
1105 gram-negative microorganisms. We see that the antibiotic  
1106 resistance to TB really needs a very specific set of drugs  
1107 and other approaches including that are non-antibiotics where  
1108 a vaccine or vaccines may be applicable such as I mentioned  
1109 the Staph aureus with MRSA but also with diagnostics as Dr.  
1110 Frieden talked about and Dr. Fauci did, that one of the ways  
1111 that we can help physicians immediately is by having point-  
1112 of-care diagnostics that allow them to make the proper  
1113 diagnosis and then prescribe the correct drugs.

1114 Mr. {Shimkus.} My time is expired. Thank you, Mr.  
1115 Chairman.

1116 Mr. {Pallone.} Thank you. I just want to join with Mr.  
1117 Shimkus's comments about the timeliness of the testimony. I  
1118 understand it came in maybe a little earlier than what he

1119 said, but the bottom line is, we didn't get it until  
1120 yesterday evening, and it is supposed to be 48 hours, and  
1121 members, not that I am trying to bemoan us but we come in for  
1122 votes at 6:30 and it is almost impossible to read the  
1123 testimony the night before when you are just arriving here  
1124 for votes, so I would just ask you and FDA, because I know he  
1125 has pointed this out several times with FDA and Human and  
1126 Health Services, we really need to get the testimony in in a  
1127 timely fashion, otherwise we really can't formulate questions  
1128 and really have an effective hearing. So I just wanted to  
1129 mention that again.

1130         The next is the gentlewoman from the Virgin Islands, Ms.  
1131 Christensen.

1132         Mrs. {Christensen.} Thank you. I didn't expect to be  
1133 coming up this quickly, and thank you both for being here and  
1134 for your testimony again.

1135         Dr. Woodcock, at the end of your testimony you gave us a  
1136 little bit of good news, so to what do you attribute the  
1137 increase or have you been able to attribute it to anything,  
1138 the increase in the new investigations of antimicrobial  
1139 drugs?

1140         Dr. {Woodcock.} We are seeing this to some extent  
1141 across the board in drug development, and I attribute it both  
1142 to the new science that has identified a lot of new targets,

1143 genetics and so forth, so that is number one. Number two,  
1144 ether is a changing structure of the industry and there are a  
1145 lot more players and different players who are getting into  
1146 development and that is probably good news for diversity, and  
1147 otherwise I don't think we know, but I think those are two of  
1148 the major factors.

1149 Mrs. {Christensen.} Thank you.

1150 Dr. Robinson, BARDA seems to have a fair amount of  
1151 authority with regard to addressing this issue. Is there any  
1152 further authority that BARDA would need to help us address  
1153 this crisis?

1154 Dr. {Robinson.} Thank you, ma'am. We have actually  
1155 looked at this very carefully and we believe right now that  
1156 with PAHPA that we do have the authority to move forward with  
1157 this multi-pronged approach that will allow advanced  
1158 development of all of these medical countermeasures to move  
1159 forward. So I think right now we are okay.

1160 Mrs. {Christensen.} And I guess to both of you, one of  
1161 the individuals on the second panel suggests that the federal  
1162 government has not really been good or as strong a partner as  
1163 they need to be so you don't need any other authority. Is  
1164 funding the limitation?

1165 Dr. {Robinson.} I will speak first on that. Because we  
1166 have a number of different mandates and the funding for

1167 advanced development only came about in really the fiscal  
1168 year 2007 budget, we certainly would need more resources to  
1169 be able to address all the different priorities that we have  
1170 including antibiotic resistance, yes.

1171 Mrs. {Christensen.} Dr. Woodcock?

1172 Dr. {Woodcock.} We accomplish what we can with the  
1173 resources that we have. There are needs for regulatory  
1174 science that are quite broad and this is one area. The  
1175 research into the endpoints in trial design could help  
1176 accelerate obviously getting guidances out in a timely manner  
1177 and so forth. The President's budget for 2011 has a request  
1178 for increasing regulatory science by the FDA commissioner.  
1179 So I think we are limited to some extent because, like Dr.  
1180 Robinson, by the large number of priorities that we deal  
1181 with.

1182 Mrs. {Christensen.} And Dr. Woodcock, you also talked  
1183 about some of the limitations in terms of the research  
1184 limitations but the plan that the interagency task force put  
1185 together has been in effect for 10 years. What percent or  
1186 how much of that plan has been implemented and what other  
1187 barriers might you have run into in implementing much of what  
1188 you have set out?

1189 Dr. {Woodcock.} Well, I believe that the plan will be  
1190 updated and republished. There have been elements of that

1191 that have been accomplished but there is a plan to reupdate  
1192 the plan and publish it with timelines for accomplishment of  
1193 various activities which I think will help move that program  
1194 along.

1195 Mrs. {Christensen.} Well, I didn't have a chance to  
1196 look at the plan but has 10 percent, 30 percent of it been  
1197 implemented over the 10 years?

1198 Dr. {Woodcock.} I am sorry. I can't give you--we can  
1199 get back to you on that.

1200 Mrs. {Christensen.} Thank you.

1201 Mr. Chairman, I will yield back my time.

1202 Mr. {Pallone.} Thank you.

1203 The gentleman from Kentucky, Mr. Whitfield.

1204 Mr. {Whitfield.} Thank you all very much for your  
1205 testimony. Dr. Woodcock, I would like to revisit this issue  
1206 of lack of clarity and simply ask the question, in your view,  
1207 is the criticism valid that the FDA does have a lack of  
1208 clarity and it is unclear as to what type of clinical trials  
1209 will be required for demonstrating safety and effectiveness?  
1210 We hear a lot of criticism of the FDA in that regard, so in  
1211 your view, is that criticism valid or not valid?

1212 Dr. {Woodcock.} I would say it is valid to say that the  
1213 scientific community has a lack of clarity on how to best  
1214 evaluate new antibiotics and that is reflected in the fact

1215 that the FDA is struggling to get new guidances out there  
1216 that reflect new evaluation methods that will be effective in  
1217 today's environment. So had there been clarity in the  
1218 scientific community, I think FDA could have effected this  
1219 change very rapidly, but due to the lack of clarity we had to  
1220 go through a great deal of effort to gain some type of  
1221 consensus on how to do this.

1222 Mr. {Whitfield.} It is seldom that the scientific  
1223 community has very much clarity anyway, isn't it?

1224 Dr. {Woodcock.} Well, we are no strangers to  
1225 controversy in the area of how to evaluate medical products.  
1226 However, this was a change that occurred between the 1980s  
1227 and 2000, 1990 to 2000, a change that happened rapidly and it  
1228 has been very difficult to get a new state of clarity about  
1229 how to do this antibiotic development.

1230 Mr. {Whitfield.} Would you explain the Orphan Drug Act  
1231 for me, please? And also it is my understanding that there  
1232 are grants available under the Orphan Drug Act and the amount  
1233 of money involved in those grants and it is also my  
1234 understanding that you all were required in the 2007 act to  
1235 have a public hearing, which I think occurred in April maybe  
1236 of this past year and what the results of that were and what  
1237 you are doing to follow up on those recommendations?

1238 Dr. {Woodcock.} The Orphan Drug Act allows for

1239 incentives, grants as well as exclusivity for products to get  
1240 onto the market for products that are intended to treat  
1241 populations smaller than 200,000 individuals in the United  
1242 States.

1243 Mr. {Whitfield.} Smaller than 200,000?

1244 Dr. {Woodcock.} Yes, and so this has been a wildly  
1245 successful program in incentivizing the development of drugs  
1246 for small populations, and I think there is agreement across  
1247 the board about that, which is very rare to get such  
1248 agreement. So it has been a very successful program. Its  
1249 applicability to antibiotics is limited to the extent that  
1250 where the population is often larger than that of treated  
1251 patients for the given indication but for small indications  
1252 where there is fewer than 200,000 people that would present  
1253 with that condition in the United States, then the orphan  
1254 provisions are germane.

1255 Mr. {Whitfield.} What is the dollar value of the grants  
1256 that would be available under that program?

1257 Dr. {Woodcock.} I don't know. We would have to get  
1258 back to you on that. I think they vary, but one of the more  
1259 valuable issues is the orphan exclusivity that is given to  
1260 the product if it successfully gets on the market.

1261 Mr. {Whitfield.} And how did that April hearing go or  
1262 forum go?

1263 Dr. {Woodcock.} Again, I would have to get back to you  
1264 on that. I don't have the details of that.

1265 Mr. {Whitfield.} Okay. You were not there?

1266 Dr. {Woodcock.} No.

1267 Mr. {Whitfield.} I yield back the balance of my time.

1268 Mr. {Pallone.} Thank you.

1269 Next is the gentleman from Maryland, Mr. Sarbanes. He  
1270 has no questions.

1271 We will go to Mr. Burgess, who actually has 8 minutes.

1272 Dr. {Burgess.} Thank you, Mr. Chairman.

1273 And again, thank you both for being here, very  
1274 informative discussion.

1275 Dr. Woodcock, you made the statement during your  
1276 testimony that the microbes have strategies. I guess that  
1277 begs the question, do we--because it does seem like we have  
1278 got a problem both with the product in the pipeline and  
1279 perhaps the pipeline itself may be old and rusty and full of  
1280 obstacles. So are we--how do you feel about how we are  
1281 updating that infrastructure to get this job done?

1282 Dr. {Woodcock.} Well, obviously we all agree that  
1283 prudent uses and preventing infection is one of the mainstays  
1284 of this but we also must have a pipeline and I feel that many  
1285 of the issues covered by the members already such as the  
1286 short-term use of antibiotics, the regulatory or scientific

1287 difficulties nowadays in the development path, until recently  
1288 probably the lack of new targets because the antibiotics were  
1289 often all focused on the same microbial targets and now there  
1290 is a broader range of targets. So I think there is room for  
1291 optimism. However, I do believe that more commercial  
1292 interest in this field needs to occur to really get the  
1293 pipeline robust.

1294 Dr. {Burgess.} Well, Dr. Robinson mentioned two issues,  
1295 but let us stay with you, Dr. Woodcock, because the FDA plays  
1296 a role here in becoming available. One was the point-of-care  
1297 diagnostics and the other were the vaccines where you go from  
1298 a broader spectrum now down to a narrower spectrum but if you  
1299 have fewer bugs that are actually able to become resistant,  
1300 then you'll reduce the likelihood of resistance. So how is  
1301 the FDA doing as far as getting those two tools that BARDA is  
1302 developing, how is the FDA doing it getting those into the  
1303 hands of clinicians?

1304 Dr. {Woodcock.} The FDA has approved several point-of-  
1305 care diagnostics recently, several diagnostics for MRSA.  
1306 However, they have to go through an additional step of the  
1307 CLIA process to be approved for use in the practitioner's  
1308 office, but I think this is very promising as far as that  
1309 rapid microbial testing can be developed.

1310 Dr. {Burgess.} But this is a problem, though, I mean,

1311 with CLIA, I wasn't here but CLIA meant that we couldn't even  
1312 make a microscopic slide and look at it under the microscope  
1313 for clinically easily recognizable pathogens because I was  
1314 not licensed to do that. So what happened, of course, I  
1315 would do it and not charge for it and not tell anyone I was  
1316 doing it say my clinical acumen tells me this is X even  
1317 though I have identified it under the microscope. What a  
1318 waste of time. Are we trying to improve that part as well or  
1319 is that beyond the scope of the FDA?

1320 Dr. {Woodcock.} CLIA, as you know, is administered by  
1321 CMS. However, this particular issue is simply to show that  
1322 the diagnostic is effective in use in the hands of the  
1323 practitioner and then it can be used in the hands of the  
1324 practitioner. So it is simply a demonstration that  
1325 practitioners can use such a diagnostic like the rapid strep  
1326 test or whatever in the setting of an office.

1327 Dr. {Burgess.} I didn't mean to get off on that. I  
1328 still have a great deal of emotional difficulty with the  
1329 affronts to my clinical judgment from CLIA.

1330 Let me ask you this. The new molecular entities  
1331 approved by the FDA in the last decade, I think for the last  
1332 hearing my staff had prepared for me a list of 10 new  
1333 molecular entities. Does that sound about right?

1334 Dr. {Woodcock.} That sounds about right.

1335 Dr. {Burgess.} Is that okay, one a year for the last  
1336 decade, or now over the last decade?

1337 Dr. {Woodcock.} Well, this reflects the slide in the  
1338 pipeline since 1987 where the new INDs have progressively  
1339 decreased every year since 1987 until recently. So it takes  
1340 about 5 or 6 years in the clinic from first in human studies  
1341 to see therapies coming out and being available to doctors.

1342 Dr. {Burgess.} Do you know, are there any applications  
1343 that have been filed with the FDA to get approval for new  
1344 diagnostics for bacterial infections? Do you know if you  
1345 have approved any? Has the FDA approved any of those new  
1346 diagnostics?

1347 Dr. {Woodcock.} As I said, we have approved several  
1348 over the last several years, yes, for rapid diagnostics.

1349 Dr. {Burgess.} You know, Mr. Waxman, who unfortunately  
1350 is not here, asked unanimous consent to insert into the  
1351 record a letter from Advanced Life Sciences, and I asked to  
1352 look at it just because I wanted to see what he was putting  
1353 into the record, but it is very interesting. I mean, here is  
1354 a company that has developed a single does or once-a-day oral  
1355 therapy for methicillin-resistant Staph aureus and we talked  
1356 about patient compliance. You tell a patient they have got  
1357 to take something every 4 hours, guess what? They aren't  
1358 going to do it. They will do what I did, which I don't

1359 recommend, which is you take the antibiotic to toxicity and  
1360 then back off, and if you feel better, you don't take it  
1361 anymore. That is what patients do. That is real-world  
1362 stuff. So if you give them one pill a day, they are much  
1363 more likely to comply with the regimen. So this actually  
1364 sounds like something that might be very useful. We have got  
1365 a pathogen that is a series pathogen for community-acquired  
1366 pneumonia and it is multiply-resistant Staph aureus, a once-  
1367 a-day therapy, and here the company has done all the stuff  
1368 they needed to do to get it going and then the rules changed  
1369 on them in the middle of the application and they had to go  
1370 back to square one. This is a small company. This is not  
1371 one of the big houses that now we say won't participate, and  
1372 this is exactly the type of company we want involved in this  
1373 and they are apparently coming to Chairman Waxman with the  
1374 information that they can't--you know, they had to start all  
1375 over again, significant cost to them because they are a small  
1376 startup company. What do you say to that? Why are we  
1377 putting these kind of obstacles out there?

1378 Dr. {Woodcock.} Well, it is a very difficult situation  
1379 when the scientific needs for scientific evaluation changed  
1380 during a development program, and it is very difficult for  
1381 small companies. We try to avoid that as much as we can but  
1382 the science may change in advance--

1383 Dr. {Burgess.} And I recognize that, but can you not,  
1384 and the advisory panels, can you not build in the flexibility  
1385 as you are going through these? I mean, you changed the  
1386 endpoints after the new drug application has been submitted.  
1387 They have already invested considerable time and money. They  
1388 could walk away from the project. Fortunately, they have not  
1389 because I think this is a product that ultimately will  
1390 benefit patients. But, really, it seems like there has got  
1391 to be more flexibility. These are relatively unique  
1392 situations that develop but more flexibility at the  
1393 regulatory side to deal with just these types of problems. I  
1394 mean, suffice it to say if Sir Alexander Fleming had come up  
1395 against this, he might have never had a statue of himself  
1396 erected by the bullfighters in Spain because he wouldn't have  
1397 been able to get penicillin cleared through your agency.

1398 Dr. {Woodcock.} We understand. I can't discuss any  
1399 specific case but we certainly try to build in flexibility  
1400 and we recognize that changing--and that is actually built  
1401 into our procedures. We try not to change our advisory  
1402 requirements during a development program if at all possible.

1403 Dr. {Burgess.} I don't mean to interrupt, but my time  
1404 is going to run out, and they are really tough on me with the  
1405 gavel here, but do you really feel like you are getting a  
1406 clear regulatory pathway so everyone can know the rules and

1407 then if we do change the rules in the middle, we at least  
1408 have some certainty for these companies that at some point  
1409 the regulations will cease and they will get either a yes or  
1410 no on their product? Because that is after all what they  
1411 need to hear.

1412 Dr. {Woodcock.} We recognize how important that is to  
1413 stimulate and sustain development in any indication area. We  
1414 definitely recognize that predictability is key.

1415 Dr. {Burgess.} Thank you, Mr. Chairman.

1416 Mr. {Pallone.} Since you suggested we should be tough,  
1417 I guess we will have to be.

1418 Dr. {Burgess.} I will give you back Mr. Waxman's  
1419 submission for the record.

1420 Mr. {Pallone.} Thank you.

1421 Next is the gentleman from Texas, Mr. Green.

1422 Mr. {Green.} Thank you, Mr. Chairman. And I have never  
1423 thought you wielded a heavy gavel. I would ask permission to  
1424 submit my opening statement for the record, Mr. Chairman.

1425 [The prepared statement of Mr. Green follows:]

1426 \*\*\*\*\* COMMITTEE INSERT \*\*\*\*\*

|  
1427           Mr. {Pallone.} Without objection, so ordered. All  
1428 members may submit their statements without even making the  
1429 request actually.

1430           Mr. {Green.} Thank you, Mr. Chairman.

1431           Dr. Robinson, you explained some of the challenges that  
1432 hinder antibiotic development and I would like to ask about a  
1433 potential solution to encouraging companies to work on  
1434 developing antibiotics, advance market commitment. I  
1435 understand the way the strategy works. The government  
1436 contracts with a company to buy a certain number of doses of  
1437 a product at a specific price. This gives the company a  
1438 certain level of assurance that there will be a market for  
1439 their product on an agreed-upon price. This is similar to  
1440 what you do for other certain countermeasures which  
1441 traditional market forces doesn't work, smallpox or anthrax  
1442 vaccines. Do you think this approach, should we consider  
1443 antibiotics for this approach?

1444           Dr. {Robinson.} Well, certainly because we have  
1445 antibiotics as part of our mainstay against biotreats, I  
1446 would have to say this is something we would have to consider  
1447 going forward. For public health reasons, it should be  
1448 openly discussed with the medical communities and also  
1449 considered as one of our possibilities to incentivize going

1450 forward, yes.

1451 Mr. {Green.} And one of my concerns about stockpiling  
1452 is, we also have shelf life to obviously antibiotics and any  
1453 other medication, and that is something you dealt with,  
1454 though, with the smallpox and anthrax vaccines, I assume?

1455 Dr. {Robinson.} Certainly with the therapeutics we have  
1456 a shelf life extension program that the FDA has so admirably  
1457 held for a number of years now, and I think that we can  
1458 utilize that going forward with new antibiotics that would  
1459 come into the stockpile.

1460 Mr. {Green.} So you don't see any logistical  
1461 challenges? I mean, you have already addressed some of the  
1462 challenges of other medications. You could do the same with  
1463 antibiotics?

1464 Dr. {Robinson.} That is correct. It would be a policy  
1465 issue at this point.

1466 Mr. {Green.} Dr. Woodcock, one of the suggestions for  
1467 creating incentives for antibiotic is expand the concept of  
1468 tropical disease priority review vouchers established under  
1469 the FDA Amendments Act. Such a voucher would entitle the  
1470 holder to get a drug reviewed with a target completion time  
1471 of 6 months. Under such an approach, FDA would give a  
1472 company a priority review voucher as a reward for developing  
1473 a qualified infectious disease product. The company could

1474 use the voucher for a drug of its choice or could sell it to  
1475 another company. Dr. Woodcock, could you tell us how the  
1476 existing tropical disease program has worked from the FDA's  
1477 perspective? Does it seem like a workable approach for  
1478 important new antibiotics, and what are the tradeoffs in  
1479 terms of FDA review of other drugs if we have that 6-month  
1480 provision in there?

1481 Dr. {Woodcock.} Well, I don't think that there has been  
1482 enough activity so far under the tropical disease provisions  
1483 to provide an assessment but we can get back to you on  
1484 exactly what has happened but, you know, I don't think there  
1485 has been enough action there to provide an assessment.

1486 As far as the tradeoffs, I think if you wanted to think  
1487 of this more broadly and apply it more broadly, what this  
1488 does would decrease the FDA review time from 10 months to 6  
1489 months for any given product and could be applied to any  
1490 product, and most likely a company would apply it to a  
1491 product that would normally be for a chronic disease,  
1492 widespread treatment, right, and might be used to treat tens  
1493 of millions of Americans, and this would mean that FDA would  
1494 have to review that much faster than ordinary because the  
1495 voucher had been applied to that. So I think there are some  
1496 limitations on that approach because when we get a lot of  
1497 priority reviews, especially where we are reviewing a drug

1498 that tens of millions of Americans might be exposed to it and  
1499 it may be for chronic but not really important condition, we  
1500 have to be really sure of the safety of that drug. We have  
1501 to do a very, very careful review, and if we had large  
1502 numbers of short reviews for products like that, I think that  
1503 would be problematic for our review structure.

1504 Mr. {Green.} I know one of the concerns I have is, I  
1505 have a district in Houston, Texas, and we are seeing many  
1506 more tropical diseases, for example, that are coming into our  
1507 country, whether it is global warming or what, but if there  
1508 is a problem, it is going to be in Houston and Dallas and San  
1509 Antonio and shortly in Chicago and other places. So that is  
1510 why I think some of that is really needed to respond to in  
1511 our own country, much less what is happening in other parts  
1512 of the world.

1513 Mr. Chairman, I actually gave you 6 seconds back. Thank  
1514 you.

1515 Mr. {Pallone.} Thank you, Mr. Green.

1516 The gentleman from Georgia, Mr. Gingrey.

1517 Dr. {Gingrey.} Mr. Chairman, I want to read an excerpt  
1518 into the hearing record from the Administration's own  
1519 interagency task force on antimicrobial resistance. The task  
1520 force wrote a public health action plan in 2008 that reads in  
1521 part, ``Existing market incentives and regulatory processes

1522 may be insufficient to stimulate the development of certain  
1523 priority antimicrobial-resistant products while fostering  
1524 their appropriate use. The goal is to investigate and act  
1525 upon potential approaches for stimulating and speeding the  
1526 entire antimicrobial-resistant product development process  
1527 from drug discovery through licensing. Drs. Woodcock and  
1528 Robinson, do you agree with that statement?

1529       Dr. {Woodcock.} It is critically important if you want  
1530 to increase the activity in a given sector to provide  
1531 adequate incentives and discovery is important because we  
1532 need new targets. We need antimicrobials that are going  
1533 against a broader range of activities of the microbes and  
1534 development is important because it requires a great deal of  
1535 investment to get a product through and there has to be seen  
1536 some type of return on investment in order to get robust  
1537 investment in that sector. So I think those things are  
1538 extremely important and we have to think them through very  
1539 carefully.

1540       Dr. {Gingrey.} So you do agree.

1541       Dr. Robinson, would you agree also as well?

1542       Dr. {Robinson.} Yes, I would agree, absolutely, because  
1543 advanced development is the area that BARDA plays that when  
1544 Dr. Fauci was here, he was talking about discovery and early  
1545 development and then the market over here. Well, that is

1546 what BARDA does. It makes sure it can get from early  
1547 development all the way to the market.

1548 Dr. {Gingrey.} Doctors, can you tell the committee what  
1549 organizations actually co-chair this task force, the  
1550 Administration's interagency task force on antimicrobial  
1551 resistance?

1552 Dr. {Woodcock.} I believe CDC, NIH and FDA.

1553 Dr. {Gingrey.} I think you are right, Dr. Woodcock.

1554 Dr. Robinson, you won't have to second-guess her. That  
1555 is exactly right.

1556 If your 2008 report is true, and it is a report that is  
1557 co-chaired by CDC, HHS and FDA, as Dr. Woodcock knew and  
1558 reported, if the report is true, and we do need to look  
1559 outside current market and regulatory incentives to stimulate  
1560 antibiotic development, what other incentives might we as a  
1561 government provide? As an example, would liability  
1562 protection in certain circumstances help support greater  
1563 innovation? Dr. Robinson?

1564 Dr. {Robinson.} With the liability relief that has been  
1565 provided previously by Congress with the PREP Act, we have  
1566 actually applied that with declarations during events that  
1567 would include some of the antibiotics, and what we were told  
1568 by industry was that that was very helpful and that some form  
1569 of liability relief is important.

1570 Dr. {Gingrey.} Sort of like in the vaccine production  
1571 when we really need something to combat H1N1.

1572 Dr. Woodcock?

1573 Dr. {Woodcock.} Well, I think I don't have further  
1574 opinion on the liability issue. Obviously any type of  
1575 incentive is important and I think any incentives have to be  
1576 considered in light of whether or not you want to have  
1577 restrictions at the other end because one of the goals here  
1578 would be to restrict the use or moderate the use or make sure  
1579 the use is very prudent of the intervention to preserve its  
1580 effect as long as possible, and that is--we have our current  
1581 problems with the pipeline but if we contemplated a pipeline  
1582 that would end up with antimicrobials that would only be used  
1583 in niche situations where they were really needed, that would  
1584 be even a further disincentive, but you have to think about  
1585 that as a goal to preserve the effect of that for a long time  
1586 to protect the population and what kind of incentives would  
1587 stimulate that.

1588 Dr. {Gingrey.} Well, certainly I have an opinion on  
1589 that and a very definitive opinion in regard to the  
1590 development of the vaccines. I felt like liability  
1591 protection was absolutely essential for us to move forward in  
1592 that direction.

1593 Now, this last question real quickly, and I don't have

1594 an opinion on this. I am just very curious to know what you  
1595 think about it, though. Do our current antitrust laws allow  
1596 companies to work together to create and expedite new  
1597 antibiotics? And if not, if those laws don't allow that,  
1598 would an easing of the law prove beneficial, do you think?

1599 Dr. {Robinson.} Sir, I will give you an example where  
1600 we actually have used the authority given to BARDA for  
1601 antitrust exemption, and we actually used with the  
1602 development of the H5N1 and the H1N1 vaccine. It was very  
1603 important that we have that. Certainly in our case, we could  
1604 actually use that and actually provide our sister agencies to  
1605 be there also, which we normally do.

1606 Dr. {Gingrey.} Dr. Woodcock?

1607 Dr. {Woodcock.} I have worked in public-private  
1608 partnerships where we have gotten companies together to  
1609 advance general societal goals and they have had to be  
1610 extremely lawyer-intensive on the antitrust issues, so there  
1611 is no doubt, I think, that it is a barrier to working  
1612 together to advance broader goals.

1613 Dr. {Gingrey.} Great. I think that is very helpful and  
1614 I appreciate your response.

1615 Mr. Chairman, you are pretty generous with that gavel.  
1616 I will yield back 1 minute late.

1617 Mr. {Pallone.} Thank you.

1618 Mr. Murphy of Pennsylvania.

1619 Mr. {Murphy of Pennsylvania.} Thank you, Mr. Chairman.

1620 I have been sitting here going over some of the FDA websites  
1621 on this information. I know you have quite a public  
1622 campaign, preserving our treasure, knowing how antibiotics  
1623 work, et cetera. Have you measured the effectiveness of your  
1624 campaigns in terms of working with the public in reducing  
1625 their demands on physicians for antibiotics when it is not  
1626 the appropriate medication?

1627 Dr. {Woodcock.} I believe especially the CDC's recent  
1628 campaign--

1629 Mr. {Murphy of Pennsylvania.} The CDC's, yes, CDC and  
1630 FDA on the same sites, yes.

1631 Dr. {Woodcock.} --did have an impact that was measured  
1632 on reducing antibiotic use in sort of inappropriate  
1633 conditions, yes.

1634 Mr. {Murphy of Pennsylvania.} Is that something we are  
1635 going to see continued and expanded? I mean, we have talking  
1636 a good bit about that today in terms of the kind of comments  
1637 you have made and members have made. I am just wondering if  
1638 that is something that you see that we should continue to  
1639 fund and push for a widespread public education on that, and  
1640 I might add, including the things you heard in my earlier  
1641 commentary about the need for prevention, and I am amazed

1642 sometimes, I will go into hospitals where you can't walk down  
1643 the hall without someone being fairly militant and making you  
1644 gown and glove and wash your hands, which is good. I have  
1645 heard of other dynamic things. To get in the ICU at  
1646 University of Miami Medical Center, you don't push a button,  
1647 there's not a sensitive sensor. To get in the door, you have  
1648 to put your hand under an alcohol dispenser, and then when it  
1649 squirts in your hands, the doors open. That is a very clever  
1650 idea. Or I have also heard of systems where the doctors wear  
1651 little monitors or anybody, and when they enter a room if  
1652 they not washed their hands, a little mini alarm goes off and  
1653 says ``Wash your hands, please,`` and then the chairman hits  
1654 them with the gavel. Not true, sir. I am continuing the  
1655 theme here. But I am just wondering about public education  
1656 campaigns that we do to reduce the need there.

1657 Dr. {Woodcock.} I believe that is extraordinarily  
1658 important. No matter what we do to the pipeline, and I think  
1659 the last 20 years have shown us that, if there is  
1660 indiscriminate use, then that will accelerate the development  
1661 of resistance and our pipeline will continue to have trouble  
1662 getting ahead of that. The recent scientific emerging  
1663 understanding about infection control and how effective these  
1664 simple measures actually can be if they are rigorously  
1665 followed I think has startled a lot of people and provides a

1666 tremendous opportunity for improving quality in health care  
1667 and decreasing infections, as you said, but each of those I  
1668 believe needs continued pressure and education and interest  
1669 to perpetuate them and they will go a long way toward dealing  
1670 with this problem.

1671         Mr. {Murphy of Pennsylvania.} Well, I want to encourage  
1672 all of you. I know when some of the recent flu outbreaks  
1673 came out, you couldn't get into a bus stop without seeing a  
1674 sign somewhere, and that was excellent. I thought it was  
1675 very helpful.

1676         The second thing I wanted to ask about has to do with  
1677 since when people are sick they want to do something, and so  
1678 there are a number of over-the-counter products, and either  
1679 of you can answer this too, in terms of what we should be  
1680 doing to help promote those for symptom assistance as opposed  
1681 to the false promise of antibiotics for virus, other things  
1682 we should be doing to encourage more OTC products, over-the-  
1683 counter products instead. Is that in any of your purview  
1684 that you want to comment on that?

1685         Dr. {Woodcock.} FDA regulates the over-the-counter  
1686 drugs, and we certainly--there is certainly a huge array of  
1687 symptomatic control available for common viral illnesses that  
1688 people suffer and also there are many other simple measures.  
1689 So I think much of this is public education about the

1690 availability of straightforward symptomatic control for viral  
1691 illnesses.

1692           Mr. {Murphy of Pennsylvania.} Do you have anything to  
1693 add on that, Dr. Robinson?

1694           Dr. {Robinson.} I would just concur with that also. I  
1695 mean, we have had a number of different sponsors come to us  
1696 for support looking at very simplistic type of products like  
1697 that.

1698           Mr. {Murphy of Pennsylvania.} I might add to my  
1699 editorial comments. I know that cuts to allow people to have  
1700 their health care plan use their monies to pay for over-the-  
1701 counter drugs, I don't like that idea because here we are  
1702 talking about a massive amount of money we have to put into  
1703 research and prescribing cots for antibiotics that we are  
1704 building resistance to when we should be encouraging people  
1705 to use other symptom remedies for that which are much less  
1706 expensive and of course appropriate for those things too, so  
1707 I hope those are things that we will restore in the future  
1708 and I want to thank you both for your testimony. It is good  
1709 to read this.

1710           I yield back, Mr. Chairman.

1711           Mr. {Pallone.} Thank you.

1712           The gentlewoman from Tennessee, Ms. Blackburn.

1713           Mrs. {Blackburn.} Thank you, Mr. Chairman.

1714 I am going to be very brief. I just want to go back to  
1715 what Chairman Pallone was talking about at the very first,  
1716 and I touched on it in my opening statement, our concern with  
1717 the uncertainty that seems to exist at the FDA. And in my  
1718 district in Tennessee, we have some wonderful groups that are  
1719 doing tremendous amounts of research in biotherapies and in  
1720 new therapies that are coming along the chain. We hear  
1721 repeatedly about concern with the uncertainty from the FDA.  
1722 You mentioned, Dr. Woodcock, that there has been a decline in  
1723 the pipeline since 1987 and then we have also touched on the  
1724 disincentives that are there. Dr. Robinson mentioned some of  
1725 those. And I think that it is important that we realize  
1726 those disincentives and the uncertainty at the FDA have a  
1727 direct effect on what is there in that pipeline, and you keep  
1728 saying, you have mentioned several times you have the  
1729 authority that is necessary, Dr. Woodcock, to finalize these  
1730 documents and provide some certainty on that pathway, and I  
1731 would just highlight with you that we think that that is  
1732 important to do. If you have the authority, maybe you have  
1733 too much authority. Maybe we need to pull some of that back  
1734 and oversight and be just a little more direct and  
1735 participatory in trying to help define that, but I would just  
1736 highlight with you that it is of concern to us. We  
1737 appreciate the work that you are doing but we do have great

1738 concerns about the uncertainty and the disincentives and the  
1739 decline in the pipeline, and with that I will yield back.

1740       Mr. {Pallone.} Thank you. And let me thank both of you  
1741 for being here today. It was obviously very helpful to us in  
1742 this sort of three-pronged effort here with three hearings to  
1743 get to the bottom of some of these problems and what is  
1744 happening. Thank you.

1745       I will ask the second panel to come forward at this  
1746 time. Let me introduce--well, first of all, welcome, and let  
1747 me introduce the second panel. Starting to my left is Dr.  
1748 Brad Spellberg, who is associate professor of medicine, the  
1749 David Geffen School of Medicine at UCLA and a member of the  
1750 Infectious Diseases Society of America Antimicrobial  
1751 Availability Task Force. Second is Dr. Sandra Fryhofer, who  
1752 is from the Council on Science and Public Health at the  
1753 American Medical Association. Then we have Dr. John Bradley,  
1754 who is speaking on behalf of the American Academy of  
1755 Pediatrics. He is the chief of the Division of Infectious  
1756 Diseases. He is with the Department of Pediatrics at the  
1757 University of California School of Medicine, clinical  
1758 director of the Division of Infectious Diseases and he is  
1759 also at Rady Children's Hospital in San Diego. That is a  
1760 long list there. And then we have Dr. Barry Eisenstein, who  
1761 is senior vice president of scientific affairs for Cubist

1762 Pharmaceuticals. I have to ask you, I keep looking at this  
1763 Cubist, is that just the drug that you--what does the Cubist  
1764 refer to?

1765 Dr. {Eisenstein.} We believe that medicine and science  
1766 involved in drug development is both an art and a science.

1767 Mr. {Pallone.} Oh, so it is reference to a cube, in  
1768 other words. Okay. Thank you.

1769 And last is Dr. Jeffrey Levi, who is executive director  
1770 of the Trust for America's Health. He has testified many  
1771 times before the committee, and I hope that we did not  
1772 contribute to your leg being broken or whatever happened to  
1773 you.

1774 Mr. {Levi.} No.

1775 Mr. {Pallone.} Thank you for being here today.

1776 So you know we have 5-minute opening statements that  
1777 become part of the record and then we may ask you, or you may  
1778 submit additional written statements if you like, and we will  
1779 start with Dr. Spellberg.

1780 Dr. {Spellberg.} Thank you. Could we cue up the  
1781 slides, please?

1782 Mr. {Pallone.} Oh.

1783 Dr. {Spellberg.} Great.

1784 Mr. {Pallone.} It is up there.

|  
1785 ^STATEMENTS OF BRAD SPELLBERG, MD, FIDSA, ASSOCIATE PROFESSOR  
1786 OF MEDICINE, DAVID GEFLEN SCHOOL OF MEDICINE AT UCLA, MEMBER,  
1787 INFECTIOUS DISEASES SOCIETY OF AMERICA ANTIMICROBIAL  
1788 AVAILABILITY TASK FORCE; SANDRA FRYHOFFER, MD, COUNCIL ON  
1789 SCIENCE AND PUBLIC HEALTH, AMERICAN MEDICAL ASSOCIATION; JOHN  
1790 S. BRADLEY, MD, ON BEHALF OF AMERICAN ACADEMY OF PEDIATRICS,  
1791 CHIEF, DIVISION OF INFECTIOUS DISEASES, DEPARTMENT OF  
1792 PEDIATRICS, UNIVERSITY OF CALIFORNIA SCHOOL OF MEDICINE,  
1793 CLINICAL DIRECTOR, DIVISION OF INFECTIOUS DISEASES, RAY  
1794 CHILDREN'S HOSPITAL, SAN DIEGO; BARRY EISENSTEIN, MD, FACP,  
1795 FIDSA, SENIOR VICE PRESIDENT, SCIENTIFIC AFFAIRS, CUBIST  
1796 PHARMACEUTICALS; AND JEFFREY LEVI, PHD, EXECUTIVE DIRECTOR,  
1797 TRUST FOR AMERICA'S HEALTH

|  
1798 ^STATEMENT OF BRAD SPELLBERG

1799 } Dr. {Spellberg.} Thank you very much, Mr. Chairman. My  
1800 name is Dr. Brad Spellberg. I am an infectious disease  
1801 specialist, as you said, at the UCLA School of Medicine and  
1802 Harbor UCLA Medical Center. I am also the author of ``Rising  
1803 Plague,'' which is a book about the antibiotic crisis, and it  
1804 is my honor today to be here representing the Infectious  
1805 Diseases Society of America, which is an organization of more

1806 than 9,000 physicians, pharmacists and scientists that all  
1807 work in infectious diseases and microbiology.

1808         In 2004, the IDSA released the ``Bad Bugs, No Drugs''  
1809 white paper to inform the public and Congress about the  
1810 looming antibiotic crisis and more recently just in the last  
1811 couple of months, the IDSA has released the 10 by 20  
1812 initiative, which calls for the development of 10 new  
1813 critically needed antibiotics by the year 2020. And the  
1814 reason why we are here today and the reason why IDSA has  
1815 released ``Bad Bugs, No Drugs'' and the 10 by 20 initiative  
1816 is because we are here to advocate for our patients that are  
1817 dying of infections and we are running out of drugs to throw  
1818 at them.

1819         [Slide.]

1820         This graph shows the number of new systemic  
1821 antibacterial agents approved by the FDA for a 5-year period.  
1822 The conclusion from this graph is inescapable: antibiotic  
1823 development is dying. And at the same time, we are  
1824 witnessing skyrocketing incidences of multidrug-resistant  
1825 bacterial infections of a variety of types, some of which are  
1826 shown on this graph, but there are many other types as well.  
1827 This of course creates a critical need for new antibiotics to  
1828 be developed right at the time when new antibiotics are not  
1829 being developed, and these infections hit hospitalized

1830 patients, infirm patients, sick patients, the elderly, but  
1831 they also hit the healthiest and strongest among us. In  
1832 particular our soldiers in Iraq and Afghanistan have been  
1833 devastated by a wide variety of multidrug-resistant bacterial  
1834 infections. And this highlights a central point, which is  
1835 that everyone is at risk for these infections including  
1836 healthy people in communities, and as shown on this slide are  
1837 examples of real patients who were healthy in communities and  
1838 have been killed or maimed by multidrug-resistant bacterial  
1839 infections. Everyone is at risk. The collective toll of  
1840 these infections in terms of number of people infected,  
1841 number killed and the multibillions of dollars per year that  
1842 these infections cost our health care system is absolutely  
1843 staggering.

1844         We have to start thinking of antibiotics as a precious  
1845 limited resource in the same way that we view forestry,  
1846 fisheries and energy policy. We need to both conserve and  
1847 restore this precious resource and currently we do neither.  
1848 We overuse and waste our antibiotics in both humans and  
1849 animals, and the antibiotic resource is not being restored,  
1850 because as we have heard, both there is an economic  
1851 disincentive because antibiotics are not economically  
1852 competitive with other drugs and there are regulatory  
1853 barriers that prevent companies from understanding how to do

1854 clinical trials to get antibiotics approved.

1855           So we need a multi-pronged approach to solving these  
1856 problems, as we have heard. We need a multi-pronged approach  
1857 to promoting antibiotic conservation. We need much better,  
1858 more effective and widespread antibiotic stewardship programs  
1859 to be used all over the country and frankly throughout the  
1860 world. We need funding to be made available to CDC and  
1861 others to develop and spread these stewardship programs. We  
1862 do need to promote the development and use of rapid  
1863 diagnostics to empower physicians to more accurately  
1864 prescribe antibiotics, and finally, we need to pass the STAR  
1865 Act, which will give us federal oversight and create the  
1866 infrastructure necessary to gather the data we need to  
1867 understand the scope of the antibiotic resistance problem in  
1868 this country.

1869           We also need a multi-pronged approach to promoting  
1870 antibiotic restoration. We need to establish orphan drug-  
1871 like economic push and pull incentives to rekindle interest  
1872 in the industry in antibiotic R&D. We need to increase  
1873 funding to relevant federal agencies like NIH, like BARDA and  
1874 we should really start thinking seriously about establishing  
1875 a nonprofit public-private partnership whose mission is to  
1876 develop critically needed small-market molecules to treat  
1877 life-threatening infections caused by resistant bacteria, and

1878 finally, we need to continue to promote regulatory clarity at  
1879 the FDA for existing pathways and also to create new pathways  
1880 to create critically needed antibiotics that have not been  
1881 developed previously.

1882 I am going to close with a brief anecdote. Congressman  
1883 Burgess mentioned penicillin. I want to go back to the  
1884 beginning of the penicillin era to remind all of us how  
1885 important it is that we have effective antibiotics. So I am  
1886 going to tell you the true story of a 4-year-old girl in late  
1887 1942 who had been in perfect health until she suddenly  
1888 developed an infection on her face, a skin infection. This  
1889 progressed relentlessly. Her face and neck became so  
1890 swollen, she could not swallow her own saliva, and it was  
1891 when she began gasping for breath that her parents in a panic  
1892 rushed her to the Mayo Clinic.

1893 [Slide.]

1894 And this is what this little girl looked like on arrival  
1895 to the hospital. Her parents were told that she would be  
1896 dead within 2 days and there wasn't anything anybody could do  
1897 to stop it. Imagine being told that about your 4-year-old  
1898 that 4 days earlier had been in perfect health. But she was  
1899 lucky because Dr. Horel at the Mayo Clinic was one of the  
1900 very few people in the United States that had access to  
1901 penicillin before the end of World War II. He went into his

1902 laboratory. He grabbed some doses of penicillin and he began  
1903 treating her, and this is what this little girl looked like  
1904 at the end of a few days of penicillin therapy.

1905           Antibiotics are the only medical intervention that can  
1906 take a patient that looks as sick as this little girl did on  
1907 arrival to the hospital and turn them into somebody as well  
1908 as she looked when she was discharged from the hospital a few  
1909 days later. To my understanding from what I am told, this  
1910 little girl is alive and well today and still receives her  
1911 care at the Mayo Clinic. Penicillin has given her a 7-decade  
1912 lease on life and counting.

1913           [Slide.]

1914           So this is my final slide. Prior generations have given  
1915 us the gift of antibiotics and today we have a moral  
1916 obligation to ensure that antibiotics continue to be  
1917 available for our children and future generations. The time  
1918 for debate has passed. The time for action is now. Thank  
1919 you.

1920           [The prepared statement of Dr. Spellberg follows:]

1921 \*\*\*\*\* INSERTS 3, 4 \*\*\*\*\*

|

1922            Mr. {Pallone.}    Thank you, Dr. Spellberg.

1923            Dr. Fryhofer.

|  
1924 ^STATEMENT OF SANDRA FRYHOFER

1925 } Dr. {Fryhofer.} Good morning, or is it afternoon now?  
1926 Chairman Pallone, Ranking Member Shimkus and other members of  
1927 the subcommittee, I am Dr. Sandra Adamson Fryhofer. I am a  
1928 general internist in Atlanta, Georgia. I am a clinical  
1929 associate professor of medicine at Emory University School of  
1930 Medicine. I am a member of the American Medical  
1931 Association's Council on Science and Public Health, and I am  
1932 pleased to testify today on behalf of the AMA about  
1933 antibiotics and the growing threat of antibiotic resistance.

1934 Antibiotics are miracle drugs but many are beginning to  
1935 lose their luster. Antibiotic resistance is now a major  
1936 public health concern. Take MRSA, for example, methicillin-  
1937 resistant Staph aureus. You can think of MRSA as a rogue  
1938 staph infection. The bacteria is smarter, so traditional  
1939 antibiotics in the methicillin family can't kill it. MRSA  
1940 infections aren't new. The new trend is where we are seeing  
1941 them. They used to be seen only in hospital settings but now  
1942 we are seeing these infections in the community and in  
1943 otherwise healthy young people including athletes. The AMA  
1944 believes that in order to reverse these trends requires a  
1945 multi-faceted approach: reduce inappropriate use of existing

1946 antibiotics, incentive research and development in order to  
1947 create new antibiotics, and finally, encourage alternatives  
1948 to reduce our dependence on antibiotics, and one such  
1949 alternative is vaccines.

1950           Inappropriate use of antibiotics, why is this important?

1951 Increasing rates of drug-resistant invasive infections  
1952 correlate directly with increases in antibiotics overuse.  
1953 Decreasing inappropriate use of antibiotics can reduce the  
1954 prevalence of antibiotic-resistant bacterial infections or  
1955 super bugs. Continued physician education about this issue  
1956 is key. The AMA has sponsored many educational conferences.  
1957 We have developed and disseminated educational tools  
1958 including one specifically focusing on MRSA. We have issued  
1959 scientific reports on antibiotic resistance. We have also  
1960 supported the CDC's campaign to prevent antimicrobial  
1961 resistance in health care settings.

1962           The Physician Consortia for Performance Improvement  
1963 called PCPI was convened by the AMA. Now, this group is  
1964 dedicated to improving patient health, safety and quality of  
1965 care. PCPI develops evidence-based clinical performance  
1966 measures and they have already developed one for managing ear  
1967 infections in children and they are in the early stages of  
1968 developing one for managing sinus infections in adults.

1969           Next, patient education must also be a part of the

1970 solution. One of the main reasons that physicians prescribe  
1971 unnecessary antibiotics is patients want them and some of  
1972 them demand them. The AMA helped launch the CDC'S Get Smart  
1973 public education campaign on why physicians should not  
1974 prescribe antibiotics for the common cold. The AMA has been  
1975 involved in several media briefings about antibiotic  
1976 resistance, and hopefully as mainstream media gives more  
1977 attention to this issue, our patients may become more  
1978 accepting of why they don't need an antibiotic.

1979 Now, we have talked a lot today about use of antibiotics  
1980 in the health care system but use of antibiotics in  
1981 agriculture and in animal husbandry also contributes to  
1982 antibiotic resistance. The AMA is opposed to use of  
1983 antibiotics at non-therapeutic levels in agriculture or as  
1984 growth promoters and urges that such use be terminated or  
1985 phased out based on sound scientific risk assessments.

1986 Another part of the solution is we need new antibiotics,  
1987 especially now that many of the ones we have no longer work.  
1988 This means fostering and incentivizing new research and  
1989 development. The AMA has supposed the call to action you  
1990 just heard about, the ``Bad Bugs, No Drugs'' and another new  
1991 initiative that Dr. Spellberg told us about, the 10 by 20, is  
1992 very exciting. This initiative will be considered for  
1993 endorsement by the American Medical Association at our annual

1994 meeting later this week.

1995           So patient education, physician education, new  
1996 antibiotics. We also need to look for innovative ways to  
1997 reduce our dependence on antibiotics. One way of staving off  
1998 infection is through vaccines, and the development of new  
1999 vaccines against resistant bugs like toxigenic E. coli, for  
2000 example, should be encouraged. However, vaccines only work  
2001 if people get them. We have vaccines available that boost  
2002 immunity to deadly strains of pneumococcal infection, but  
2003 even in this era of ever-increasing antibiotic resistance,  
2004 immunization rates against pneumococcal infection remain low  
2005 in adults.

2006           In summary, the American Medical Association is  
2007 committed to getting antibiotic resistance under control and  
2008 we are making some headway. CDC data over the last 10 years  
2009 shows a 20 percent decrease in use of antibiotics to treat  
2010 upper respiratory infections and a 13 percent decrease in  
2011 prescribing antibiotics overall for all office visits. The  
2012 American Medical Association will continue to support these  
2013 efforts and we appreciate the opportunity to be here with you  
2014 today.

2015           [The prepared statement of Dr. Fryhofer follows:]

2016 \*\*\*\*\* INSERT 5 \*\*\*\*\*

|  
2017            Mr. {Pallone.} Thank you, Doctor.  
2018            Dr. Bradley.

|  
2019 ^STATEMENT OF JOHN S. BRADLEY

2020 } Dr. {Bradley.} Thank you very much, Mr. Chairman. It  
2021 is a real pleasure to be here today to share some information  
2022 with you about children. My name is John Bradley. I am a  
2023 fellow of the American Academy of Pediatrics, or the AAP,  
2024 which is a nonprofit professional organization of more than  
2025 60,000 primary care pediatrics, pediatric medical  
2026 subspecialists and pediatric surgical specialists dedicated  
2027 to the health, safety and well-being of infants, children and  
2028 adolescents. I am a member of the Academy's committee on  
2029 infectious disease, and with Dr. Spellberg, the IDSA's task  
2030 force on antimicrobial drug availability. My oral testimony  
2031 this morning is going to focus specifically on the challenges  
2032 of antibiotic resistance in children.

2033 The successful treatment of infections in children  
2034 requires the availability of safe and effective antimicrobial  
2035 therapy and especially for children I emphasize both safe and  
2036 effective. Antimicrobials are among the most commonly  
2037 prescribed drugs in children but the appropriate use of  
2038 antibiotics in the treatment of true infections, and kids do  
2039 get otitis media and strep throat, combined with the  
2040 inappropriate use of antibiotics has led to the development

2041 of resistance. This resistance has had a significant impact  
2042 on our ability to treat children in both clinics and in  
2043 hospitals. Antibiotic choices for treatment of infections  
2044 are more limited for children than adults. However, we have  
2045 the same critical need for new antibiotics in children as is  
2046 present in adults as these same antibiotic-resistant  
2047 organisms that cause infections in adults cause infections in  
2048 children who are hospitalized. However, for most of the  
2049 newer, more potent antibiotics approved for adults over the  
2050 past 5 to 10 years, inadequate information exists on the  
2051 safety and efficacy of these antibiotics in newborns, infants  
2052 and children but we are using them anyway because we have to.

2053 Please consider the following specific pediatric issues.  
2054 First, children are uniquely vulnerable to infections.  
2055 Newborn infants, particularly premature infants who are now  
2056 surviving with birth weights of only 1 pound, babies this  
2057 large, have horribly suppressed immunity that is a necessary  
2058 component of survival during growth in the womb. In  
2059 addition, all children up to age 2 years have immature immune  
2060 systems and are particularly susceptible to bacterial  
2061 bloodstream infections and spinal meningitis. Further, many  
2062 infants have anatomic or genetic abnormalities that increase  
2063 their susceptibility to infection and many of these children  
2064 die of infections during childhood, so my colleagues who care

2065 for adults have never taken care of these children or watched  
2066 them die.

2067         Second, the safety of drugs is a critical factor for  
2068 children, a population that the FDA and human research  
2069 committees recognize as vulnerable. Drug toxicity such as  
2070 irritation or damage to the brain, heart, bones or joints may  
2071 last a lifetime.

2072         Third, damage from the infection itself may last a  
2073 lifetime, particularly if the wrong antibiotic is used for  
2074 the treatment of an antibiotic-resistant organism.

2075         Fourth, children are incredibly efficient at spreading  
2076 infections. Not only do they cough, sneeze and drool over  
2077 each other, but they spread infection to siblings, parents  
2078 and grandparents. Diarrhea is a scourge of daycare centers.  
2079 Clean diaper-changing facilities and sinks are critical but  
2080 are often lacking, and the CDC and public health departments  
2081 around the country have documented many outbreaks of  
2082 bacterial infections in infants caused by increasingly  
2083 resistant bacteria as we reported in our written testimony.  
2084 Antibiotic resistance is a serious problem in children, and  
2085 the AAP has worked for over a decade to teach pediatricians  
2086 and families about judicious use of antibiotics beginning in  
2087 earnest in 1998 with our collaboration with the CDC in a  
2088 series of articles published in our official medical journal

2089 called Pediatrics. We have shared CDC materials. We have  
2090 created AAP materials to distribute to our members and to the  
2091 families they care for and to emphasize over and over again  
2092 the importance of appropriate use. One toddler in a daycare  
2093 center who receives inappropriate therapy leading to the  
2094 development of resistant bacteria can spread that organism to  
2095 classmates and family members, making treatment of both the  
2096 child and the contacts including adults more difficult. We  
2097 know this and we are committed to programs to enhance  
2098 appropriate use to decrease resistance.

2099         Just like our colleagues in adult medicine, we are  
2100 running out of antibiotics for these multi-resistant  
2101 bacteria, and in our written testimony we provide a current  
2102 reference to a journal article describing the deaths of four  
2103 out of seven premature infants who were exposed to an  
2104 antibiotic-resistant strain of acinetobacter, the gram-  
2105 negative bacteria that is coming back from Iran and Iraq in  
2106 our soldiers.

2107         Vaccination is another critical component of combating  
2108 the spread and severity of antimicrobial-resistant  
2109 infections, and the AAP has taken pride in being the  
2110 professional pediatric organization that has developed and  
2111 promoted an immunization schedule for all children in the  
2112 United States for the past 72 years. Universal immunization

2113 of children for pneumococcus, the antibiotic-resistant  
2114 bacteria that infects the respiratory tract, causes ear  
2115 infections and pneumonia, has actually decreased antibiotic  
2116 resistance in invasive infections in both children and adults  
2117 as immunization prevents this resistant bacteria from living  
2118 in the nose and throat of immunized children, therefore  
2119 limiting the spread of these bacteria to adults who kiss them  
2120 and share food with them.

2121         In summary, antibiotic resistance is a moving target and  
2122 requires ongoing intense commitments to develop better  
2123 surveillance tools, better vaccines and better antibiotics.  
2124 We support the initiatives that were presented by Dr.  
2125 Spellberg from the IDSA and notably H.R. 2400, or the STAR  
2126 Act. The Pediatric Research Equity Act and the Best  
2127 Pharmaceuticals for Children Act have helped us tremendously  
2128 encouraging the pharmaceutical industry to develop  
2129 information on pediatrics that they ordinarily would not have  
2130 done.

2131         I have just a few slides that I would like to show of  
2132 premature infants here just to give you an idea of how small  
2133 and frail they are, and some of the slides that I wish to  
2134 show--

2135         Mr. {Pallone.} Dr. Bradley, I know you are like a  
2136 minute and a half over so--

2137 Dr. {Bradley.} I am sorry.

2138 Mr. {Pallone.} Just show us the slides and then we will  
2139 move on.

2140 Dr. {Bradley.} Yes, sir.

2141 [Slide.]

2142 This is a gut infection in a newborn infant resistant.

2143 This is MRSA destroying the lung, and Dr. Spellberg showed  
2144 the picture of this child who is posted on the IDSA website.

2145 This is a child who had open heart surgery for congenital  
2146 heart disease and is now on a lung bypass machine, and he is  
2147 such a setup for antibiotic-resistant bacteria.

2148 Thank you. I appreciate the opportunity to testify.

2149 [The prepared statement of Dr. Bradley follows:]

2150 \*\*\*\*\* INSERT 6 \*\*\*\*\*

2151 | Mr. {Pallone.} Dr. Eisenstein.

|  
2152 ^STATEMENT OF BARRY EISENSTEIN

2153 } Dr. {Eisenstein.} Chairman Pallone, Ranking Member  
2154 Shimkus and members of the subcommittee, thank you for the  
2155 opportunity to testify on the urgent need to spur greater  
2156 innovation and accelerate the development of new therapeutics  
2157 to combat the threat of antimicrobial-resistant bacterial  
2158 infections. I am Dr. Barry Eisenstein, senior vice  
2159 president, scientific affairs, at Cubist Pharmaceuticals.  
2160 Cubist is a biopharmaceutical company headquartered in  
2161 Lexington, Massachusetts. We currently market Cubicin, also  
2162 known as daptomycin for injection, a first-line intravenous  
2163 antibiotic against methicillin-resistant Staph aureus, MRSA,  
2164 and other gram-positive infections as well as Staph aureus  
2165 blood infections. Cubist has a growing pipeline of  
2166 antibiotic candidates against other resistant and difficult-  
2167 to-treat infections.

2168 We believe antimicrobial resistance is a public health  
2169 crisis. You have already received testimony from the CDC,  
2170 NIH, FDA, BARBA, and today, the IDSA, AMA and AAP combined  
2171 with numerous independent studies is unanimous is two key  
2172 points. First, antibiotic resistance is an increasingly  
2173 severe threat to our public health, and second, that gaps in

2174 our therapeutic options are growing rapidly by the month,  
2175 making it urgent that we develop more drugs, more new drugs  
2176 to develop resistant infections. We are approaching a crisis  
2177 point with antibiotic resistance and the lack of new drugs  
2178 against gram-positive bacteria such as Staph, gram-negative  
2179 bacteria such as acinetobacter.

2180 Mr. Chairman, you yourself noted in the subcommittee's  
2181 last hearing that gram-negative infections have become a  
2182 significant health issue for many servicemen and servicewomen  
2183 returning from the Middle East with untreatable infections,  
2184 so why so few antibiotics in development? There are critical  
2185 economic disincentives at work that profoundly and adversely  
2186 impact the willingness of companies and others to pursue  
2187 cutting-edge antimicrobial R&D. As you have heard, the  
2188 number of new antibiotics approved by the FDA has decreased  
2189 by 70 percent since the mid 1980s, and a recent peer review  
2190 study found only five new antibiotics in the R&D pipeline out  
2191 of more than 506 in development, less than 1 percent. But  
2192 proven incentives exist to encourage antimicrobial  
2193 innovation. Three years ago with your leadership, a  
2194 provision in FDAAA required FDA to answer whether the Orphan  
2195 Drug Act could be applied in this matter. Regrettably, the  
2196 agency concluded that they cannot under the law as written.

2197 Despite this setback, like you, Cubist believes there

2198 are still options available. We commend IDSA for their 10 by  
2199 20 initiative and we strongly support enactment of H.R. 2400,  
2200 the STAR Act, but we believe that neither the 10 by 20 nor  
2201 STAR Act includes provisions that would directly encourage  
2202 development of new therapeutics. As one of the very few  
2203 American companies discovering and commercializing novel  
2204 anti-infectives, we believe that incentives must attract more  
2205 small, mid-market and large companies into pursuing both  
2206 human clinical studies and earlier stage research. Congress  
2207 and the Administration need to correct market failures just  
2208 as they have already for rare diseases, pediatric drug use  
2209 and medical countermeasures. I believe such incentives must  
2210 include the following: one, enhanced market and data  
2211 exclusivity for qualified infectious disease products; two,  
2212 exempt qualified infectious disease products from the  
2213 pharmaceutical excise tax and 340(b) drug discount expansion  
2214 enacted in health reform; three, authorize the study and  
2215 establishment of guaranteed market contracts and other pull  
2216 market mechanisms as well as the use of other transactions  
2217 authority by the HHS; four, expand tropical disease priority  
2218 review vouchers as established under FDAAA to apply to  
2219 qualified infectious disease products; five, create  
2220 infectious disease product development grants modeled on  
2221 FDA's successful orphan product development grants; six,

2222 codify the task force on global antimicrobial resistance; and  
2223 seven, improve access to home infusion antibiotic treatment,  
2224 especially in the Medicare program.

2225           In conclusion, Mr. Chairman, thank you for the  
2226 opportunity to testify today. Antimicrobial resistance is a  
2227 very real threat to public health and one that is only  
2228 getting worse. I urge Congress to act on the consensus  
2229 recommendations that I and many others offer as steps toward  
2230 ensuring the development of the next generation of first-line  
2231 drugs to combat resistant infections.

2232           [The prepared statement of Dr. Eisenstein follows:]

2233 \*\*\*\*\* INSERT 7 \*\*\*\*\*

|

2234 Mr. {Pallone.} Thank you, Dr. Eisenstein.

2235 Dr. Levi.

|  
2236 ^STATEMENT OF JEFFREY LEVI

2237 } Mr. {Levi.} Thank you, Mr. Chairman, thank you, Ranking  
2238 Member Shimkus. I am Jeff Levi. I am the executive director  
2239 of Trust for America's Health. We are a not-for-profit non-  
2240 partisan public health advocacy organization.

2241 Antimicrobial resistance, or AMR, is not an abstract  
2242 concern. As we have heard, we live in a world where  
2243 antibiotic resistance is believed to be responsible for over  
2244 90,000 deaths a year in the United States. That is more than  
2245 die of diabetes or Alzheimer's or HIV. And AMR poses a  
2246 totally unnecessary burden on the U.S. health care system.

2247 We face this problem in part because the market has  
2248 failed to meet the need for new antimicrobials. My oral  
2249 testimony, I am going to focus on the primary research and  
2250 development questions that I think we need to address this  
2251 market failure, but my written testimony discusses two other  
2252 critical components to this effort, and that is federal  
2253 leadership and prevention, and I would like to briefly  
2254 comment on those first.

2255 First, the Administration has taken a major step forward  
2256 in creating new locus for leadership regarding AMR by  
2257 establishing the new position of deputy assistant secretary

2258 for health and infectious diseases. This new leadership, we  
2259 hope, will provide the development and oversee the updated  
2260 public health action plan to combat antimicrobial resistance  
2261 and that will be a robust and comprehensive plan that  
2262 addresses the many issues outlined in the testimony you are  
2263 hearing today.

2264       Until we develop new antimicrobial agents, we must  
2265 depend on prevention. While much has been started, we hope  
2266 that the Administration will embrace a far more aggressive  
2267 national education campaign about appropriate use of  
2268 antimicrobials and non-pharmaceutical approaches to prevent  
2269 transmission of resistant bacteria. Above all, we hope the  
2270 Administration will step back from its proposed cut of \$8.6  
2271 million in funding for State and local health departments to  
2272 track and control antibiotic resistance.

2273       Ultimately, the problem of antimicrobial resistance will  
2274 not be resolved until we have better diagnostics, new  
2275 antimicrobial agents and new vaccines, but few new products  
2276 are in the pipeline, as we have heard. This is primarily  
2277 because the market has failed. We need to change that  
2278 equation. To date, the largest federal investment in  
2279 creating market incentives is through BARDA. Unfortunately,  
2280 while BARDA has the authority to do the research we need to  
2281 do, it is chronically underfunded. Even the proposed \$476

2282 million for fiscal 2011 for BARDA is a fraction of what BARDA  
2283 needs to incentive development of a range of countermeasures,  
2284 not just antimicrobials. With scarce funding the federal  
2285 government has been unable to demonstrate to industry that  
2286 they will be full partners. The existing options beyond  
2287 BARDA including potential expansion of the Orphan Drug Act,  
2288 prioritization of vouchers for companies that focus on  
2289 neglected tropical diseases and advanced purchase  
2290 arrangements are all necessary but we believe probably  
2291 insufficient to create the research and manufacturing  
2292 capacity and/or the demand for developing new antimicrobial  
2293 agents. These financial and regulatory incentives may  
2294 continue to attract small companies but we worry that they  
2295 will not attract the larger companies with the manufacturing  
2296 and marketing capacity to bring new antimicrobial products to  
2297 scale.

2298         Even if we successfully address the market issues, we  
2299 still need policies and programs that will also create the  
2300 intellectual capital in the academic and private sector-based  
2301 biomedical research community if we are to answer the range  
2302 of basic research questions and then develop new products.

2303         In short, I think we are left with more questions than  
2304 answers, and so we need a collaborative effort between the  
2305 private sector and the public sector, and I hope it will be

2306 reflected in the forthcoming action plan and that it can  
2307 address some of the following questions. What is the right  
2308 mix of direct financial incentives and regulatory protections  
2309 to bring new companies to the table? What policies and  
2310 incentives can the government create that will result in a  
2311 willingness of venture capital to invest in development of  
2312 new antimicrobial agents? Government financing a loan does  
2313 not need to be the answer. We have begun to see venture  
2314 capital play a new role in development of new influenza-  
2315 related products and we learn from this experience and bring  
2316 more players to the table. What investments does the NIH  
2317 need to make to incentivize biomedical researchers to re-  
2318 engage with the field of antimicrobial development so they  
2319 see a long-term future in this field? What policies can FDA  
2320 put in place in advance so that potential investors in  
2321 research know the pathway to approval? And finally, and just  
2322 as important, what policy and financial arrangements will  
2323 assure that new products developed with special federal  
2324 financial support or regulatory incentives will be accessible  
2325 and affordable to domestic consumers reflecting the  
2326 taxpayers' early investment in their development? Any plan  
2327 should come with a professional judgment budget so that the  
2328 Congress and the Administration can make appropriate  
2329 estimates of the potential return on an increased federal

2330 investment. If the HHS plan fails to address these issues  
2331 properly, an independent entity should be empowered to  
2332 develop that plan.

2333 AMR is a solvable problem if we are creative enough in  
2334 our policies and our investment strategies. As the bugs  
2335 adapt, so must we.

2336 Thank you again for the opportunity to share our views  
2337 today.

2338 [The prepared statement of Mr. Levi follows:]

2339 \*\*\*\*\* INSERTS 8, 9 \*\*\*\*\*

|  
2340 Mr. {Pallone.} Thank you, Dr. Levi. Let me thank all  
2341 of you. As you know, we are going to take questions now, and  
2342 I will start with myself.

2343 Some of you mentioned that antibiotics are unique among  
2344 drugs because the more they are used, they less effective  
2345 they become, so in order to preserve their effectiveness,  
2346 they need to be used infrequently. That is a very different  
2347 situation from drugs used, for example, to treat a rare  
2348 cancer. Yet even with these differences, a couple of you  
2349 suggested that we should look at extending the market  
2350 exclusivity provided to antibiotics like we did with the  
2351 Orphan Drug Act and exclusivity, of course, delays generic  
2352 competition and deprives patients and the overall health care  
2353 system of the critical savings they provide. You know, we  
2354 are always worried about saving money around here. So if we  
2355 are going to consider this kind of incentive, we need to have  
2356 every confidence that it is justified and it will work. So  
2357 let me ask those of you who addressed this, beginning with  
2358 Dr. Eisenstein, if you can explain how adding 6 months or  
2359 even 2 years of exclusive marketing would result in companies  
2360 investing in antibiotic development when, as I mentioned, the  
2361 only way to preserve an antibiotic's effectiveness is to  
2362 minimize its use. You understand, it seems a little

2363 disingenuous. In other words, during the period of exclusive  
2364 marketing, the public health goal would be to minimize use of  
2365 the drug and thus minimize its sale. So under those  
2366 circumstances, why would additional market exclusivity be a  
2367 successful inducement for antibiotic development? I am  
2368 confused. How do you juxtapose those two?

2369 Dr. {Eisenstein.} I think you are talking about really  
2370 two answers to the same problem, the problem that we have  
2371 today about antibiotic resistance, and I am not an economist,  
2372 but as has been explained to me from smart economists who  
2373 have looked at this, there is an issue of supply and an issue  
2374 of demand. The issues of demand have been very well  
2375 discussed by the panelists here today, I believe, in terms of  
2376 things like antimicrobial stewardship, which by the way I as  
2377 a physician working at a pharmaceutical company strongly  
2378 subscribe to and agree with. What this means is that a given  
2379 company like Cubist would actually forego profits that it  
2380 might otherwise be able to get if it were not selling  
2381 antimicrobials, if it were selling some other product. So  
2382 make up for that, because of the otherwise perverse aspects  
2383 that controlling the demand side is perversely then hurting  
2384 the supply side by providing an extra disincentive, you give  
2385 back to the company extra time to regain the investment that  
2386 they have made previously, albeit in several more years out.

2387 Mr. {Pallone.} Right, but I guess what I am--

2388 Dr. {Eisenstein.} Albeit, it is not at the same level.

2389 Mr. {Pallone.} Maybe you have answered this but maybe I  
2390 don't understand. I understand that, but, I mean, what about  
2391 this other factor which is that you have this health goal to  
2392 minimize use of a drug and doesn't that mean minimize its  
2393 sale? So how do you address that in the context of the  
2394 market exclusivity?

2395 Dr. {Eisenstein.} Well, again, market exclusivity would  
2396 provide the innovative company with a longer launch pad.

2397 Mr. {Pallone.} So the fact that they were trying to  
2398 minimize use as a public health goal wouldn't be significant  
2399 because you have a longer period of time?

2400 Dr. {Eisenstein.} It would tend to balance that out,  
2401 and that is how you give back for the degree of control at  
2402 the front end.

2403 Mr. {Pallone.} All right. I want to ask two more and I  
2404 am going to be quick here. Dr. Spellberg, you think 15 to 20  
2405 years of exclusivity is necessary. Now, that far exceeds any  
2406 other terms of market protection that we in place today, so  
2407 why do you give it such a long period? Unless I  
2408 misunderstood, I thought you said 15 to 20 years.

2409 Dr. {Spellberg.} So from my understanding, the current  
2410 orphan drug, if you can apply the orphan drug to a product

2411 for 7 years.

2412 Mr. {Pallone.} Yes, and we have others. In health care  
2413 reform, we did for generic follow-up biologics, I think that  
2414 was 14 or maybe 12. But you are at 15 to 20.

2415 Dr. {Spellberg.} Well, I think this was just a concept  
2416 that we are in really bad shape with antibiotics and we have  
2417 to do something potent to fix it, and I think one of the  
2418 really important central concepts that IDSA believes is that  
2419 there isn't going to be one incentive that fixes this  
2420 problem, there is going to be a panel of them, and whatever  
2421 panel is felt to be most fiscally responsible and effective  
2422 is fine.

2423 Mr. {Pallone.} So it is one of the pieces?

2424 Dr. {Spellberg.} Exactly.

2425 Mr. {Pallone.} And that is sort of what Dr. Levi says,  
2426 so I will end with you. You expressed skepticism about  
2427 whether exclusivity would work, and I think you did give us a  
2428 whole panoply, so just give me a little more information  
2429 about why you have questions on exclusivity and how important  
2430 that is by comparison to some of the other things you  
2431 mentioned.

2432 Mr. {Levi.} I am not sure I know the answer to what is  
2433 the right balance.

2434 Mr. {Pallone.} I know. None of us do. But I would

2435 like your opinion.

2436           Mr. {Levi.} But I think market exclusivity plays a role  
2437 but I think we are not entirely clear about how major a role,  
2438 how much of an incentive it is going to be, and I think we  
2439 have this very strange situation where on the one hand we  
2440 want to discourage use, which even with some additional  
2441 exclusivity, will that be enough to bring big manufacturers  
2442 to the table, and that is what we really need. We need both  
2443 the intellectual capital that these big companies have and  
2444 the production and marketing capacity that they have. If it  
2445 is dramatically successful and becomes a new major  
2446 antibiotic, we wouldn't necessary--we want prudent use but it  
2447 may then have a very large market that goes beyond what was  
2448 ever intended in the Orphan Drug Act. So I think we have to  
2449 try to figure out what that right balance is, and I guess I  
2450 have to come back to my bottom line as to why all these  
2451 questions still remain is that we haven't invested the money  
2452 that it is going to take and a lot of this is going to take  
2453 federal dollars, and we have the authority in agencies like  
2454 BARDA to promote this development and I think industry feels  
2455 this is a much improved process but we haven't put enough  
2456 resources into it. We put a fraction of the resources into  
2457 to even develop the products that are already on the agenda  
2458 that BARDA has and so it is going to take a significant mix.

2459           Just one last thought, which is, once we make those  
2460 federal investments, we need to make sure that these are  
2461 indeed accessible to consumers and that the federal  
2462 government doesn't pay twice so that I would suggest that the  
2463 340(b) program is actually very important. If we are  
2464 subsidizing care for people, whether it is through Medicaid  
2465 or the community health centers, if the federal government is  
2466 paying for the direct care, we shouldn't be paying for it  
2467 twice if we have already invested in the development of those  
2468 products.

2469           Mr. {Pallone.} All right. Thank you.

2470           Mr. Shimkus.

2471           Mr. {Shimkus.} Wow, so many questions, so little time,  
2472 all the doctors at the table. I have learned a couple things  
2473 from listening to the testimony and perusing. This is  
2474 serious business, and I just don't know if we are serious  
2475 about it yet. So I think you are helpful in the testimony.  
2476 Some of you like the STAR Act and the STAR man is here, so I  
2477 am going to talk with him about it, but also some of you said  
2478 it is not enough, so there is probably some building that has  
2479 to be done and I look forward to working with Congressman  
2480 Matheson, who is a good friend and an honest broker, which I  
2481 think you need in this business.

2482           Dr. Levi, I'm just making comments and I am going to try

2483 to get to questions, but you mentioned market failure, and I  
2484 think the charts in both testimonies shows that we don't  
2485 have, and I don't know if Dr. Woodcock mentioned the small  
2486 little uptick, if this was really just Pollyannaish or, you  
2487 know, trying to feed up some optimism based upon FDA, but I  
2488 think there needs to be a discussion of market failure or  
2489 government failure, that there may be both here, and that is  
2490 where I want to encourage you all to continue to talk. If we  
2491 really believe that there is a serious problem, we can get to  
2492 a solution but we all have to be working together and we will  
2493 develop a consensus, and so I think there is hope for that  
2494 because we have had successes in marketing new drugs from  
2495 pediatric exclusivity to other things, what we have done on  
2496 the biologics, and we have done this stuff. So there are  
2497 things that we can do.

2498 I have stayed off beating up my friends on the new  
2499 health care law and also some panelists here, so my intent is  
2500 not to do that, but I do think, Dr. Eisenstein, you did  
2501 mention the excise tax on pharmaceuticals in your testimony.  
2502 One of your solutions is, we need to get relief from that as  
2503 an incentive, which if you then go on to take it to its  
2504 natural conclusion, which means that the excise tax must be  
2505 an inhibitor to certainty or return on investment or  
2506 something to the pharmaceutical practices, which also was

2507 mentioned that President's fiscal year 2011 \$8.6 million cut  
2508 in preventive and education, which I think a lot of people  
2509 don't talk about it, or was highlighted in the last panel  
2510 also was if we want to move people off antibiotics, we want  
2511 to move them to--and this was Congressman Murphy's point. He  
2512 is not here right now. But we want to move them way out of  
2513 prescriptive antibiotics so we should want to encourage them  
2514 initially to do over-the-counter but what we did in the  
2515 health care law for flexible spending accounts was  
2516 disincentivize people using over-the-counter. In fact, we  
2517 took away their ability to use their flexible spending  
2518 accounts to do that. So I end up walking away having more  
2519 questions than answers. And some of the questions I kind of  
2520 already mentioned based upon the statements.

2521 Does anyone want to--I guess let me just finish with a  
2522 question with Dr. Spellberg, if I may. In your testimony you  
2523 comment--we talked about this pipeline and development. Do  
2524 you buy--I mean, you sat in here, and Dr. Woodcock left, and  
2525 she was here for most of the testimony, which I have great  
2526 respect for. Do you buy their arguments that they are doing  
2527 all they can and there is a little uptick? You heard me ask  
2528 them about regulatory authority, do they need more. I really  
2529 didn't get any answer. So they seem to think they have the  
2530 power to move forward but I have got a feeling that you are

2531 not convinced.

2532 Dr. {Spellberg.} Well, let me start by saying that I  
2533 think all of us are very appreciative of the tremendous  
2534 energy and effort that Dr. Cox, Dr. Woodcock and the new  
2535 leadership under Drs. Hamburg and Sharfstein have infused  
2536 into the agency. Just in the last year or two we have seen a  
2537 tremendous uptick of energy and efficiency and work product  
2538 output. We have been asking for guidance documents for years  
2539 on these diseases and we are finally starting to get some. I  
2540 don't think that they need more statutory authority. I think  
2541 that--there are two issues that I would raise with Dr.  
2542 Woodcock's testimony. First is that it is not true that  
2543 companies have a clear path to approval for superiority  
2544 drugs. I consult for companies that develop antibiotics.  
2545 They don't know how to do those studies. Those studies have  
2546 never been done before. It may be philosophically true that  
2547 that is an open path but for something that has never been  
2548 done before, companies are not going to take a risk on  
2549 hundreds of millions of dollars of capital invested to do a  
2550 trial that has never been done before. They wanted to go to  
2551 tried-and-truth pathways. So we think that we need guidance  
2552 documents to do those studies. The superiority studies for  
2553 highly drug-resistant bacteria do not exist. There is no  
2554 pathway for that, and we need guidance on that, one.

2555           Two, I think the issue with the non-inferiority studies  
2556 that Dr. Woodcock mentioned, I don't think that there is--I  
2557 would not personally characterize it as scientific  
2558 controversy. What there is, is statistical controversy. If  
2559 you talk to the physicians and the investigators who do these  
2560 studies, there is pretty clear consensus on what these  
2561 studies should look like, and when you look at the advisory  
2562 committee panel votes, it is split, clinicians, scientists  
2563 and statisticians. So I would personally go back to Samuel  
2564 Clemens: There are three kinds of lies: lies, damn lies and  
2565 statistics, and I think statistics are very valuable, but  
2566 when you start to weigh them more heavily than clinical  
2567 reality, I think that is a problem and I would like to see a  
2568 philosophical balance. I think this is a philosophical  
2569 problem, not a scientific problem at the FDA.

2570           Mr. {Shimkus.} Thank you, Mr. Chairman. I want to  
2571 apologize to the rest of the panelists for not asking follow-  
2572 up questions but you can tell I was listening and I took in a  
2573 lot of information. I yield back, Mr. Chairman.

2574           Mr. {Pallone.} Sure.

2575           Next is, he has been characterized as our star, the  
2576 gentleman from Utah, Mr. Matheson.

2577           Mr. {Matheson.} Well, thank you, Mr. Chairman. I have  
2578 been called a lot worse, so I will take the positive

2579 descriptions when I get them.

2580 I want to thank the panel. I am sorry I have been  
2581 bouncing between two hearings, so trying to be in two places  
2582 at once, but I do appreciate the panel being here. I  
2583 appreciate your insight and your indicated support for what  
2584 we are trying to do with the STAR Act, and Mr. Shimkus, I  
2585 agree, there is always room to look for improvements and I  
2586 have always tried to be an honest broker, and that is why we  
2587 hold these hearings, to get more information and we want to  
2588 do the best we can. Sometimes process does help if you go  
2589 through the process, and so I hope we can continue to do that  
2590 on this issue.

2591 And I wanted to acknowledge Dr. Spellberg. You  
2592 participated in a briefing just last month for Congressional  
2593 staff that I think helped highlight this issue and it is good  
2594 to see you again, and I appreciate your engagement on the  
2595 issue, and both Dr. Spellberg and Dr. Bradley, I appreciate  
2596 you bringing some examples of how infectious disease and  
2597 disease-resistant bugs that cause the problems for actual  
2598 patients because ultimately that is what we are talking  
2599 about, the patients. And I have a bias because my wife is a  
2600 pediatric infectious disease doc as well as the Children's  
2601 Hospital in Salt Lake City, so this is an important issue for  
2602 me and that is why I have tried to get engaged in this

2603 legislation.

2604 Dr. Spellberg, let me ask you just a couple of  
2605 questions. How often are seeing in your practice are you  
2606 finding patients with resistant infections, and are you  
2607 seeing a trend that is going in an upward way?

2608 Dr. {Spellberg.} Yes. I am in an academic hospital so  
2609 my patient care is inpatient, and we encounter multidrug-  
2610 resistant bacteria daily, every day on rounds, and I will  
2611 just give you an example. Over a 1-month period at my  
2612 institution, we had 23 patients that were infected with  
2613 extreme drug-resistant acinetobacter that is resistant to  
2614 everything except one last-ditch drug, Colistin, which was  
2615 abandoned in the 1960s because it is so toxic and that is all  
2616 we have left. Twenty-three patients in one month for one  
2617 bacteria. That is the scope of the problem.

2618 Mr. {Matheson.} And that was your last hope, that one  
2619 medication?

2620 Dr. {Spellberg.} Yes, that is it. And I should also  
2621 mention, we don't routinely test for susceptibility to that  
2622 drug so we don't know, some of those 23 patients may have  
2623 been resistant to it as well. We don't know. Getting back  
2624 to the STAR Act, we need data collection to know what the  
2625 extent of the resistance problem is.

2626 Mr. {Matheson.} Right. Part of the STAR Act is, it

2627 does create this, we call it the public health antimicrobial  
2628 advisory board, and it is going to include infectious disease  
2629 experts, public health, pharmacy, vets and other experts to  
2630 provide sort of advice to this interagency task force to try  
2631 to bring some accountability to federal efforts. Do you  
2632 think that--how do you think that type of advisory board is  
2633 going to benefit this issue?

2634 Dr. {Spellberg.} I think there are at least two really  
2635 important reasons why we need that advisory board. One is  
2636 that this stuff is very complex and it takes a tremendous  
2637 amount of very broad scientific expertise. I think it is  
2638 unrealistic to expect that one government agency is going to  
2639 have that breadth of expertise. An external advisory panel  
2640 can bring a very broad and deep expertise to oversee the  
2641 issue. The second issue is that an external board can help  
2642 hold the feet to the fire, help make sure that goals are met  
2643 and provide some accountability externally.

2644 Mr. {Matheson.} In your practice, when you--well, you  
2645 say you are at an academic hospital, teaching hospital, so in  
2646 terms of your involvement with looking for development of new  
2647 meds, new antibiotics that can address these tougher bugs, we  
2648 had a lot of discussion today about the available incentives  
2649 to encourage the research and development. Do you think the  
2650 existing incentives, there are some that are working and not

2651 working in addition to what we ought to add in the future but  
2652 are there some efforts we try to do to encourage development  
2653 of new meds that just aren't getting traction at all?

2654 Dr. {Spellberg.} Yes, I don't think we have any  
2655 existing mechanisms that apply to antibiotics. We have tried  
2656 to access the orphan drug program. It has been made very  
2657 clear, explicitly clear that the orphan drug program does not  
2658 apply to antibiotics for whatever reason. We need orphan-  
2659 drug-like mechanisms. There is no existing incentive  
2660 mechanism to bring companies back to the drawing board.

2661 Mr. {Matheson.} Mr. Chairman, I will yield back.  
2662 Thanks.

2663 Mr. {Shimkus.} Will the gentleman just yield for  
2664 follow-up on that?

2665 Mr. {Matheson.} Yes.

2666 Mr. {Shimkus.} In the orphan drug and because of the  
2667 population of 200,000, is that basically why the FDA is  
2668 saying that the orphan drug does not qualify? And since  
2669 these are bacteria, they don't know the population?

2670 Dr. {Spellberg.} You know, I think we could very much  
2671 quibble with the fact that there are, you know--

2672 Mr. {Shimkus.} Is this statistical stuff that you were  
2673 talking about on my question?

2674 Dr. {Spellberg.} I don't understand the exact reasons

2675 why the FDA counts the numbers as being more than 200,000.  
2676 if we talk about all bacterial infections, certainly it is  
2677 more than 200,000. If we talk about extremely drug-resistant  
2678 acinetobacter, it can't be more than 200,000. But either  
2679 way, fine. If we can't access orphan drug, let us look at  
2680 other push-pull mechanisms and let us look at, you know,  
2681 increasing funding at NIH so we can get better science to  
2682 lead target discovery and establish a clinical trials  
2683 network. There are lots of other things we could be doing.

2684 Mr. {Matheson.} Thanks, Mr. Chairman.

2685 Mr. {Pallone.} Thank you.

2686 Dr. Burgess.

2687 Dr. {Burgess.} Thank you, Mr. Chairman. I can't tell  
2688 you how refreshing it is to have a panel where four of the  
2689 five panelists are MDs. You know, we did the health care  
2690 bill and all the hearings leading up to that. We just heard  
2691 from economists and political scientists and theoretical  
2692 folks. It would have been great to have you guys here while  
2693 we were actually doing that work, but you are here today and  
2694 I appreciate the fact that you are.

2695 Dr. Bradley, Dr. Spellberg, you guys took me back to the  
2696 1970s when I was in medical school, and on the pediatric  
2697 wards, the pediatric attending told us that let us use  
2698 gandamycin because we are saving gentamicin for the days when

2699 gandamycin will no longer be effective. And then Dr.  
2700 Spellberg, when I did an elective in infectious disease, I  
2701 was told by the professor why did you pick gandamycin for  
2702 this child. I said well, because we are saving gentamicin.  
2703 He said well, you need to go down and talk to the orthopedist  
2704 because they are not saving it, they are using it on anybody  
2705 who walks in the door, which just--that is part of the  
2706 problem because it is like our air quality issues. They  
2707 don't live in a single jurisdiction, they tend to migrate  
2708 throughout society.

2709 But the 10 by 20 issue, Dr. Spellberg, you heard me  
2710 questioning Dr. Woodcock from the FDA, and the new molecular  
2711 entities in the last decade have been about 10, so is 10 by  
2712 20, are we just talking about the status quo with development  
2713 of new stuff or is 10 by 20 really a breakthrough?

2714 Dr. {Spellberg.} You are talking about 10 new molecular  
2715 entities on a declining scale, so if you look at the last 5  
2716 years, it is way less than that. If we got 10 new meaningful  
2717 drugs to treat really resistant bacteria by the year 2020,  
2718 that would be a dramatic improvement from where we are right  
2719 now. Do I think one drug per year is enough in the long  
2720 term? Probably not. But if each of those drugs is a  
2721 meaningful advance, it is not a ``me too'' drug, then one to  
2722 two per year in the long run is probably enough to get us

2723 where we need to go.

2724 Dr. {Burgess.} Let me interrupt you because, again,  
2725 they are just the devil on me with the gavel in this  
2726 committee. What are some of the new things that are out  
2727 there? What have you got in the pipeline? Tease us with  
2728 what is over the horizon. What are we going to be able to  
2729 treat?

2730 Dr. {Spellberg.} To be honest with you, first of all,  
2731 let us remember that if we are lucky, one in five drugs, one  
2732 in five antibiotics in the pipeline is going to get approved.  
2733 When you talk about the pipeline, you are talking about late  
2734 pre-clinical early phase I clinical trials. It may be as bad  
2735 as one in 10. So if you have 15 antibiotics in the pipeline,  
2736 which is what the IDSA and the European Centers for Disease  
2737 control and EMEA identified, we are going to be lucky to have  
2738 two, maybe three of those drugs get approved in the next 5 to  
2739 10 years or so.

2740 Dr. {Burgess.} Well, you talked quite passionately and  
2741 eloquently about the need for funding, and I don't disagree  
2742 with that, but 15 months ago we passed an enormous bill, it  
2743 was called a stimulus bill. We pumped so much money into  
2744 NIH, we thought they were going to pop, and now how do you  
2745 get those discoveries into the hands of clinicians if we have  
2746 got this pipeline problem at the FDA?

2747           Dr. {Spellberg.} Well, I think you have got two  
2748 problems there. One is putting money into NIH, and we are  
2749 calling for \$500 million to go into NIAID specifically, is  
2750 not enough. We need that money to go to the critical areas,  
2751 and in our analysis with NIAID's help, the vast majority of  
2752 the dollars they spent on antimicrobial resistance is not  
2753 spent on solving multidrug-resistant bacteria, it is  
2754 primarily spent on things like HIV and tuberculosis. We need  
2755 to have that money go to lead compound, discovery of new lead  
2756 molecules that are going to treat multiresistant infections.  
2757 A tiny fraction of that money goes there.

2758           The other thing is, in discussions with Dr. Woodcock, we  
2759 need a clinical-trial network so that very sophisticated  
2760 clinical trials can get done that will open up the antibiotic  
2761 pipeline during clinical development and we would like to see  
2762 public-private partnerships, large grants that bring together  
2763 academia and industry to help solve these problems.

2764           Dr. {Burgess.} Well, after all, that was the penicillin  
2765 story because--

2766           Dr. {Spellberg.} That is exactly right.

2767           Dr. {Burgess.} --your 1942 pictures, however dramatic  
2768 they are, that was only a handful of patients who could be  
2769 treated at that time and it was not until the defermentation  
2770 process occurred toward the end of the second World War that

2771 it became clinically efficacious to treat large numbers of  
2772 people and that was the story of D-Day, saving life and limb  
2773 when they stormed the beaches of Normandy.

2774 Dr. Fryhofer, I just have to ask you a question about  
2775 the health care bill, because, after all, your organization  
2776 supported it. I am a member of the AMA. I did not support  
2777 it. I voted it against it. But on the issue of class II  
2778 medical devices, and we are going to get--you are going to  
2779 get hit, your members are going to get hit with a significant  
2780 tax on class II medical devices in physician offices.  
2781 Syringes, needles will be taxed and I think it is 2.9  
2782 percent. That is going to be a hard cost to pass on to the  
2783 patient, to the consumer because you are under contractual  
2784 arrangement with the insurance companies and it is not likely  
2785 that they are going to pick up the cost of that tax. But  
2786 what about some of these point-of-diagnosis tests that have  
2787 been talked about, the tests are being developed by BARDA and  
2788 some of the tests that Dr. Woodcock from the FDA talked  
2789 about? Those tests, are they not going to be classified as  
2790 class II and class II devices?

2791 Mr. {Pallone.} Dr. Burgess, why don't we do this? Your  
2792 time has run out but the three of us, since we are here, I am  
2793 going to have each of us have another 5 minutes.

2794 Dr. {Burgess.} We ought to let Dr. Fryhofer answer the

2795 question.

2796 Mr. {Pallone.} Answer that one and then--

2797 Dr. {Burgess.} Since it has been so eloquently posed.

2798 Mr. {Pallone.} Then we are going to have another round  
2799 just for those--

2800 Dr. {Burgess.} Is this tax going to have a chilling  
2801 effect on you being able to do those tests?

2802 Dr. {Fryhofer.} Well, I think that the tests that you  
2803 are talking about would not necessarily be done in doctors'  
2804 offices. I think many of these diagnostic tests would  
2805 probably be done by a laboratory.

2806 Dr. {Burgess.} Well, if I can interrupt for a minute,  
2807 that is exactly what we were told, that these would be point-  
2808 of-diagnosis tests that would be done. The rapid strep was  
2809 alluded to, and I tried to get some information on some of  
2810 the others but they will be done in the office.

2811 Dr. {Fryhofer.} Well, they may be collected in the  
2812 office, but in order to be done in the office, you have to be  
2813 CLIA approved to perform that level of test. So certainly I  
2814 think some of these initial tests might not be performed in  
2815 the office, and those are concerns and certainly as you say,  
2816 there is a lot more work we need to do on this new health  
2817 care bill but I think there are a lot of things we did  
2818 accomplish. I have children, I have two college students,

2819 and I am glad to know that they can stay on my health  
2820 insurance until they are 26. I am glad we have gotten rid of  
2821 this preexisting-condition problem for so many of our  
2822 patients. So there are some good things that happened but we  
2823 still have a lot of work to be done and we are depending on  
2824 you and Congress to work out the bugs and including these  
2825 bugs we talked about today and move forward to help our  
2826 patients.

2827         Mr. {Pallone.} Now you have another 5 minutes after,  
2828 myself, Shimkus and you.

2829         I wanted to ask a question of how we can promote the  
2830 stewardship of antibiotics, encouraging more judicious use.  
2831 In our first hearing on antibiotics, we heard about the CDC's  
2832 Get Smart campaign, which is an effort to educate physicians  
2833 and encourage better prescribing habits. We heard about some  
2834 of the successes of that venture and some of the shortfalls  
2835 in the funding for it. But even if Get Smart were fully  
2836 funded, I am wondering if that goes far enough, especially if  
2837 patients are demanding antibiotics. I am worried that a  
2838 volunteer campaign won't be able to effectively address this  
2839 issue or that even the interagency collaboration and what is  
2840 proposed by Mr. Matheson under STAR might not be enough.

2841         So let me just ask three questions in this regard, first  
2842 of Dr. Bradley because I don't think we even asked you

2843 anything. As a pediatrician, can you talk about the  
2844 pressures you face from parents to give antibiotics for your  
2845 patients?

2846 Dr. {Bradley.} Yes, sir. In the past that has been  
2847 sort of standard. Both the parents ask for antibiotics for  
2848 their children with sore throats, grandparents ask, and we  
2849 have had a campaign with teaching materials in the waiting  
2850 rooms, in the exam rooms to say don't ask for an antibiotic  
2851 if your doctor doesn't think your child has an infection.  
2852 There are programs we have put into place that have decreased  
2853 antibiotic use, some of the CDC, some of them Academy of  
2854 Pediatrics, and it is an education issue, and I think all of  
2855 the press that--the lay press has a lot of information about  
2856 antibiotic resistance. Parents are now understanding that we  
2857 can't just give antibiotics out.

2858 In another constructive way in different medical groups  
2859 that are clinical pathways being developed where if a child  
2860 has an ear infection, they come in with a supposed ear  
2861 infection. There are specific ways that the doctor needs to  
2862 evaluate that to make sure it is a true infection so there is  
2863 the little checklist: is the eardrum red and bulging, is  
2864 there pain, is there fever. And if not all of those are  
2865 present, then there is no antibiotic that should be  
2866 prescribed. We are putting together the same things for

2867 pneumonia so that we are designing methods for physicians and  
2868 clinicians to assess children in a systematic way to reduce  
2869 inappropriate antibiotic use. So it is a huge problem and we  
2870 are working hard and we are not there.

2871 Mr. {Pallone.} All right. I only have 2 minutes. I  
2872 wanted to get into the hospital setting because I can see how  
2873 these quality measures like Dr. Fryhofer, you mentioned  
2874 better quality measures to tract antibiotic use and I can see  
2875 how that would work where someone has a cold or sinus and  
2876 antibiotics shouldn't be used, but what about quality  
2877 measures in the hospital setting? I will ask you, Dr.  
2878 Fryhofer.

2879 And then Dr. Spellberg, you laid out a comprehensive  
2880 campaign for stewardship and you talked about comprehensive  
2881 hospital programs. So let me start with you, same question.  
2882 What do we do in the hospital setting? I will ask you and  
2883 then Dr. Spellberg.

2884 Dr. {Fryhofer.} Well, certainly the hospital setting is  
2885 a much different setting than the ambulatory setting. In the  
2886 hospital, there is an opportunity for a very collaborative  
2887 approach with the primary care or admitting physician, with  
2888 infectious disease specialist colleagues, with clinical  
2889 pharmacologists, also with the laboratory. So it is more of  
2890 a real-time situation so you can sort of change your approach

2891 to the patient, you know, every hour, every minute, so to  
2892 speak. In an ambulatory setting, right now we don't have as  
2893 many quick diagnostic ways to know exactly what the patient  
2894 has when they come in the office, and I think all of us were  
2895 very impressed by the photo of that young woman that you  
2896 showed us at the end of your presentation, Dr. Spellberg.  
2897 But as a primary care physician seeing patients in my office  
2898 every day, I don't want my patient to get like that. So we  
2899 don't want every patient that gets an antibiotic to be on the  
2900 verge of death. We want to use them judiciously. At the  
2901 same time, we don't want to handcuff doctors because we are  
2902 going to lose patients that way also.

2903 Mr. {Pallone.} Dr. Spellberg?

2904 Dr. {Spellberg.} I have to answer your question in  
2905 three parts but I will go quick. Okay. So there are three  
2906 strategies for stewardship. There is nagging, which I am  
2907 going to make more comments about in a minute, and that is  
2908 really important. There is diagnostics and there is  
2909 approving drugs through the FDA in a completely new way, and  
2910 all three of these things need to be done. In terms of the  
2911 nagging, which is the traditional antibiotic stewardship  
2912 program, I just want to point out what we are up against. If  
2913 you go back to the historical literature which I spent a lot  
2914 of time reading over the last several years, there were

2915 physicians in the 1940s that were begetting their colleagues  
2916 not to overprescribe antibiotics. This is not a new  
2917 conversation. It is very difficult to change human behavior.  
2918 Stewardship programs have generally not been widely  
2919 disseminated because there is no mechanism to pay for them.  
2920 Hospitals won't pay people to spend their time nagging people  
2921 not to prescribe drugs. So one of the issues is, we need the  
2922 CDC to develop stewardship programs and that we need to  
2923 figure out how to convince medical systems to pay for their  
2924 implementation.

2925         The second thing, probably the most powerful way we can  
2926 prevent overuse of antibiotics is exactly what was just  
2927 mentioned, look at the psychology of why antibiotics are  
2928 overprescribed. It is fear, and I don't mean specific fear  
2929 about lawsuits, I mean brain stem, we don't know why we are  
2930 afraid fear because we don't know which of our patients have  
2931 bacterial infections or not. We have a patient with  
2932 symptoms, it may be bacteria, it may be viruses. If 95  
2933 percent of the time it is viruses, it means 5 percent of the  
2934 time it is bacteria, and I don't want to guess wrong. If we  
2935 had rapid diagnostics, physicians have a printout that says  
2936 this is not a bacterial infection, that will end  
2937 inappropriate antibiotic prescription, so new diagnostics  
2938 would be very powerful.

2939           And the third thing is new FDA indications. If a drug  
2940 is only indicated for the treatment of multidrug-resistant  
2941 bacteria, it can only be marketed by law for what it is  
2942 indicated for. That will prevent overuse of the drug in  
2943 other settings.

2944           Mr. {Pallone.} Okay. Thank you.

2945           Mr. Shimkus.

2946           Mr. {Shimkus.} Thank you, Mr. Chairman.

2947           First of all, I have been told and I believe, although  
2948 obviously you have heard me address some misgivings that FDA  
2949 historically has been the gold standard and it has been able  
2950 to help and roll out things. Obviously there are hiccups and  
2951 there are problems now that we really want to address. There  
2952 is also a concern in the pharmaceutical debate just in  
2953 essence regular chemical compound drugs and maybe biologics  
2954 that the new European Union and their pathway might  
2955 eventually incentivize and have a quicker pathway which not  
2956 only then moves new drugs and development over the European  
2957 but then the factories and the jobs and then we lose that  
2958 gold standard. Now we are talking about this continued  
2959 problem here now with the antibiotic issue. You all are the  
2960 experts and maybe Dr. Levi, maybe Dr. Spellberg, Dr. Bradley,  
2961 some of whom are nodding as I look at facial expressions,  
2962 does anyone want to weigh in? Is this European Union

2963 takeover, their ability to have a quicker pathway, one, is  
2964 that a real threat? Two, is there stuff that we can learn in  
2965 their processes which might help us move rapidly? Can  
2966 anyone?

2967 Dr. {Spellberg.} I will make a couple of comments and  
2968 then I suggest that Dr. Eisenstein may be the most qualified  
2969 to answer that.

2970 Mr. {Shimkus.} Dr. Bradley wants to answer.

2971 Dr. {Spellberg.} Oh, I am sorry. Go ahead.

2972 Dr. {Bradley.} I can tell you that the way that the  
2973 EMEA is approving antibiotics now includes strong programs  
2974 for pediatrics upfront so after the first phase I trials  
2975 where the drugs preliminarily tested in adults, they are not  
2976 beginning to get testing in children so that they will have  
2977 drugs for their children probably 5 years or so sooner than  
2978 we would have them in the United States. Our FDA is talking  
2979 to them, and I hope that we can get earlier programs in  
2980 pediatrics, but yes, the EMEA and the Europeans have come at  
2981 this with a completely fresh view and they are rattling cages  
2982 and some of their ideas are quite good. Thank you.

2983 Mr. {Shimkus.} Dr. Eisenstein?

2984 Dr. {Eisenstein.} Yes. We get the impression, as Dr.  
2985 Bradley just stated, that the EMEA is moving ahead in a more  
2986 forward-looking way. I think that unfortunately the FDA had

2987 a hiccup with the approval process with Ketek. That has been  
2988 very well documented. I won't go into details. But  
2989 unfortunately, they, I believe, have gone into more of a  
2990 risk-averse mode over the last 4 or 5 years, and one of my  
2991 favorite expressions I learned from the director of  
2992 infectious diseases at the time, Janice Sheref, let us not  
2993 have the perfect be the enemy of the good, and unfortunately,  
2994 Janice is no longer at that position anymore, in part because  
2995 of the fallout from Ketek and I think is very unfortunate.

2996 Mr. {Shimkus.} Dr. Levi?

2997 Mr. {Levi.} I guess the two things that I would add is,  
2998 one, I think we do have something to learn from how the  
2999 Europeans are doing overall drug approval, but I also think  
3000 that sometimes we are--you know, we need to recognize that  
3001 the United States, for example, when we want the FDA process  
3002 to move quickly, it can. We had the first approved H1N1  
3003 vaccines in the United States, even though our system is  
3004 allegedly so much more cumbersome. So I think when we want  
3005 to, we can make that system work.

3006 The second is, we can't lose sight of the fact that it  
3007 is not just--you know, the fact that there are so few new  
3008 molecular entities entering the FDA stream is not because--it  
3009 is not exclusively and probably not primarily because of the  
3010 FDA approval process. We don't have the intellectual capital

3011 up front to create those, and we need to be investing in  
3012 creating that intellectual capital and then maybe some of the  
3013 financial capital will follow.

3014       Mr. {Shimkus.} Let me just finish with this. I agree  
3015 with you, Dr. Levi. The bioterrorism response that we did a  
3016 couple Congresses ago and BARDA as an example of us when we  
3017 realize that there is a real need to move, we can move.  
3018 There are probably things to be learned in that process that  
3019 would help us. I am concerned about the European Union and  
3020 their ability to usurp us if we don't straighten out our  
3021 processes to some extent, and this risk issue, the perfect is  
3022 the enemy of the good is something that I think we just have  
3023 to be careful about. I go back to the drug, the last drug,  
3024 everything else is not of use. You go back to the drug  
3025 developed in the 1960s that was super toxic but if I was a  
3026 parent and that was the last hope, that also brings in  
3027 liability issues. So there are processes, and I talked with  
3028 Mr. Matheson. I think there are processes that members of  
3029 good will can get some compromise on to move this forward,  
3030 and I do appreciate the testimony today.

3031       Mr. {Pallone.} Thank you.

3032       The gentleman from Texas, Mr. Burgess.

3033       Dr. {Burgess.} Thank you, Mr. Chairman.

3034       Dr. Levi, you are right. We did get that vaccine, that

3035 H1N1 vaccine out in very, very short time, and the vaccine  
3036 produced in this country turned out to be much safer than the  
3037 vaccine produced in particularly some of the eastern European  
3038 countries. So I will be the first to criticize the FDA, but  
3039 I did want to point out that yes, they do sometimes do things  
3040 right, and we do take safety in this country, we just  
3041 stipulate that drugs are always going to be safe, but Dr.  
3042 Eisenstein, you are right, we just clobbered them over Ketek.  
3043 We had them in here every day for what seemed like weeks on  
3044 end and it was a wonder that there was anyone left standing  
3045 at the FDA. It wasn't this committee but the Oversight and  
3046 Investigation Subcommittee that I am also on that was really  
3047 pretty aggressive on that, not that there weren't problems  
3048 but I think you are right, I think we as a subcommittee  
3049 probably bear some of that responsibility because of the  
3050 punishment we extracted on the folks on the FDA after that  
3051 Ketek story broke.

3052         Let me just ask you, Dr. Eisenstein, on the issue--I  
3053 talked to Dr. Spellberg about this a little bit but the  
3054 antibiotics in the pipeline concept. Do we have some good  
3055 molecules in the pipeline that are going to be coming  
3056 forward?

3057         Dr. {Eisenstein.} I can speak mostly about Cubist. We  
3058 are focused on acute health care. We have most of our

3059 expertise in the anti-infective space. We have now had  
3060 daptomycin/Cubicin on the market for 7 years to specifically  
3061 fight MRSA, and with that head of steam that we have  
3062 established, we have three additional antimicrobials that are  
3063 in human testing. One of them is for a disease called  
3064 Clostridium difficile associated with diarrhea. You are a  
3065 physician. You understand the importance of what. What  
3066 others might not appreciate is that that is starting to come  
3067 up on the horizon to become even as important perhaps as MRSA  
3068 in the hospital setting. We are working on an antimicrobial  
3069 specifically for that. We recently acquired a small company,  
3070 an even smaller company than ours because we consider  
3071 ourselves a madcap company looking at a new molecule to go  
3072 after one of the six key escape pathogens, in this case  
3073 pseudomonas, through a new mechanism of action that we are  
3074 very excited about and we have yet another antibiotic also in  
3075 the clinic that goes after some of the other escape pathogens  
3076 including pseudomonas, acinetobacter and Klebsiella.

3077       Let me underscore, though, something that Dr. Spellberg  
3078 just said earlier, and that is, it is very difficult to be  
3079 able to develop antimicrobials specifically for drug-  
3080 resistant organisms because by definition, you don't have  
3081 anything to compare it with so you therefore can't do a  
3082 controlled clinical trial. This is exactly the comment made

3083 earlier about the statistics getting in the way of clinical  
3084 judgment that makes otherwise great sense.

3085 Dr. {Burgess.} Let me just ask you a question on that.  
3086 Some of the so-called market failures aren't really caused by  
3087 a failure of science, they are caused more by the  
3088 difficulties that we impose in the regulatory process?

3089 Dr. {Eisenstein.} I would say that is part of it, and  
3090 the other part is that then the market size later given the  
3091 constraints that we have of putting some of these, I would  
3092 say enormously potentially very valuable antibiotics. We  
3093 talked some about personal interaction. I have a  
3094 granddaughter who because of birth defects at birth, she is 3  
3095 years now, she has been through six urinary tract infections,  
3096 three of which have been caused by these escape pathogens. I  
3097 worry every moment that the next infection she is going to  
3098 get is going to be due to an organism that is not going to  
3099 allow her to live anymore. I mean, I am very personally  
3100 invested in this. But the difficulty then is that we have  
3101 the opportunity to come up with new antibiotics but then they  
3102 have to be put behind a glass plate that says crack only in  
3103 case of an emergency.

3104 Dr. {Burgess.} Yes, and I am going to interrupt you  
3105 there because I am running out of time, and Dr. Spellberg,  
3106 you referenced that and you said use only as indicated, but

3107 doctors, we use stuff off label all the time.

3108 Dr. {Spellberg.} What we are talking about is a total  
3109 rethink of how antibiotics are developed in this country and  
3110 throughout the world. We can no longer afford the luxury of  
3111 having a drug like tigecycline come out, which is a  
3112 lifesaving drug for people with really resistant  
3113 acinetobacter and then have it get FDA approved to treat skin  
3114 infections where we have 20 other antibiotics we can be  
3115 using.

3116 Dr. {Burgess.} I just want to ask one last question on  
3117 the advisory panel because this is a fight that the chairman  
3118 and I had 3 years ago during the reauthorization of the Food  
3119 and Drug Act, and you talked about philosophical flexibility  
3120 in the advisory panels. We restricted the advisory panels  
3121 such that anyone who had actually worked on development of a  
3122 compound was restricted off of the panel, and this seemed to  
3123 me to be awfully shortsighted. The Institute of Medicine in  
3124 fact I think said restrictive to no more than 25 percent.  
3125 But the way we went about that seemed awfully pernicious,  
3126 particularly in some of the pediatric fields. The universe  
3127 of people that has worked on the compound is--I mean, they  
3128 are the people who know, the only people who know about the  
3129 drug. So is what we have done with the advisory panels and  
3130 the reauthorization 3 years ago, has that been part of the

3131 problem?

3132 Dr. {Spellberg.} Well, I think the advisory panels have  
3133 done the best they can overall. The real dissention recently  
3134 has been a true clinician-statistician split, not an overall  
3135 scientific spilt, although I do agree with you that I think  
3136 the people who are the most experienced with clinical  
3137 investigations are the people who tend to get consulted by  
3138 companies. So if you exclude the most experienced, informed  
3139 people, it does create problems, and Dr. Bradley has spent a  
3140 lot of time in the advisory committee so I wonder if you want  
3141 to make some comments.

3142 Dr. {Bradley.} I thank you for your comment, sir, and I  
3143 believe that keeping people off the committee who have any  
3144 experience in developing the drugs has been a problem.

3145 Dr. {Burgess.} I thank both of you. I am glad the  
3146 chairman was here to hear that. I will yield back my time.

3147 Mr. {Pallone.} Well, listen, this has been very helpful  
3148 obviously and I think we learned a lot today, and again, we  
3149 are doing three hearings in an ongoing effort and then we may  
3150 move some legislation, so I really appreciate your input. We  
3151 may give you additional written questions within the next 10  
3152 days or so and I would like you to get back to us promptly  
3153 with that.

3154 But thank you again, and without objection, the meeting

3155 of the subcommittee is adjourned.

3156 [Whereupon, at 1:06 p.m., the subcommittee was

3157 adjourned.]