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6 EXAMINING MEDICAL PRODUCT MANUFACTURER

7 COMMUNICATIONS

8 WEDNESDAY, JULY 12, 2017

9 House of Representatives

10 Subcommittee on Health

11 Committee on Energy and Commerce

12 Washington, D.C.

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16 The subcommittee met, pursuant to call, at 10:15 a.m., in
17 Room 2322 Rayburn House Office Building, Hon. Michael Burgess
18 [chairman of the subcommittee] presiding.

19 Members present: Representatives Burgess, Guthrie, Barton,
20 Upton, Shimkus, Blackburn, Lance, Griffith, Bilirakis, Bucshon,
21 Brooks, Mullin, Hudson, Collins, Carter, Walden (ex officio),
22 Green, Engel, Schakowsky, Butterfield, Matsui, Castor, Sarbanes,
23 Kennedy, Cardenas, Eshoo, and Pallone (ex officio).

24 Staff present: Adam Buckalew, Professional Staff Member,
25 Health; Daryll Dykes, Health Fellow; Paul Edattel, Chief Counsel,

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26 Health; Adam Fromm, Director of Outreach and Coalitions; Jay
27 Gulshen, Legislative Clerk, Health; Alex Miller, Video Production
28 Aide and Press Assistant; Jennifer Sherman, Press Secretary;
29 Danielle Steele, Policy Coordinator, Health; John Stone, Senior
30 Counsel, Health; Hamlin Wade, Special Advisor, External Affairs;
31 Jeff Carroll, Minority Staff Director; Samantha Satchell,
32 Minority Policy Analyst; Andrew Souvall, Minority Director of
33 Communications, Outreach and Member Services; Kimberlee
34 Trzeciak, Minority Senior Health Policy Advisor; and C.J. Young,
35 Minority Press Secretary.

36 Mr. Burgess. The Subcommittee on Health will now come to
37 order. I will recognize myself for 5 minutes for the purpose
38 of an opening statement.

39 From last year's 21st Century Cures Act to this year's Food
40 and Drug Administration reauthorization, this subcommittee has
41 been committed to bringing federal regulation into the modern
42 era of medicine. Today, we continue that work by examining
43 legislation to update the regulatory framework affecting the
44 dissemination of truthful and non-misleading information about
45 products approved by the Food and Drug Administration.

46 I practiced medicine for several decades. I know firsthand
47 how challenging it is it and how challenging it can be for
48 providers to stay up to the minute with cutting edge information
49 in both medicine and science. Following the Food and Drug
50 Administration's approval of a product, the use of that product
51 rapidly evolves based on patient and provider experience.
52 Frequently, the standard of care for a condition is outside of
53 the Food and Drug Administration approved labeling. Ensuring
54 that healthcare providers have access to new information
55 generated by real-world evidence is critical to optimizing
56 patient care and outcomes. Particularly in medicine, the old
57 adage holds true, knowledge is power.

58 Our legal framework for the regulation of manufacturer
59 communications sometimes prevents healthcare professionals from
60 receiving the most current scientific information available about

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61 the benefits and risks of FDA-approved medicines. A lack of
62 relevant information can lead to physicians making patient care
63 decisions with incomplete information. This is both unfair to
64 the physician and unsafe for the patient.

65 We owe it to the patient and medical communities to ensure
66 that there is free and full dissemination of truthful and
67 non-misleading scientific and medical information for healthcare
68 professionals.

69 I certainly want to thank two of our committee members, the
70 vice chairman of the committee, Brett Guthrie, and Representative
71 Morgan Griffith from Virginia for offering the bills that will
72 be under discussion today. I feel they offer a targeted
73 approach to addressing the problems presented by our regulatory
74 framework for medical product communication. And if he would
75 like time, I am prepared to yield to the gentleman from Kentucky,
76 if he would like time for an opening statement.

77 Mr. Guthrie. Thank you, Mr. Chairman. There is another
78 very important hearing on opioids going on downstairs and we have
79 our Kentucky Justice Secretary there.

80 Mr. Chairman, I want to thank you for holding this hearing
81 today to examine communications between manufacturers and
82 healthcare payers which I addressed in my bill, H.R. 2026, the
83 Pharmaceutical Information Exchange Act. My bill will enable
84 greater information exchange in order to guide health plans,
85 pharmacy benefit managers, and others who develop prescription

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86 drug formularies and medical devices to make well-informed
87 decisions about the benefits and costs of medications and medical
88 devices for the populations they cover.

89 Patients benefit when these formulary decisions are informed
90 by the most recent and reliable scientific evidence on drugs and
91 devices beyond just what we learn from the clinical trials
92 conducted by FDA approval. Our committee has addressed
93 post-approval information exchange. We should take the next
94 logical step by addressing what information can and should be
95 exchanged pre-approval by considering the updated discussion
96 draft we are examining today.

97 I would like to submit for the record a letter of support
98 for my bill into the record by a number of organizations including
99 the Academy of Managed Care Pharmacy, Humana, Sanofi, and Mayo
100 Clinic.

101 Mr. Burgess. Without objection, so ordered.

102 Mr. Guthrie. Thank you, Mr. Chairman. I yield back.

103 Mr. Burgess. The chair thanks the gentleman. The chair
104 would like to recognize the gentleman from Virginia, Mr. Griffith,
105 if would seek time for an opening statement.

106 Mr. Griffith. Thank you very much, Mr. Chairman, I do
107 appreciate it. Mr. Guthrie and I were both downstairs
108 introducing former colleagues from the House of Delegates, so
109 we apologize that we came rushing in, but we got that done.

110 The draft version of my bill that we are discussing today

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111 will responsibly set the rules of the road so that manufacturers
112 have the most accurate and up-to-date information about their
113 products that can provide doctors and researchers with that
114 information, and in the appropriate context, to improve patient
115 care and facilitate additional research.

116 Not only does the lack of clear rules have a public health
117 ramification, but also it has legal consequences. There have
118 been a number of court decisions that raise significant First
119 Amendment questions about the FDA's authority to restrict a drug
120 or device manufacturer from communicating truthful and
121 non-misleading off-label information about their products.

122 The Judiciary Branch should not be turned into de facto
123 policy makers because of FDA's misunderstanding of the law or
124 our inaction here in Congress.

125 I remain open to any and all suggestions from both sides
126 of the aisle and from stakeholders as to how this legislation
127 may be improved, but I am glad we are continuing the dialogue.

128 Also, I also forward to hear from witnesses today about how the
129 FDA's vague policies hinder the facilitation of information to
130 healthcare providers and how this legislation could be a first
131 step in addressing some of the challenges that we will hear about.

132 Thank you. I yield back.

133 Mr. Burgess. The gentleman yields back and the chair yield
134 back. The chair recognizes the ranking member of the
135 subcommittee, Mr. Green, 5 minutes for an opening statement,

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136 please.

137 Mr. Green. Thank you, Mr. Chairman. Today, we are
138 considering two draft bills addressing pharmaceutical
139 manufacturer communications on medical products. The Medical
140 Product Communications Act and the Pharmaceutical Information
141 Exchange Act suggest the changes of the rules surrounding the
142 communications from medical product manufacturers will likely
143 have far-reaching implications for decisions made by healthcare
144 providers about which therapies are appropriate for their
145 patients. It is critically important for us to fully consider
146 and appreciate the impact those proposed changes could have on
147 patient safety, health outcomes, and the promotion of value in
148 our healthcare system.

149 My concern with the two bills we are considering today is
150 that as drafted they would undermine public health, discourage
151 pharmaceutical research, and undermine the FDA's central capacity
152 to ensure medical products used on patients have demonstrated
153 safety and efficiency. Opening the floodgates for off-label
154 communication puts patients at risk, puts a dent in the armor
155 that ensures patients get effective therapies, and not snake oil.

156 Broadening off-label communications could erode FDA's
157 approval standard as it would enable the uses of products never
158 found to be safe or effective in patients and weaken consumer
159 confidence in the FDA approval process. FDA's approval standard
160 of safety and efficiency is considered to be the gold standard

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161 globally. As the FDA Commissioner Dr. Scott Gottlieb has said,
162 the most important incentive to developing useful information
163 remains the ability for companies to market drugs based on what
164 has been proven scientifically. There is an incentive currently
165 for companies to seek FDA's approval for all uses of a drug product
166 if they wish to market the product for those uses and gain coverage
167 for these uses.

168 Allowing manufacturers to communicate about unproven uses
169 of their products reduces the incentive to go through the FDA's
170 approval process as clinical trials are the most expensive part
171 of the development. Thus, it is not hard to imagine a scenario
172 where a company seeks the narrowest indication for their product,
173 gets on the market, and forgoes on continuing large, well
174 controlled, randomized clinical trials that would prove a product
175 is both safe and effective for broader populations or indications.

176 Patients and doctors should fully be empowered to make joint
177 decisions about their care. This includes the efficiency, risk,
178 and cost of their options.

179 Information is key, however, and the best decisions are based
180 on accurate, evidence-based information, not just for information
181 that may be incomplete, inconclusive, or at worst inaccurate.

182 The discussion draft of the Medical Product Communications Act
183 would not provide or ensure that patients and care providers have
184 access to better research and evidence. Rather, it would allow
185 drug manufacturers to communicate information about prescription

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186 drugs that have not been approved by the FDA. The lack of approval
187 may be due to contradictory evidence or the lack of any evidence
188 at all, or the need for additional research.

189 While I have concerns with both discussion drafts as written,
190 I do appreciate that our audience matters. The discussion draft
191 of the Pharmaceutical Information Exchange Act would expand the
192 ability of drug and device manufacturers to communicate
193 healthcare economic information, and scientific information to
194 payers, formularies, technology review committees, or other
195 entities about unapproved uses of products. These audiences are
196 sophisticated and have an inherent interest in being skeptical
197 of claims made outside a product's label. Therefore, it is less
198 problematic in its premise than the other bill we are considering.

199 While I am willing to work with my colleagues on the proposal,
200 it is critical that these communications promote patient safety,
201 public health, and the appropriate safeguards are in place to
202 avoid damaging unintended consequences. As we consider the issue
203 of off-label communication, we must always keep in mind that the
204 way to truly help patients get the most effective treatments is
205 to maintain the highest standards of safety and evidence and
206 appropriate risk of benefit balance.

207 Scientifically validated safety and efficiency and the
208 incentives for manufacturers to seek FDA approval are clear and
209 should be preserved. I look forward to hearing from our witnesses
210 and if anybody wants time, I will yield my 45 seconds back. Thank

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211 you, Mr. Chairman.

212 Mr. Burgess. The gentleman yields back. The chair thanks
213 the gentleman. The chair recognizes the gentleman from Oregon,
214 the chairman of the full committee, Mr. Walden, 5 minutes for
215 an opening statement, please.

216 Mr. Walden. I thank the subcommittee chairman, Chairman
217 Burgess. Thanks for this holding this hearing. It is a really
218 important topic and it is a topic that has been important for
219 our members for some time.

220 Approximately 40 percent, 40 percent of prescriptions in
221 the United States are for indications or uses not included in
222 the FDA approved product labeling. Although off-label uses of
223 drugs and devices are often the recognized standard for care for
224 treating many conditions, the lack of clarity in the statute and
225 implementing regulations has stifled important information about
226 such uses for being communicated in a responsible and
227 non-promotional manner by manufacturers.

228 The FDA has attempted to address this issue, but it has been
229 in a piecemeal fashion or the last 2 decades with various
230 non-binding guidance documents and policy statements that frankly
231 fall woefully short, particularly given the criminal penalties
232 in play.

233 As the Supreme Court affirmed in 2011 that First Amendment
234 commercial speech protections extend to medical product
235 manufacturers, every subsequent judicial decision, every

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236 decision, has raised significant questions about the extent of
237 FDA's authority to restrict truthful and non-misleading off-label
238 communications.

239 So where are we today? The regulators and the courts have
240 spoken. Everyone is left with a vast amount of uncertainty that
241 does nothing to protect or benefit patients. So it is time for
242 Congress to act. And as FDA's authorizing committee, it is our
243 job to clarify this statute and get it right which brings us to
244 this hearing. Neither of these bills are new to my fellow
245 committee members. We discussed an earlier version of both bills
246 during a markup in this subcommittee back in May and we reviewed
247 these updated versions of the full committee markup of the FDA
248 Reauthorization Act last month. Both bills were ultimately
249 withdrawn as amendments to FDARA with a commitment from our
250 colleagues on the other side of the aisle to work with us together
251 to iron out a compromise so we could move these important policies
252 forward and speak as the Congress and not leave this up to a
253 mishmash of court decisions. So I look forward to
254 continuing that work today.

255 I believe Morgan Griffith's bill, H.R. 1703, is a serious,
256 well thought out policy proposal that responsibly sets the rules
257 of the road in a constitutionally-sound manner. I greatly
258 appreciate his willingness to continue to address concerns. He
259 has heard about the legislative language.

260 I also appreciate Ranking Member Pallone's commitment at

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261 the user fee markup to work with us in good faith on this issue
262 through regular order which starts with this important hearing.

263 In addition. Representative Guthrie's amended version of
264 H.R. 2026 would clarify how drug and medical device companies
265 can share healthcare, economic, or scientific information related
266 to investigational uses of their products with payers and similar
267 entities. These bills do not provide manufacturers with free
268 reign to communicate any and all information about their products.

269 They establish targeted, statutory boundaries within which
270 manufacturers may responsibly disseminate accurate and
271 up-to-date information about medical products. These
272 clarifications will lead to a better informed healthcare system.

273 They will ensure that patients receive high-quality care based
274 on current sound, scientific, and clinical information.

275 Today, we continue the dialogue. I look forward to a
276 productive discussion and I appreciate the input of our witnesses
277 who are before us today and with that, unless there are other
278 members who would like to use the balance of my time, I will yield
279 back the balance of my time.

280 Mr. Burgess. The chair thanks the gentleman. The
281 gentleman yields back. The chair recognizes the gentleman from
282 New Jersey, the ranking member of the full committee, 5 minutes
283 for an opening statement, please.

284 Mr. Pallone. Thank you, Mr. Chairman. I want to thank you
285 for holding today's hearing. The issue before us today is an

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286 important one and I hope that our discussion today will help to
287 inform whether or not it would be appropriate for this committee
288 to take further action.

289 Today, under current law, medical product manufacturers are
290 required to demonstrate the safety and effectiveness of each
291 intended use of their medical product. This review process has
292 been critical to protecting and promoting public health by
293 ensuring that the benefits of medical products that are prescribed
294 to patients outweigh the risk. It also is common sense. Just
295 because a medical product approved for one use may be found to
296 be safe and effective for that use, doesn't necessarily mean that
297 it will be safe and effective for another use or for another
298 population.

299 Recognizing that physicians may prescribe treatments
300 off-label in response to individual patient needs, FDA allows
301 the communication of truthful and non-misleading scientific or
302 medical information regarding unapproved uses of medical products
303 that may assist physicians in making treatment decisions. In
304 those instances, FDA has allowed for manufacturers to respond
305 to requests from physicians about unapproved uses and provide
306 peer reviewed journal articles, scientific or medical texts, and
307 clinical practice guidelines.

308 Following 21st Century Cures, manufacturers are also now
309 able to share healthcare economic information with payers to help
310 them better understand the economic benefits of an approved

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311 treatment.

312 These are common-sense approaches that allow doctors to
313 address the individual needs of a patient, but also ensure that
314 patients are not unnecessarily exposed to unproven or harmful
315 medical products.

316 Now today, we are here to examine discussion drafts from
317 Representatives Griffith and Guthrie that would greatly expand
318 the types of scientific information that manufacturers could
319 share without any FDA oversight. While I understand that medical
320 product manufacturers have voiced concerns about their ability
321 to communicate with doctors about their products, I am concerned
322 that these drafts would severely undermine the current
323 protections against marketing unsafe and ineffective medical
324 products.

325 During this hearing, I hope to hear what materials
326 manufacturers want to share with healthcare professionals and
327 payers that they feel they can't under current law.

328 The scientific exchange discussion draft would severely
329 restrict the types of evidence the FDA has always relied on to
330 determine the intended use of a medical product. It would also
331 hamstring the Agency from holding bad actors who distribute
332 dangerous drugs or medical devices accountable.

333 The pre-approval communication discussion draft will blow
334 a hole in the current approval process by allowing the
335 communication of any scientific evidence or healthcare economic

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336 information to payers or formularies without any recourse to the
337 FDA to prevent bad actors from communicating false or misleading
338 information. Allowing manufacturers to communicate about
339 unapproved products and unapproved uses of their products reduces
340 the incentive of those through FDA's approval process and that
341 is grossly irresponsible in my opinion.

342 For example, the proposed discussion draft would allow for
343 a manufacturer to publish a biased, scientific study in any medium
344 to constitute scientific exchange. This could simply include
345 posting results of a non-peer reviewed study on a company's
346 website and there is no requirement that this information be
347 truthful.

348 I am also concerned that these two discussion drafts could
349 expose more patients to medical products that have never been
350 proven to be safe or effective. One study found that 81 percent
351 of medications prescribed for off-label purposes had poor or no
352 scientific support, while another found that patients who
353 received off-label prescriptions were 54 percent more likely to
354 experience an adverse event, as compared to on-label use. And
355 these are risks that we simply cannot ignore.

356 So Mr. Chairman, if there is a need for greater certainty
357 and clarity on the types of communications that manufacturers
358 are permitted to use under current law, I am willing to have that
359 discussion. However, broadening communication in the way it is
360 proposed under these discussion drafts would, in my opinion,

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361 undermine FDA's regulatory review process and the safety and
362 effectiveness approval standard.

363 I have about a minute. I don't know if anybody wants it.
364 If not, I yield back, Mr. Chairman.

365 Mr. Burgess. The gentleman yields back. The chair thanks
366 the gentleman. This concludes member opening statements and I
367 would like to remind members that pursuant to committee rules
368 all members' opening statements will be made part of the records.

369

370 And we want to thank our witnesses for being here with us
371 this morning, for taking time to testify before the subcommittee.

372 Each witness will have the opportunity to give a summary of their
373 opening statement, followed by questions from members.

374 This morning, we are going to hear from Coleen Klasmeier,
375 a partner of Sidley Austin, LLP; Alta Charo, the Warren Knowles
376 Professor of Law at the University of Wisconsin; Dr. George Van
377 Hare, the Division Chief, Pediatric Cardiology; Louis Larrick
378 Ward, Professor of Pediatrics at Washington University School
379 of Pediatrics; and Co-Director of the St. Louis Children's and
380 Washington University Heart Center; Aaron Kesselheim, Associate
381 Professor of Medicine, Harvard Medical School, Director of
382 Program on Regulation, Therapeutics and Law from the Division
383 of Pharmacoepidemiology and Pharmacoconomics at the Brigham and
384 Women's Hospital; Linda House, President of the Cancer Support
385 Community; and Katherine Wolf Khachatourian, Vice President,

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386 Delegation Oversight, Pharmacy Services of QualchoiceHealth Plan
387 Services.

388 We appreciate all of you being here today and Ms. Klasmeier,
389 you are recognized for 5 minutes for the purpose of an opening
390 statement. Thank you for being here.

391 STATEMENT OF COLEEN KLASMEIER, PARTNER; SIDLEY AUSTIN LLP; ALTA
392 CHARO, WARREN P. KNOWLES PROFESSOR OF LAW, UNIVERSITY OF
393 WISCONSIN; GEORGE VAN HARE, CO-DIRECTOR, ST. LOUIS CHILDREN'S
394 AND WASHINGTON UNIVERSITY HEART CENTER; AARON KESSELHEIM,
395 ASSOCIATE PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL, DIRECTOR
396 OF PROGRAM ON REGULATION, THERAPEUTICS AND LAW FROM THE DIVISION
397 OF PHARMACOEPIDEMOLOGY AND PHARMACOECONOMICS AT THE BRIGHAM AND
398 WOMEN'S HOPSITAL; LINDA HOUSE, PRESIDENT OF THE CANCER SUPPORT
399 COMMUNITY; AND KATHERINE WOLF KHACHATOURIAN, VICE PRESIDENT,
400 DELEGATION OVERSIGHT, PHARMACY SERVICES OF QUALCHOICEHEALTH PLAN
401 SERVICES

402

403 STATEMENT OF COLEEN KLASMEIER

404 Ms. Klasmeier. Thank you, Mr. Chairman. Chairman Burgess,
405 Vice Chairman Guthrie, Ranking Member Green, Chairman Walden,
406 members of the subcommittee, my name is Coleen Klasmeier. I am
407 a partner and the head of the FDA Regulatory Practice at Sidley
408 Austin in Washington, D.C. I am appearing today on behalf of the
409 Medical Information Working Group.

410 Today, I would like to make three points. First, FDA's rules
411 governing manufacturer communications are neither clear nor
412 precise. Decisions to prescribe and use lawfully-marketed drugs
413 and medical devices in ways that differ from the FDA authorized
414 labeling, so-called off-label use, are a constituent part of
415 medical and surgical practice and can also be the standard of

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416 care. FDA has long recognized the need for prescribers to receive
417 and for manufacturers to have some ability to provide information
418 outside of product labeling to help support clinical decision
419 making. As a result, although a manufacturer is prohibited from
420 promoting its product for new uses, it can lawfully provide
421 information about off-label uses within defined circumstances.

422 Currently, there are four safe harbors. Only one is set
423 forth in a binding regulation. The others are in non-binding
424 documents. They therefore lack the force of law. Moreover, two
425 of the four safe harbors have been the subject of on-going FDA
426 proceedings since 2011. Under these policies, a manufacturer
427 can provide off-label information ostensibly without fear of
428 enforcement in four scenarios involving scientific exchange,
429 responses to unsolicited requests, continuing education, and
430 reprints of journal articles, reference texts, and clinical
431 practice guidelines. Each safe harbor is subject to a number
432 of qualifying criteria and additional requirements which are
433 unclear in many key respects.

434 Moreover, FDA has been unable to complete its process of
435 revising the safe harbor policies, so questions frequently arise
436 regarding the relationship between the old policies and the new
437 policies.

438 In addition, there is a lack of symmetry between the safe
439 harbors that apply to drugs and those that apply to medical
440 devices. In short, the safe harbors are a mess. As a result,

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441 manufacturers cannot confidently rely on the safe harbors and
442 that has public health consequences. For example, it is common
443 for the Advisory Committee on Immunization Practices, a federal
444 statutory advisory committee to the CDC, to make recommendations
445 for vaccines that are arguably off-label. ACIP recommendations
446 might vary the dosing schedule or recommend use of a vaccine in
447 a new patient population. The vaccine manufacturer would
448 reasonably fear that communicating about the ACIP recommendation
449 to physicians or payers could be characterized by government as
450 unlawful, off-label promotion. Ultimately, the public health
451 would not be advanced because physicians would not receive
452 manufacturer communications reinforcing that recommendation.

453 The regulatory scheme also has legal consequences. The
454 First Amendment case law makes clear that FDA is limited in its
455 power to prohibit drug and device manufacturers from engaging
456 in accurate communications about their product. FDA's
457 regulatory scheme also implicates the due process laws of the
458 Fifth Amendment which requires government agencies to establish
459 rules that are clear and to give fair notice of what is prohibited,
460 particularly in the context of free expression.

461 Second, the existing FDA regulatory scheme for manufacturer
462 communication is highly unstable. The lack of clear rules to
463 allow manufacturers an appropriate measure of latitude to
464 communicate about their products is only a part of the problem.

465 FDA and the Justice Department impose aggressive restraints on

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466 manufacturers' speech. Although manufacturers have indeed
467 settled many cases involving off-label promotion allegations in
468 recent years, in some instances individuals and firms have raised
469 First Amendment arguments in court and those arguments have
470 succeeded. FDA's regulatory scheme continues to burden
471 constitutionally-protected speech and is therefore at risk from
472 additional lawsuits.

473 The Medical Information Working Group has for more than 10
474 years and across more than 20 submissions, requested targeted
475 clarifications to the existing FDA safe harbors and to key
476 statutory terms such as labeling and intended use. We have not
477 asked for and we do not want a healthcare system in which
478 manufacturers can market their product based on spurious or
479 unsubstantiated claims of safety or efficacy.

480 Third, legislation could dramatically improve the
481 regulatory scheme. Although the MIWG has been dedicated to
482 direct engagement with FDA on manufacturer communication issues
483 since 2006, we also recognize the paramount role of Congress and
484 we believe that legislation may be necessary for several reasons.

485 For one thing, FDA action has been slow and ineffectual.
486 It has been almost 6 years, for example, since FDA published
487 a notice in the Federal Register asking for comment on scientific
488 exchange and responses to unsolicited requests. Where FDA has
489 taken action, the policy has tacked in the wrong direction
490 becoming less clear and even more speech restrictive. For these

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491 reasons, it would be helpful for Congress to step in and set the
492 overall policy direction for FDA to implement.

493 Legislation is also more durable than unilateral FDA action.
494 Statutory law is not subject to the same variability as agency
495 pronouncements and cannot be undone in a future administration.
496 Legislation would be less susceptible to legal challenge than
497 a regulation or an FDA guidance document. Regulations have the
498 force of law, but the Administrative Procedure Act creates a
499 vehicle for challenge in court, whereas a statutory change could
500 only be challenge successfully in court on constitutional
501 grounds.

502 Legislation may also be necessary given the likelihood of
503 continued judicial involvement in this area. Although we value
504 the contributions that recent judicial decisions have made to
505 the body of relevant law, we also believe that litigation is not
506 the best way to make law on important public health issues where
507 there is little room for error. We are especially concerned that
508 some future lawsuit might eviscerate the FDA regulatory scheme.

509 We see great value in congressional engagement with FDA on
510 manufacturer communication issues to help assure the regulatory
511 scheme is put on to a more stable and sustainable footing. Thank
512 you very much for the opportunity to testify today and I look
513 forward to your questions.

514 [The prepared statement of Ms. Klasmeier follows:]

515

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*****INSERT 1*****

517

Mr. Burgess. I thank the gentlelady for her testimony.

518

Ms. Charo, you are recognized for 5 minutes, please.

519 STATEMENT OF ALTA CHARO

520

521 Ms. Charo. Chairman Burgess, Vice Chairman Guthrie,
522 Congressman Green, and members of the committee, thank you for
523 the opportunity to address you on issues surrounding
524 communication and marketing of off-label uses.

525 My name is Alta Charo. I am the Warren P. Knowles Professor
526 of Law at the University of Wisconsin. I am an elected member
527 of National Academy of Medicine, formerly known as the Institute
528 of Medicine, where I have served on a number of committees
529 including the one that produced a report on ensuring the safety
530 of the U.S. drug system. I also served as an advisor in the Office
531 of the Commissioner at FDA from 2009 to 2011, but I would like
532 to note for the record that I speak for myself only and not for
533 FDA and not for the National Academies.

534 There are two possible reasons to expand communication about
535 off-label uses. One is to ensure that the law is consistent with
536 the requirements of the First Amendment. The other is to protect
537 public health by increasing patient access to safe and effective
538 drugs. And I share those two goals. I don't, however, believe
539 that the two amendments under discussion are necessary to achieve
540 those goals. Indeed, I fear the unintended consequence of
541 adopting the language in these amendments would be to undermine
542 public health, to discourage pharmaceutical research, and to set
543 pharmaceutical regulation back by more than 100 years.

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544 As noted in an article I co-authored with Josh Sharfstein,
545 formerly the principal deputy at FDA, our drug regulation system
546 has prohibited false or misleading advertising since 1906. And
547 in 1962, broad marketing for secondary uses of thalidomide caused
548 thousands of severe birth defects worldwide, and Congress then
549 recognized that a product can be "safe and effective" for one
550 intended use where the benefits exceed the risks, but not "safe
551 and effective" for another which why approval of a drug for a
552 labeled indication does not mean it will be safe and effective
553 for off-label uses and precisely why additional studies are
554 needed.

555 This requirement to demonstrate safety and effectiveness
556 for an intended use applies both to the first approval of a new
557 compound or a new drug, as well as to any supplemental indication.

558 And while it is true there have been a handful of cases narrowing
559 constraints on commercial speech regarding unapproved
560 "off-label" uses, the courts have consistently upheld commercial
561 speech restriction with respect to the first approval of a new
562 product. If the First Amendment means that off-label promotion
563 must be permitted, then promotion of entirely untested,
564 never-approved drugs should also garner the same protection.

565 In both cases, the majority of drugs will fail to show that they
566 are safe and effective when the testing has been completed and
567 the substantial public interest in achieving that certainty is
568 the same regardless of whether it is an entirely new drug or a

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569 supplemental indication for an existing drug. If we were to
570 eliminate the restrictions on commercial speech for entirely
571 unapproved drugs, it would return us to the 1906 law where
572 prosecution for false and misleading marketing took place only
573 after people had been harmed.

574 Scientific journals and conferences are already allowed to
575 present information about off-label uses. Sponsors can answer
576 questions from physicians and provide reprints of peer-reviewed
577 articles, even if related to off-label uses. And in April 2017,
578 the FDA further clarified these rules and used guidances as a
579 more flexible mechanism to provide that information.

580 Legislation, regulation, and court decisions have not the kind
581 of flexibility that guidances have. We have entered an era in
582 which communication takes on many new forms ranging from tweets
583 to Facebook to any number of internet sources and it is important
584 to maintain flexibility in how we regard communication and its
585 influence and its intended purpose, rather than solidifying it
586 in legislation which can be difficult to change over time.

587 Now the proposed amendment of Section 201 muddies the
588 exceptions that FDA has outlined and I fear it risks eviscerating
589 the general rule against off-label promotion even if that is not
590 its intent. It also has the effect of immunizing sponsors from
591 responsibility even if they know and take advantage of the now
592 blurry line between legitimate scientific exchange and illegal
593 marketing.

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594 The proposed amendment of Section 502, I fear, will
595 exacerbate this problem, by allowing premature information to
596 be delivered to formularies and payers with the probable effect
597 of increasing patient use of unproven and unsafe therapies. And
598 as has been noted already by members here on the committee, studies
599 have repeatedly shown that even products that look promising in
600 early trials will usually be shown to be unsafe or ineffective
601 when larger trials are completed. And indeed, overall only about
602 one in five compounds, only one in five, will successfully move
603 from Phase 2 to Phase 3 trial, with lack of efficacy as the most
604 common reason for failure.

605 In a series of articles recently produced by Professor
606 Christopher Robinson at the University of Arizona, we can also
607 see that multiple studies show that the majority of off-label
608 uses also will turn out to be either unsafe or ineffective.
609 Encouraging coverage before approval is to encourage expanded
610 use before approval of treatments that we now know empirically
611 are likely to fail. And I fear that the effect would be to
612 increase use that will harm more patients than it helps.

613 History amply demonstrates there is a compelling public
614 interest in unbiased evaluation of evidence; in clear, accurate
615 communication; in maintaining incentives for research. The
616 combined effect of these amendments is to expand promotion and
617 payment for unproven uses of drugs. It undercuts the marketing
618 advantages that the law now uses as an incentive for sponsors

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619 to complete the research needed to see which uses are, in fact,
620 safe and effective. And in turn, it leaves physicians, patients,
621 formularies, and payers without independently verified
622 information. For complex products like drugs, the marketplace
623 of ideas cannot work properly with unvetted information from
624 necessarily self-interested sources. And when using the wrong
625 drug can injure patients or cause them to miss out on effective
626 treatment, it is an invitation to another tragedy when we prevent
627 FDA from doing its job to protect the public.

628 Thank you very much.

629 [The prepared statement of Ms. Charo follows:]

630

631 *****INSERT 2*****

632 Mr. Burgess. The chair thanks the gentlelady.

633 The chair recognizes Dr. Van Hare 5 minutes for your opening

634 statement, please.

635 STATEMENT OF GEORGE VAN HARE

636

637 Dr. Van Hare. Good morning, Chairman Burgess, Ranking
638 Member Green, and members of the subcommittee. Thank you for
639 holding this hearing and for inviting me to testify on this
640 important topic. My name is George Van Hare. I am Chief of
641 Pediatric Cardiology at St. Louis Children's Hospital in St.
642 Louis, Missouri. My clinical practice is focused on caring for
643 children with heart rhythm disorders. This year I have the honor
644 of serving as the president of the Heart Rhythm Society. The
645 Heart Rhythm Society is the international leader in science,
646 education, and advocacy for cardiac arrhythmia professionals.

647 Its members include

648 6,100 physicians, scientists, nurses, and other allied health
649 professionals in more than 90 countries.

650 Sharing comprehensive, scientifically valid data is
651 critical to the practice of medicine generally, and it is even
652 more critical for particular specialties. It is sometimes
653 claimed that the use of drugs or devices off-label is the result
654 of a choice by physicians. Sometimes this is
655 true. However, for pediatric sub-specialists, this is usually
656 not the case. This is due to the fact that very few of the
657 medications for arrhythmias that are on the market are formally
658 approved for use in children. Thus, using treatments off-label
659 is often our main method of

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660 treatment of children. Similarly, catheters that we use for
661 catheter ablation procedures are labeled for a limited number
662 of specific arrhythmias, but are used for treating and curing
663 all types of arrhythmias in adults and children.

664 By way of example, I would like to cite the specific drug,
665 amiodarone, brand name Cordarone. This is one of our most
666 important medications for the treatment of potentially
667 life-threatening arrhythmias, particularly in patients who have
668 undergone successful surgical repair of complex
669 congenital heart defects. The FDA-approved label simply states
670 "The safety and efficacy of Cordarone Tablets in
671 pediatric patients have not been established." This means that
672 the manufacturer is not allowed to share prospectively any data
673 that they may have concerning experience with this drug in
674 children.

675 Another example, not specific to children, is a labeling
676 of ablation catheters. These devices are used in performing
677 catheterization procedures to cure arrhythmias. In the last 25
678 years, these procedures have essentially replaced open heart
679 surgery as the best option for a curative procedure. Their
680 labeling is limited to only certain arrhythmias. For example,
681 the Cryocath, a cryoablation catheter manufactured by Medtronic,
682 is only labeled for treating one common arrhythmia, AVNRT, despite
683 the fact that it is ideal for treating other, more dangerous
684 arrhythmias. It would be absurd to use a different catheter for

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685 these other arrhythmias on the basis of the labeling, and even
686 more absurd if you consider open heart surgery. However, because
687 of the labeling, technical support representatives of the
688 manufacturer are not allowed to discuss other indications
689 directions and prospectively, despite the fact that the use of
690 this catheter for these other indication sis widely agreed to
691 be the standard of care.

692 There is an important way in which information sharing among
693 physicians may also be adversely affected. When a medical
694 conference is directly sponsored by a manufacturer, these
695 conferences do not qualify as official continuing medical
696 education events. Consequently, physician speakers are
697 considered to be "agents" of the manufacturer sponsoring the
698 event, and they are also limited to discussing only the labeled
699 indications. Any discussion between physicians regarding
700 experiences with drugs or devices that are off-label at such
701 events must occur informally, rather than as part of the program,
702 and thus these discussions do not benefit from the great potential
703 for information sharing among physician attendees.

704 The good news is that it doesn't have to be this way. It
705 is likely that there is a large amount of data maintained by
706 manufacturers, which under the current rules they are not allowed
707 to proactively share with clinicians. I urge the committee to
708 explore ways to define acceptable types of real-world evidence
709 that manufacturers might proactively share with medical decision

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710 makers. These types of data might include observational studies,
711 pharmacokinetic studies, and information on particular
712 sub-populations. The data must be truthful, presented in
713 context, and scientifically valid.

714 There is some concern that manufacturers might overwhelm
715 physicians with data taken out of context or data that are
716 misleading and skewed to present a more favorable picture than
717 is realistic. However, physicians are trained to analyze data.

718 We know how to evaluate the validity of studies. If regulatory
719 restrictions provide guard rails to ensure that data are truthful
720 and presented in context, physicians are fully capable of
721 analyzing such data effectively.

722 In my opinion, a reasonable regulatory paradigm lies
723 somewhere between no communication and completely unrestricted
724 communication. The current structure is not optimal for
725 fostering the advancement of medical knowledge, and it leaves
726 many patients and their physicians at an unnecessary
727 disadvantage. Additionally, it seems incongruous to me that the
728 manufacturer, the entity with the most robust data related to
729 a product, cannot share information they hold proactively while
730 any lay person with an internet connection can freely disseminate
731 whatever information they like about that same product however
732 biased and unreliable.

733 In closing, I hope that my testimony has provided the
734 committee with a real-world perspective on how the current rules

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735 often prevent physicians from receiving valuable, clinical
736 information in a timely fashion. I respectfully suggest that
737 Congress should establish ways to unlock
738 data maintained by manufacturers related to off-label use of drugs
739 and devices. I thank the committee for its time. The Heart
740 Rhythm Society would welcome the opportunity to work with you
741 on policy proposals related to this topic. Thank you.

742 [The prepared statement of Dr. Van Hare follows:]

743

744 *****INSERT 3*****

745 Mr. Burgess. The chair thanks the gentleman for his
746 testimony.

747 Dr. Kesselheim, you are recognized for 5 minutes for your
748 statement, please.

749 STATEMENT OF AARON KESSELHEIM

750

751 Dr. Kesselheim. Good morning, Chairman Burgess, Ranking
752 Member Green, and other members of the committee, thank you for
753 the opportunity to join you today. In my time I want to make
754 four main points.

755 First, the current restrictions on manufacturers' ability
756 to market their drugs for non-FDA approved indications is not
757 a bureaucratic or paternalistic effort to prevent manufacturers
758 from communicating. These rules were developed in response to
759 major public health problems caused by the lack of such
760 regulation. Evidence of the public health dangers that arise
761 from widespread off-label marketing can be seen in the drug
762 paroxetine or Paxil, an antidepressant that was promoted
763 off-label for use in children leading to at its peak over two
764 million prescriptions per year for use in children until it was
765 ultimately linked to self-injury and suicide in that population.

766 Or, the off-label promotion of anti-psychotic medications to
767 control behavioral symptoms in elderly patients with dementia,
768 uses that are not only generally ineffective, but that also
769 increase the risk of death by 60 to 70 percent. At one
770 point, due to off-label promotion approximately one in seven
771 elderly nursing home residents reportedly received these drugs.

772 Over and over again, these episodes show us, as former Chief
773 Justice William Rehnquist originally put it that "there are

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774 sufficient dangers attending [the] widespread use [of
775 pharmaceuticals] that they simply may not be promoted in the same
776 manner as hair creams, deodorants, and toothpaste."

777 Second, the dangers from off-label promotion do not come
778 simply from the spread of false information about these products,
779 although that does happen on occasion of course. Rather, in one
780 study that I led, we found that off-label promotion most commonly
781 involved presenting reports of individual cases or
782 poorly-designed studies as definitive evidence supporting an
783 off-label use, while de-emphasizing data that didn't fit the
784 narrative the manufacturers were creating. In each of these
785 particular cases, the words themselves may not have been false
786 or strictly misleading, but the benefits of the drug overstated
787 and the risks down played in ways that the physicians might have
788 needed advanced training in epidemiology or access to the
789 underlying clinical trial data to understand which they simply
790 do not have. This is why we need the diligent, independent
791 assessment of safety and efficacy provided by the FDA. The
792 complexity of the assessment that is required, along with the
793 high stakes of getting that assessment wrong provides the
794 rationale for having a formal drug approval process in the first
795 place.

796 Third, the Griffith and Guthrie discussion drafts directly
797 risk these outcomes. The Guthrie discussion draft, for example,
798 defines scientific information that could support an off-label

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799 marketing claim as including pre-clinical data in petri dishes
800 or in mice, and all it requires is a study that was conducted
801 that the manufacturer anticipates could be sufficient to support
802 FDA approval.

803 The Griffith draft, in creating a so-called safe harbor for
804 scientific exchange, purports to require manufacturers to
805 disclose appropriate contextual information for their
806 statements, but it would be highly risky to give a manufacturer
807 with a strong financial and intellectual stake in the product's
808 success free reign to determine what is or isn't proper context
809 or what is or isn't contradictory for its product. At the same
810 time, it is unrealistic to expect each individual physician to
811 have the time and expertise to subject such claims to the same
812 kind of scrutiny that the FDA would exercise when it reviews a
813 drug application or a request for a new indication.

814 The drafts also purport to protect the public health by
815 attaching disclaimers to these off-label communications, but I
816 led a systematic review of the evidence about the impact of such
817 disclaimers, most of which currently come in the context of
818 promotional statements for herbal remedies and dietary
819 supplements for which Congress eliminated FDA oversight of
820 promotion more than 20 years ago. Many of these products
821 advertise health-enhancing effects despite no legitimate
822 evidence that they work with disclaimers that the FDA has not
823 evaluated the promotional claims, but the massive collective

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824 evidence reveals that such disclaimers fail to adequately inform
825 or modify consumer behavior. So when anybody proposes a
826 disclaimer, I suggest that there be a disclaimer, that disclaimers
827 don't actually work.

828 Finally, I want to emphasize that the current system helps
829 protect patients from widespread promotion of drugs and devices
830 for potentially unsafe and ineffective off-label uses, while
831 still permitting off-label prescribing at the discretion of
832 physician and patients and providing well- circumscribed avenues
833 for manufacturer communication about these issues such as in
834 response to bona fide questions arising from physicians. By
835 contrast, the Griffith and Guthrie discussion drafts would reduce
836 manufacturers' incentives to conduct well-controlled trials of
837 potential off-label uses in the first place. Instead, as
838 Representative Green mentioned, manufacturers would be
839 incentivized to seek approval of drugs and devices for the
840 narrowest indication possible, and then conduct "studies" of
841 variable quality showing the utility of these products for
842 unapproved indications that would not meet current FDA standards
843 for scientific rigor.

844 I strongly recommend that the committee not pursue these
845 drafts and instead consider how we can give the FDA the proper
846 resources and authorities to continue to review emerging data
847 efficiently so that evidence that does support new uses of drugs
848 and devices can be incorporated into their labels and clinical

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849 practice while uses that the totality of the data show are unsafe
850 can be identified for the benefits of patients. Thank you very
851 much.

852 [The prepared statement of Dr. Kesselheim follows:]

853

854 *****INSERT 4*****

855 Mr. Burgess. The chair thanks the gentleman.

856 Ms. House, you are recognized for 5 minutes for an opening
857 statement, please.

858 STATEMENT OF LINDA HOUSE

859

860 Ms. House. Good morning. My name is Linda House and I am
861 the president of the Cancer Support Community. I would like to
862 thank the committee for allowing us to be here and share this
863 testimony today.

864 The Cancer Support Community is an international nonprofit
865 organization whose mission is to ensure that all people impacted
866 by cancer are empowered by knowledge, strengthened by action,
867 and sustained by community. Our organization sees over 100,000
868 patients and families each year through a network of affiliates
869 around the world. We also have a Cancer Support Helpline where
870 we administer through both of those properties, over \$50 million
871 of evidenced-based care and support each year free of charge to
872 patients and their families. Importantly, CSC is also home to
873 the only Research and Training Institute of its kind whose mission
874 is to collect and analyze information from patients to elevate
875 the voice of the patient and the caregiver as it relates to their
876 cancer experience.

877 I am here today to bring you what I feel is the most important
878 voice to this conversation and that is the voice of the patient.

879 The last 20 years have delivered unprecedented growth in
880 innovation across all aspects of health care. Never before has
881 a patient had so many options for diagnosis, treatment, and
882 follow-up care as they do now. Patients are more educated. They

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883 are more engaged. They are more empowered consumers of health
884 care than ever before. Yet, despite the emergence of patients
885 as important players, and even leaders of their care teams,
886 accessibility to comprehensive information continues to be
887 elusive.

888 We will be releasing data next week from our Cancer
889 Experience Registry where we have learned that 50 percent of
890 patients engage in shared treatment decision making with their
891 healthcare professionals. Only about eight percent report
892 allowing healthcare professionals to make decisions without their
893 input. Yet, only 25 percent indicate that they feel like they
894 are prepared to have those treatment decisions.

895 Importantly, our data reflects a growing concern about
896 inadequate collection, reporting, and label updating of endpoints
897 that are meaningful to patients. In our research, 93 percent
898 of respondents considered quality of life as very important when
899 making treatment decisions. Quality of life measured higher than
900 length of life, and these are people with cancer, yet product
901 labels continue to focus very little on fully measuring
902 comprehensive quality of life metrics. Further, product labels
903 almost never reflect updates when there are findings beyond the
904 clinical trial setting including findings about long-term effects
905 which would be meaningful for patients. A system that does not
906 proactively collect, publish, and share data poses a significant
907 risk to patient care.

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908 There are a few issues I would like to raise as current
909 limitations and we do support the work that the FDA does and we
910 do support the work of the clinical trial systems and we do support
911 accurate, meaningful, non-promotional communication.

912 Pre-approval information, as you know, is when clinical data
913 is available on a product prior to the product having an FDA label.

914 According to PhRMA, it takes an average of 10 to 15 years for
915 a drug to make it to market. And during that time, much is learned
916 about the way in which the drug works in the body, how the body
917 works with the drug, what is the accurate dose, what is the toxic
918 dose, and what are the side effects associated with that drug.

919 Yet, this treasure trove of information remains out of reach
920 from individuals other than the sponsor or potential trial
921 investigators.

922 Number two, limiting communication of information to only
923 that which is reflected in the label poses a significant challenge
924 to patients. CSC appreciates the work of the FDA and sponsors
925 of phase IV studies, in particular, but recognizes that these
926 studies do not capture comprehensive data for the use of the
927 product as was mentioned in the real world. Also, it is a rare
928 occurrence for the label to be updated in a manner that would
929 allow for proactive communications of findings outside of the
930 controlled clinical trial setting. And as we know, once trials
931 go into broader, less controlled situations, they perform
932 differently in those patients.

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933 Number three, data accumulated through Investigator
934 Initiated Trials on diseases that would never reach the investment
935 potential for registration in a label is extremely important to
936 clinical care. This information may never be communicated to
937 clinicians and will almost certainly not be made available to
938 patients who may benefit from the findings and this is
939 particularly important in patients with rare disease.

940 Number four, information learned outside of the clinical
941 trial setting and not captured in the label can also have a true
942 impact on the patient experience. And as I submitted in my
943 written testimony, this could be things like burning at the
944 injection site, a reduction in fatigue by understanding how to
945 better supplement the treatment. That information is not in the
946 label and cannot be shared in a proactive way.

947 Number five, there are several elements in general clinical
948 practice that are continuing to contribute to the limitation that
949 patients have to access comprehensive medical information through
950 their healthcare team. And in particular, as there is an active
951 evolution of the care delivery systems from volume to value, it
952 has brought with it efficiency and cost containment strategies
953 that focus on limiting treatment decisions. And I am talking
954 about hospital-based formularies and clinical pathways that are
955 currently being used in physician practices.

956 Number six, there is an inconsistent practice and
957 reinforcement of publishing clinical trial data results in

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958 scientific journals and other databases. This information has
959 to be published and as mentioned in my written comments, the ratio
960 of trials that have been opened, closed, and published, the
961 compliance rate with that abysmal and there must not only be
962 requirements, but also enforcement of the requirements to ensure
963 that all results of trials be posted whether those results are
964 positive or negative.

965 Finally, industry interpretation of the current regulations
966 is applied inconsistently across companies. This impacts the
967 way in which industry communicates with all stakeholders and most
968 certainly the way in which industry communicates with patients
969 and families forcing them only through the direct-to-consumer
970 marketing channel.

971 So in conclusion, while the comments that I have made have
972 simply scratched the surface on what is a much broader and deeper
973 issue, it is my hope that I have highlighted in your mind the
974 perspective of patients who are living with chronic and
975 life-threatening illness across the United States.

976 And to summarize in specific areas where we would like to
977 continue to work with the committee and the FDA, patients and
978 healthcare providers must have access to medical research
979 findings in a comprehensive and real-time manner. Product labels
980 should be updated in a timely manner and include data from
981 endpoints that matter most to patients and/or there must be
982 another mechanism by which to capture and proactively communicate

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983 findings that are clinically meaningful and relevant.
984 Scientifically sound communications about safe and effective uses
985 of a product are essential and should be made available to all
986 stakeholders. Clinical trial results, positive and negative,
987 should be published by the trial sponsor in a period of time that
988 is reasonable to allow full and meaningful data review while
989 ensuring timely access to information. Data, positive and
990 negative, collected outside of the clinical trial process,
991 inclusive of real-world evidence that is collected and analyzed
992 with appropriate scientific rigor should be published and made
993 available to stakeholders. And finally, proactive medical
994 communication should be tailored to meet the needs and literacy
995 levels of specific stakeholders and should not, for any
996 stakeholder, be limited only to the product label which may not
997 yet exist or be outdated.

998 Thank you for allowing us to be here.

999 [The prepared statement of Ms. House follows:]

1000

1001 *****INSERT 5*****

1002

Mr. Burgess. Thank you. Thank you for your testimony.

1003

Ms. Khachatourian, you are recognized for 5 minutes, please.

1004 STATEMENT OF KATHERINE WOLF KHACHATOURIAN

1005

1006 Ms. Khachatourian. Thank you to Chairman Burgess, Ranking
1007 Member Green, and members of the Subcommittee on Health for
1008 providing me the opportunity to speak before you today.

1009 I am Katherine Khachatourian, a pharmacist working in
1010 Medicare health insurance and a member of the AMCP Professional
1011 Practice Committee.

1012 Imagine a world where you are required by federal and state
1013 laws to determine a budget and coverage criteria for all drugs
1014 8 to 12 months in advance of the coverage year using limited
1015 available information while knowing there is information that
1016 could help you make more accurate and informed decisions. You
1017 just don't have the key to unlock the consistent release of that
1018 information. This is the world we live in as payers and
1019 population health decision makers.

1020 The limitations on information we are able to obtain results
1021 in a hindrance to patient access to novel and emerging therapies,
1022 limits our ability to accurately forecast, plan, and budget for
1023 anticipated expenditures, and it precludes our ability to
1024 contract on value rather than volume. This is the reason I am
1025 here before you today, to demonstrate the need for a legislative
1026 framework in support of House Bill 2026 which will provide the
1027 key to unlock additional information needed for us to make
1028 informed benefit decisions for better patient access to

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1029 treatment. These concepts have been discussed in depth with a
1030 diverse group of stakeholders including payers, manufacturers,
1031 clinicians, and patient advocacy groups who provide consensus
1032 recommendations for how, who, and what information should be
1033 exchanged prior to FDA approval. This information should be
1034 limited to a narrow audience inclusive of payers and population
1035 health decision makers. This scope does not include manufacturer
1036 communications with patients or prescribers prior to FDA
1037 approval.

1038 Let me share a few personal examples where lack of
1039 information has decreased patients' timely access to treatment.

1040 In December of 2013 and October of 2014, the FDA approved
1041 breakthrough treatments for the treatment of hepatitis C. These
1042 drugs had novel mechanisms of action which changed the landscape
1043 for patients with this diagnosis. Note, these approval dates
1044 were several months after we had already -- one of the payers
1045 had already analyzed costs and planned benefit. Had we been able
1046 to discuss in advance of the approval of these treatments, we
1047 would have had a better understanding of the landscape, timing
1048 of approval of multiple products, the relevant patients for each
1049 treatment, and any clinical information that would help us to
1050 make better decisions and ultimately been able to treat more
1051 patients in a more effective manner without the subsequent
1052 criteria revisions that proceeded after the approval of these
1053 products.

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1054 More importantly, the lack of needed information can impede
1055 patient access as seen in the new treatments for Duchenne's
1056 Muscular Dystrophy. In this instance, the level of evidence
1057 required to deem products safe and effective met the requirements
1058 for FDA approval. However, due to the inability of payers and
1059 manufacturers to openly discuss the level of evidence required
1060 for coverage, payers are not covering these therapies at this
1061 time. This is why the bi-directional information exchange is
1062 important to understand the level of evidence available and
1063 necessary for coverage. This example has left patients in a
1064 situation where they cannot access therapy. Had payers been able
1065 to convey the level of evidence required for coverage, could we
1066 have avoided this situation? Perhaps.

1067 Another patient access issue was one I experienced in the
1068 past year for a request for oncology. On September 21, 2016,
1069 we received a coverage request for a treatment of a patient
1070 diagnosed with inoperable lip cancer that had recently spread
1071 to their tongue. The FDA granted accelerated approval to expand
1072 the indications of an existing chemotherapy treatment on August
1073 5, 2016 to include head and neck cancer. However, when we
1074 received the request for coverage, the labeled indications and
1075 data supporting the expanded indication were not publicly
1076 available. In this situation, had I had the ability to discuss
1077 the data in advance with the manufacturer, I could have been better
1078 prepared to discuss the requested treatment with the provider,

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1079 rather than scrambling through clinicaltrials.gov and requesting
1080 a copy of the clinical trial from the manufacturer while the
1081 insured patient awaited my coverage decision.

1082 Because we can only estimate when therapies will be approved,
1083 if we receive a coverage request shortly after FDA approval, the
1084 landscape still remains one of chaos and special requests to
1085 manufacturers until the data is published, compendia and
1086 guidelines are updated, and coverage criteria reflect these new
1087 and novel treatments.

1088 I have demonstrated in the previous examples each of these
1089 breakthrough therapies represent innovations and the potential
1090 to change a patient's life, if they are able to gain access to
1091 treatment. The barrier to access to novel therapies is a
1092 population health decision maker's ability to have sufficient
1093 data and sophisticated discussions with those most informed about
1094 the utility of the products in a timely enough fashion to budget,
1095 plan and forecast it for the therapies coming to market.

1096 In conclusion, this is an issue of great importance for
1097 patient access to emerging therapies where a diverse group of
1098 stakeholders have come together to develop consensus
1099 recommendations. This includes a very narrow audience and scope
1100 of exchange between manufacturers and payers only. We need your
1101 legislative support to better care for our patients. Thank you.

1102 [The prepared statement of Ms. Khachatourian follows:]

1103

1104

*****INSERT 6*****

1105 Mr. Burgess. I thank you for your testimony. I want to
1106 thank all of our witnesses. It has certainly been compelling
1107 testimony this morning. People will note that I allowed the clock
1108 to run over because you had important information to provide us.

1109 I guess we will underscore that I will not be so generous with
1110 members, so try to confine your time to the 5 minutes allotted
1111 to these products that have not been evaluated by the FDA. This
1112 product is not intended to diagnose or prevent any condition,
1113 just to get through the appropriate label disclaimer.

1114 Let me begin the questioning and I will recognize myself
1115 for 5 minutes. And Ms. House and Ms. Khachatourian, thank you
1116 so much for your testimony.

1117 Ms. House, while you were talking and I actually wrote down
1118 a note to myself about when you mentioned about clinical trials
1119 and I was going to ask you about the utility of getting the
1120 information off of clinicaltrials.gov and then Ms. Khachatourian
1121 actually referenced that as well. So this is a real-world
1122 phenomenon where payer decisions are unable to be made, but the
1123 data is sort of accumulating on the data side of the docket, but
1124 it is not coming up to the payer's side. So it sounds like both
1125 of you have dealt with that.

1126 And Ms. Khachatourian I thank you for bringing up the issue
1127 with the new hepatitis C drugs, because we were sitting on these
1128 panels in 2012 and 2013. And I would suggest it is not just an
1129 issue of commercial payers. Our state Medicaid directors, our

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1130 state prison directors, our federal prison directors were going
1131 to have to deal with this information in very short order and
1132 they did not have it available to them.

1133 And I would be happy to listen to what both of you have to
1134 say, particularly on the clinicaltrials.gov. Are we doing a good
1135 enough job getting that information out there in a usable way
1136 so that you can actually begin the process of what are we going
1137 to have to do as far as on the payer's side?

1138 Ms. House, we will start with you, and then I would like
1139 to hear Ms. Khachatourian's thoughts on that.

1140 Ms. House. Thank you, but I didn't share my comments that
1141 I have in my written testimony. I included two studies that were
1142 done on the clinicaltrials.gov database where there was a random
1143 sampling of 600 trials originally. And 50 percent of those trials
1144 did not have a corresponding article. The second study was even
1145 more alarming in that there was a look at 13,327 trials and 1
1146 year post-data closure, only 13 percent of those has posted
1147 clinical trials information. And even when they gave a bit of
1148 a grace period and extended that for another couple of years,
1149 only 38 percent had clinical trials posted there. So not only
1150 is the system extremely difficult to sort of use and find and
1151 especially as we are moving into the age of personalized medicine
1152 to get to trials that are relevant for me, the data results aren't
1153 there.

1154 And I will give you an example that happened to me just last

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1155 week is that a patient of ours reached out and he has a certain
1156 type of lung cancer, ALK positive lung, in which there are a number
1157 of solutions and options available for him. His physician wanted
1158 to put him on a phase 2 trial with a new product and he said what
1159 do you think about this? And so I went on line to try to find
1160 information because I was trying to decide why would they put
1161 him on a phase 2 trial instead of the phase 3 trial and I am an
1162 educated consumer and I have worked in clinical trials for a long
1163 time. After about an hour and a half I could find two sources
1164 on line to your point. One of them was with a reputable medical
1165 society and the other was an opinion piece on the way in which
1166 this product worked.

1167 They are in a phase 3 setting already, so there is a lot
1168 of evidence on this particular drug and not available to even
1169 educated consumers.

1170 Mr. Burgess. Okay. Ms. Khachatourian.

1171 Ms. Khachatourian. Thank you, Mr. Burgess. I actually
1172 pulled some dates more relevant to some recently approved
1173 therapies. In the hepatitis space the products, Zepatier and
1174 Eplclusa, were approved January 28, 2016 and June 28, 2016 per
1175 the FDA website. However, results on clinicaltrials.gov were
1176 not published until September 27, 2016 and April 26, 2017
1177 respectively. So just to give perspective regarding when data
1178 is available and results are published, those are key dates that
1179 I was able to glean. I have some oncology examples as well, but

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1180 I think that proves the point regarding the delay in access to
1181 information that is necessary for coverage decisions.

1182 Mr. Burgess. Dr. Van Hare, you referenced the rich data
1183 sets that would be available by a drug or device manufacturer,
1184 but that data is sort of locked away from the clinician. I guess
1185 you have to go the bar to have those discussions? You can't have
1186 those discussions in the hearing room or the continuing education
1187 room? You have to go offsite?

1188 Dr. Van Hare. On the stairwell.

1189 Mr. Burgess. On the stairwell, okay. Very well. And you
1190 see what we are talking about today as a way of unlocking those
1191 data sets being available to the clinicians?

1192 Dr. Van Hare. I think so. I think it is really pretty
1193 simple for allowing off-label use. A physician who prescribes
1194 something off-label is responsible for ensuring that they have
1195 evaluated the most appropriate clinical data before they make
1196 a decision about prescribing something off-label and some of that
1197 data is actually held by the manufacturers.

1198 They are allowed, as I understand it, to provide it to us
1199 privately and in response to an unsolicited request, but you know,
1200 there is 300 of me in the country, the pediatric cardiologists
1201 who do what I do in the country. Every single one of us has to
1202 independently call up the drug company to get the information.
1203 It is not particularly efficient.

1204 Mr. Burgess. No. I think my time is expired. I want to

1205 be respectful of everyone's time.

1206 Mr. Green, you are recognized for 5 minutes for questions,
1207 please.

1208 Mr. Green. Thank you, Mr. Chairman. Long ago, Congress
1209 recognized the importance of requiring manufacturers to provide
1210 evidence demonstrating the safety and efficiency of the product.

1211 In marketing under current law, drug and medical device
1212 manufacturers can disseminate certain medical and scientific
1213 information about unapproved uses of approved or cleared products
1214 to health care professionals and other entities. Recent
1215 court cases cited as a source of uncertainty around the types
1216 of communication about these unapproved uses are permissible.

1217 Ms. Charo, in your written testimony, you said if the First
1218 Amendment means that the off-label promotion must be permitted,
1219 then the promotion of entirely untested, unproved drugs should
1220 also garner the same protection. Is that true?

1221 Ms. Charo. I fear that the logic would be the same in both
1222 cases. Now it is true that for things that have been approved
1223 at least once, one does have some, at least, early information
1224 that the drug is not highly toxic because that is what we are
1225 going to get from the early Phase 1 or 2 trials. But the reality
1226 is over time, both the drugs that have never been approved before
1227 or the off-label indications for things that have been approved
1228 turn out to fail which means that one begins with a presumption
1229 that any unapproved use or any unapproved drug is probably not

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1230 safe or not effective until it is proven to be so.

1231 Mr. Green. Well, this is an issue that this subcommittee
1232 and our committee has wrestled with for a number of years. Can
1233 you help us understand what restrictions the Constitution does
1234 and does not allow? Does the First Amendment prohibit the FDA
1235 from restricting promotion of unapproved uses?

1236 Ms. Charo. No, there are a number of federal cases that
1237 have upheld the FDA's authority to do just that. There is
1238 constitutional protection for commercial speech and there are
1239 standards for that protection and in the area of commercial speech
1240 it is a fair amount of protection although not the same degree
1241 of protection as you would get for political speech or other forms
1242 of speech. And those restrictions on commercial speech are
1243 permitted when there is a substantial public interest in doing
1244 so. In this case, by restricting off-label promotion, one is
1245 able to create both a stick and a carrot that drives the
1246 pharmaceutical industry toward the research needed to actually
1247 figure out which things are safe and which things are effective.

1248 If one is able to simply promote without restriction and gets
1249 no market advantage by going in and investing in the research,
1250 one loses that system entirely and we really do risk having an
1251 absence of information for people like Dr. Van Hare to solicit
1252 or to develop on his own, let alone to share with his colleagues.

1253 Mr. Green. Ms. House, I note in your focus on your testimony
1254 the fact that so much clinical trial data is unpublished. One

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1255 thing that concerns me is the bias in what is published. Multiple
1256 studies have shown that positive trial results are more likely
1257 to be published than negative results. And in particular,
1258 industry sponsorship has been demonstrated to be a factor
1259 contributing to the biased publication. Industry has no
1260 incentive to publish or promote negative findings.

1261 My question is if industry is more likely to publish positive
1262 than negative results, do you also worry that positive results
1263 will be promoted more than negative results, even if there is
1264 a particular research being communicated is truthful and not
1265 misleading? Doesn't selected provocation create a distorted
1266 view of the safety and effectiveness of the unproven use?

1267 Ms. House. I am going to answer this very carefully because
1268 I have not seen the data that you re referencing that would suggest
1269 that there is more positive data than negative data. What I would
1270 say is that our position is is that both positive and negative
1271 data needs to be published in an equal manner and should be
1272 available for communication because we do know that there are
1273 patient harms as well as benefits.

1274 Mr. Green. And I think that is what we want to get to.
1275 If I am a pharmaceutical or if I am advertising anything else,
1276 I am going to talk about how great it is. If we are running for
1277 office, I am not going to talk about our bad side. We are going
1278 to talk about the good side. So we need to have it, but we need
1279 some agency to be able to say this is what you are doing and the

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1280 FDA is what we have. That is my frustration, I guess.

1281 Dr. Van Hare, in your testimony you note that Pediatric
1282 Research Equity Act has not been sufficient in producing the
1283 amount of shareable data we might like particularly in the older
1284 drugs and clinical decisions are often made. I think you raised
1285 an important point about the need for the robust data to allow
1286 clinicians to make the best decisions they can. My concern is
1287 there is nothing in this legislation we are talking about today
1288 would actually encourage drug companies to conduct those clinical
1289 trials that could answer important questions for pediatric
1290 populations. And again, our subcommittee for decades has
1291 wrestled around what may be appropriate for an adult is just not
1292 appropriate for children and we need to do a lot more work on
1293 that to make sure that we don't leave out the pediatric population.

1294 Mr. Chairman, I know I am over time, so I yield back my time,
1295 unless you want to give it Dr. Van Hare?

1296 Mr. Burgess. Dr. Van Hare, did you want to comment?

1297 Dr. Van Hare. I think that legislation has actually helped
1298 children in terms of getting a lot more information about drugs.

1299 And certainly in the pediatric world, originally for some
1300 companies or actually enticed some companies to actually do some
1301 trials. For the most part though companies are not really
1302 interested in the pediatric market. We are very, very small
1303 market and sort of thinking about the carrot and stick sort of
1304 approach, none of the carrots are really going to help us in

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1305 pediatrics because it is a fairly small market. So we are left
1306 in a situation where no one is going to do the type of clinical
1307 trial that was actually going to allow labeling for pediatric
1308 application for a lot of the things that we actually use.

1309 Despite that, we are talking care of our children and we
1310 need the best available data to make those decisions.

1311 Mr. Burgess. Thank you. The chair recognizes the
1312 gentleman from Illinois, Mr. Shimkus, 5 minutes for questions,
1313 please.

1314 Mr. Shimkus. Well, thank you. I am going to follow up with
1315 Dr. Van Hare first of all saying for my colleagues that the
1316 Washington University School of Medicine is one of the preeminent
1317 institutions in our country. And VJC which they are affiliated
1318 with, that is the go-to for major deals. So welcome.

1319 Dr. Van Hare. Thank you.

1320 Mr. Shimkus. And I know that because -- please extend my
1321 hello to Dr. Braverman and Dr. Damiano, who I know personally
1322 from personal medical stuff. I am a Homer for these folks and
1323 I have great confidence in your testimony and your word. But
1324 I would like to follow up on the question in that how often do
1325 you assess the various information to try to treat kids? I mean
1326 so we are talking about FDA approval, but you have given testimony
1327 about outside information to make sure you can best care for kids.

1328 How often do you go and search outside information to try to
1329 bring the best medical care to the kids in the cardiology aspects?

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1330 Dr. Van Hare. It really depends on what the condition is
1331 that we are actually trying to treat. I would say that we do
1332 have the process of developing consensus documents that actually
1333 summarize the medical evidence, the clinical trials and things
1334 like that that actually sort of express and certainly our society,
1335 the Heart Rhythm Society does this all the time to create these
1336 consensus documents to give physicians guidance. But you know,
1337 I guess pediatrics and also really sub-specialty medicine in
1338 general, we take care of a lot of very unusual types of conditions
1339 that don't really fall under the labels and the recommended uses.

1340 And so I guess for those less common, more unusual types of
1341 situations, we are often looking to our colleagues. We are
1342 calling around. We are finding what has your experience been
1343 with this? What has your experience been with that?

1344 Interestingly, I am a real proponent of the concept of
1345 partnership between industry and physicians. We often work elbow
1346 to elbow when we put pacemakers in and when we do different kinds
1347 of procedures. They have a lot of information just from their
1348 experience and it is an important source for us.

1349 Mr. Shimkus. Great. Thank you. Let me go to Ms.
1350 Klasmeier. In your testimony you talked about, and I quote,
1351 "strict scrutiny" the test. What does that mean, strict scrutiny
1352 in a test in court?

1353 Ms. Klasmeier. As a practical matter, Congressman, it means
1354 the government loses. So strict scrutiny is a bit of a legal

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1355 fiction that we indulge. It reflects the notion that when
1356 you examine government regulation that affects core speech such
1357 as political speech, it is very, very hard for the government
1358 to sustain its burden of justifying that speech regulatory
1359 provision against First Amendment is solvent. So as a practical
1360 matter, if the court concludes the applicable standard is strict
1361 scrutiny, the government loses.

1362 Mr. Shimkus. Maybe my colleague, Mr. Griffith, will follow
1363 up on that. He is our legal mind here on the committee and does
1364 a good job.

1365 Let me finish with Dr. Kesselheim. I am somewhat confused
1366 in your testimony because you used numerous times the term
1367 promotion over and over again in your testimony. But on page
1368 2 of the Griffith draft, it explicitly excludes promotional
1369 communications. Am I missing something?

1370 Dr. Kesselheim. Well, no. I mean I think this is part of
1371 an example of how the Griffith draft actually makes something
1372 that is fairly clear a lot less clear because you know, if the
1373 pharmaceutical company defines something as promotion determines
1374 whether or not they fall into this safe harbor.

1375 Mr. Shimkus. What do you mean by promotion? You used it
1376 numerous times.

1377 Dr. Kesselheim. Sure. When a pharmaceutical company
1378 promotes a drug, it goes out and it tells people about the use
1379 of the --

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1380 Mr. Shimkus. For their ability to sell it?

1381 Dr. Kesselheim. Yes. It goes out and it tells physicians
1382 about how to use the product and it sort of promotes the use of
1383 the drug through one of the various advertising --

1384 Mr. Shimkus. I am reclaiming my time. I will let
1385 Congressman Griffith kind of hash this out more, but again, on
1386 page 2, it is pretty clear. It says communication is not
1387 advertising or otherwise promotional in nature. So I just had
1388 a concern with your statements in your opening statement because
1389 you said it over and over again. I think it gives the wrong
1390 indication of what my colleague is trying to do. With that, I
1391 yield back my time.

1392 Mr. Burgess. The chair thanks the gentleman. The
1393 gentleman yields back. The chair recognizes the gentlelady from
1394 Illinois, Ms. Schakowsky, 5 minutes for questions, please.

1395 Ms. Schakowsky. Thank you. I think it is really important
1396 that we step back and remember that the FDA approval process really
1397 is the gold standard, the universal gold standard to determine
1398 safety and efficacy. And efforts to undermine that standard are
1399 very worrisome to me and I think that is what happens in these
1400 drafts. I think that Ms. Charo put it best in her testimony when
1401 she stated "for complex products like drugs, the marketplace of
1402 ideas cannot work properly with unvetted information from a
1403 self-interested source."

1404 I mean I think that often this committee is inclined to say

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1405 whatever PhRMA wants, PhRMA gets. But I want to ask Dr.
1406 Kesselheim, we have heard compelling testimony, I think, about
1407 access for patients to drugs. And so it is very important, I
1408 think, for you to explain what -- -does access trump safety or
1409 does it have to by having these kind of off-label procedures?

1410 It seems to me that safety ought to come first, but are there
1411 ways to guarantee that safety without the process of approval
1412 by the FDA?

1413 Dr. Kesselheim. Well, I mean so sure and I think that part
1414 of some of the testimony that we heard was a little bit
1415 disingenuous because the access to the products was not defined
1416 necessarily by the communications that occurred. The access in
1417 the case of the hepatitis C drugs, the effectiveness of the
1418 hepatitis C drugs is not a secret. Everybody knew how well they
1419 worked. Access to them was determined by the high cost of the
1420 product, not the evaluation, not whether or not there could have
1421 been communication in the few months before the drug was approved.

1422 So I mean I think the issue is really about getting high quality
1423 evidence or high quality communications out to help inform the
1424 market so that patients can make well-informed decisions based
1425 on the highest quality information that is out there possible.

1426 And the way to do that is to make sure that a neutral, third
1427 party body of experts like the FDA is able to vet the information.

1428 And I think what we should be doing is talking about how to make
1429 sure that more information is published, more trials are

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1430 published, more trials are available, open access, and that the
1431 FDA has more power and more authority to review information so
1432 that they can make those kinds of determinations so patients can
1433 benefit.

1434 Ms. Schakowsky. Is there a way for the FDA to move more
1435 quickly? We heard about 9, 10 years, or whatever?

1436 Dr. Kesselheim. I think if the FDA had more resources, it
1437 would be able to move more quickly. There are plenty of examples
1438 where the FDA has gone out and has been concerned about new safety
1439 issues that emerge, about off-label uses and ultimately goes
1440 through the process of revising the label to try to integrate
1441 those kinds of changes. If the FDA had more resources added and
1442 more people doing that kind of post-market surveillance, label
1443 updating kind of work, then I think we would get that information
1444 out to patients and vetted information out to patients more
1445 efficiently and more quickly.

1446 Ms. Schakowsky. Ms. Charo, one of the most compelling
1447 things I heard from you saying that, in fact, when you look at
1448 these drugs, the majority of them, in fact, would probably not
1449 meet the test. Am I hearing you right?

1450 Ms. Charo. You are hearing me correctly, and I believe,
1451 in fact, it was Ranking Member Green who referenced some of those
1452 studies in his opening comments.

1453 You know, scientific research is often somewhat equivocal
1454 for a very long time. I think what we are discussing here is

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1455 really what to do in that interim period where the evidence is
1456 shifting around. Do we presume everything is going to work and
1457 therefore everything people want to say is likely to be true and
1458 should be allowed or are we going to presume that it probably
1459 isn't going to work out and we should restrain the speech until
1460 we have actually proved it will.

1461 From my perspective, given that the risk of incorrect
1462 information is that people will actually be harmed, or they won't
1463 go for the effective treatment, they will go for the ineffective
1464 one, we need to err on the side of caution here and protect the
1465 larger population.

1466 That said, there are certainly going to be some occasions
1467 in which it turns out that something does work and it would have
1468 been wonderful if we could have seen it earlier and talked about
1469 it earlier, but those incidents will be fewer than those in which
1470 it would be damaging.

1471 Ms. Schakowsky. In the last 30 seconds, Dr. Kesselheim,
1472 what does history tell us about off-label promotion? Are there
1473 some things we should be recognizing here?

1474 Dr. Kesselheim. Sure, I mean over and over and over again
1475 throughout history and you don't even have to go back to the
1476 thalidomides 50 years ago, more recent history tells us that
1477 off-label promotion drives physician practices in ways that favor
1478 the drug being promoted, not in ways that favor the overall state
1479 of the evidence and the overall state of practice. I think that

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1480 we need to be very wary about efforts to try to expand that
1481 promotion when it covers non-evidenced based -- potentially
1482 non-evidenced based communications.

1483 Ms. Schakowsky. I think we need to when it comes to patient
1484 access, discuss more about the cost. Thank you.

1485 Mr. Burgess. The gentlelady yields back. The chair thanks
1486 the gentlelady. The chair recognizes the gentleman from New
1487 Jersey, Mr. Lance, 5 minutes for questions, please.

1488 Mr. Lance. Thank you, Mr. Chairman. Let me state that I
1489 don't believe any of the testimony has been disingenuous in my
1490 judgment. This is a very difficult issue and we are trying to
1491 balance the equities on this committee and I am pleased that every
1492 member of the panel is here and I do not question the integrity
1493 of any member of the panel.

1494 Counselor Klasmeier, do you believe that the standard will
1495 be strict scrutiny or will it be rational basis or will it be
1496 some intermediate standard, based upon your professional judgment
1497 as a distinguished member of the bar?

1498 Ms. Klasmeier. Congressman, my judgment is that the
1499 standard will be some variation of intermediate scrutiny.

1500 Mr. Lance. Intermediate scrutiny, yes.

1501 Ms. Klasmeier. And it will be most likely the Central Hudson
1502 standard with a garnish of heightened scrutiny as a result of
1503 the Supreme Court's decision in Sorrell in 2011.

1504 Mr. Lance. Yes, that is my judgment as well, and I think

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1505 that there is a history of decisions in this regard that would
1506 indicate that that is probably where we would be eventually as
1507 a matter of legal analysis. Thank you.

1508 Dr. Van Hare, we have all heard that some off-label uses
1509 are well established in clinical practice, and supported by
1510 high-quality evidence, and are the standard of cure for many
1511 conditions. From your perspective, based upon your
1512 distinguished history, how does the pieces of legislation before
1513 this committee stand to improve care for patients?

1514 Dr. Van Hare. Well, to the extent that the legislation
1515 proposed by Congressman Griffith allows or improves the
1516 efficiency of sharing data that the device companies and
1517 pharmaceutical companies actually have, for physicians who are
1518 prescribing off-label, I think it will actually help.

1519 Mr. Lance. Thank you, and other members of the panel are
1520 certainly welcome to comment.

1521 Ds. Khachatourian, what are the odds that if we pass
1522 legislation we are considering today, sophisticated population
1523 health decision makers like payers, provider sponsored health
1524 plans, pharmacy-benefit managers, and other organizations would
1525 be misled by unscrupulous drug and device manufacturers who make
1526 unfounded claims about their products?

1527 Ms. Khachatourian. So first let me acknowledge my testimony
1528 by no means disingenuous.

1529 Mr. Lance. I am sure and that is why I raised it. And if

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1530 I might interrupt you, I try to lead by example in the Congress,
1531 both on the floor and in committee, and I enjoy the testimony
1532 of every witness who comes before us. Those who know me know
1533 that disingenuous is not a word that I find attractive in
1534 vocabulary here on Capitol Hill. Yes, please continue.

1535 Ms. Khachatourian. Thank you. So population health
1536 decision makers and clinicians that we are discussing here are
1537 well trained to look at things with scrutiny and to determine
1538 what level of evidence is acceptable. And during the
1539 multi-stakeholder discussions that we have had, we did address
1540 the need to determine a level of evidence and to have an agreement
1541 on what is acceptable and non-misleading. And as evidence
1542 continues to evolve and as new therapies continue to emerge, that
1543 is the goal, is to develop strict criteria that will be used to
1544 apply to any level of evidence in order to ensure that it is high
1545 level and with the patient's best interest in mind.

1546 Mr. Lance. Certainly, and that is what we are attempting
1547 to get to a place where we can make sure that always there is
1548 the greatest standard of care. It is the jurisdiction of the
1549 subcommittee and ultimately of the full committee to promote the
1550 better health of the American nation, and we recognize this is
1551 a difficult issue and I certainly commend my colleagues, including
1552 the gentleman to my immediate right, the distinguished member
1553 from Virginia, as we undertake an analysis of how best to protect
1554 the American people recognizing that that is the goal of this

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1555 subcommittee in a bipartisan nature. I yield back 22 seconds,
1556 Mr. Chairman.

1557 Mr. Burgess. The chair thanks the gentleman. The chair
1558 recognizes the gentlelady from California 5 minutes for
1559 questions, please, Ms. Matsui.

1560 Ms. Matsui. Thank you very much, Mr. Chairman. This
1561 committee recognizes the important role that FDA plays to ensure
1562 public health and safety as evidenced by the bipartisan User Fee
1563 Reauthorization that we intend to pass out of the House this
1564 afternoon.

1565 Now we can't tolerate efforts to jeopardize that role as
1566 patients across America who take drugs to treat or cure conditions
1567 rely upon the FDA to monitor the safety of these drugs and devices.

1568
1569 I am really glad that we are holding this hearing today to
1570 examine issues that arise around information sharing,
1571 particularly for those so-called off-label use and what could
1572 be done to alleviate those issues without detracting from FDA's
1573 ability to regulate safety.

1574 I am particularly interested in the situation that many rare
1575 disease and cancer patients find themselves in. As many as one
1576 in five prescriptions are written for drugs off-label, meaning
1577 that they are prescribed for a condition or population that has
1578 not been FDA approved as safe and effective. Oftentimes,
1579 off-label drugs are the only treatment available and even the

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1580 standard of care for rare disease patients with limited options.

1581 Ms. House, thank you very much for your advocacy on behalf
1582 of cancer patients. Can you please discuss prevalence of
1583 off-label use in cancer patients?

1584 Ms. House. So there was a physician posted by the Friends
1585 of Cancer Research just yesterday that indicated that the use
1586 in cancer off-label was close to 80 percent. And part of -- one
1587 of the problems that I just wanted to raise is I was looking at
1588 some other discussion is I am going to give you an example. It
1589 is an older example, but it really talks about how the current
1590 labels are out of date. There was a time around 2000 where this
1591 is the time prior to personalized medicine, so it was still in
1592 the era of poisons for cancer, that there was a combination being
1593 used off-label as standard of care for the treatment of lung
1594 cancer. That particular combination failed at that time 13 Phase
1595 3 trials which is the gold standard for the evaluation for the
1596 FDA, yet it continued to be used standard of care for many, many,
1597 many years beyond that.

1598 This morning, I went on the FDA website and pulled up the
1599 label for the lead drug in that and today in 2017, still has not
1600 been updated to reflect the use of that combination which is a
1601 problem.

1602 Ms. Matsui. It is a problem, right. Now, you know when
1603 a family gets a cancer diagnosis, I think the world stops. And
1604 you are sort of grasping at what can we do? And I think we all

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1605 go to the internet. That is where we go right now.

1606 What types of information is generally available to patients
1607 and their providers when a drug is used off-label and even when
1608 you are an educated consumer, you really kind of hit a brick wall.

1609 What kinds of solutions might you recommend to address these
1610 challenges?

1611 Ms. House. I think creating solutions that again are
1612 tailored to the stakeholder, to their literacy level, to their
1613 educational level. There is really no reason why we can't create
1614 forums that would be peer reviewed, scientifically sound
1615 analysis, and presentation of clinical data. What it does
1616 prevent then is people going to the internet and getting into
1617 a chat room that may be facilitated out of another country or
1618 by somebody who has absolutely no medical background. And we
1619 see that happening all the time. And furthermore, if a patient
1620 calls a pharmaceutical company and says I am a patient, can you
1621 give me information about XYZ, the response will almost uniformly
1622 be, I cannot answer your question. You will have to go speak
1623 with your doctor.

1624 Ms. Matsui. Thank you very much. Ms. Charo, I know you
1625 have concerns about the legislation that we are discussing today.

1626 Are there ways that we can refine the legislation to reach our
1627 shared goal of promoting public safety by increasing patient
1628 access to safe and effective drugs? I think there is information
1629 out there and you know, we are in a time now where there is much

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1630 more research and innovation and I would hate to just have a hard
1631 and fast rule regarding this.

1632 Ms. Charo. Thank you. I completely agree with you that
1633 there are other avenues that need to be explored. For one thing,
1634 it may make sense to try to distinguish those areas where off-label
1635 use really is a necessary and important part of medical care as
1636 we just heard in the area of cancer, and some other areas there
1637 it really is not as prevalent and is not as needed. And I would
1638 suggest that pediatrics may be another good example.

1639 And the Congress has made great strides in trying to create
1640 new systems for both incentives and even possibly rewards for
1641 continuing the necessary research to find what really is safe
1642 and effective, for example, in the pediatric population. Working
1643 on making sure that there is a proper incentive and reward to
1644 fill in the gaps in those areas would be a good step forward and
1645 might accomplish many of these goals without some of the risks
1646 that are intended upon some of the ambiguities and what
1647 constitutes promotional marketing or what constitutes accurate
1648 information.

1649 Ms. Matsui. Thank you. I have run out of time. I yield
1650 back.

1651 Mr. Burgess. The chair thanks the gentlelady. The
1652 gentlelady yields back. The chair recognizes the gentleman from
1653 Indiana, Dr. Bucshon, for 5 minutes for questions, please.

1654 Mr. Bucshon. Thank you, Mr. Chairman. I was a practicing

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1655 cardiothoracic surgeon prior to coming to Congress and I just
1656 have a comment, not a question, but the medical community is
1657 relatively small and I think Dr. Van Hare said there is 300
1658 pediatric cardiologists. There is about 4,500 to 5,000 cardiac
1659 surgeons. Information travels quickly. Physicians are always
1660 looking for better ways or effective ways to treat their patients
1661 whether it is on label or off-label and information passes
1662 quickly.

1663 Frustration with labeling can be really high amongst
1664 different physician communities because of the delay in updating
1665 what may or may not be FDA approved. Patients are desperate and
1666 are getting information potentially from incorrect sources
1667 including the internet as has been pointed out and so I would
1668 suggest that we definitely need reform so that patients have the
1669 opportunity to get more accurate information.

1670 With that, I am going to yield the remainder of my time to
1671 Mr. Griffith.

1672 Mr. Griffith. Thank you very much. I appreciate it
1673 greatly. Let me first say that I appreciate everybody being here
1674 today and appreciate all of your testimony. I am open to continue
1675 to work on the language to make sure that we get it right. So
1676 that is something that I would invite you all, if you have issues
1677 with the language that we currently have, please get those
1678 suggestions to us because we want to try to do this in the best
1679 way that we can. We do believe that we need to do something on

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1680 a legislative side.

1681 Also, Mr. Chairman, I have some letters in support of the
1682 bill and a draft language and if I could have unanimous consent
1683 to enter those into the record I would appreciate it.

1684 Mr. Burgess. If the gentleman will share those with us,
1685 I will seek unanimous consent in a moment.

1686 Mr. Griffith. I also want to make sure that we are all
1687 working on the language that we currently have. And so what the
1688 bill says is when we are talking about communication if you look
1689 on page 2 it says "(A) the communication is not advertising or
1690 otherwise promotional in nature; (b) the communication is
1691 supported by competent and reliable scientific evidence." And
1692 then (c) and this was to address some of the concerns that have
1693 been raised here today, we put this language in: "The
1694 communication clearly discloses appropriate contextual
1695 information about the data presented including information about
1696 limitations." And I probably should put numbers in front of
1697 these. "(1) Limitations of the data; (2) the scientific and
1698 analytical methodologies used; and (3)" -- and I think very
1699 importantly, "any contradictory data or information known to the
1700 manufacturer or sponsor."

1701 We are never going to solve all of the problems if somebody
1702 is not doing what they are supposed to do, but our intent is to
1703 try to make sure that both sides are presented. I think somebody
1704 mentioned that earlier in their testimony, that both sides are

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1705 presented and that the negative evidence is out there as well.

1706 And then we talk about situations related to the rare
1707 diseases. Cancer has been mentioned today and the children
1708 because one of the problems you have in those situations and Dr.
1709 Van Hare, you touched on this is that there may not be a sufficient
1710 number of patients to actually warrant doing a clinical study.

1711 Nothing compared to what you deal with your families Dr. Van
1712 Hare, but my son who is now 11 had two thirds of his body covered
1713 with eczema when he was about 3 months old. I kept telling my
1714 wife because of the history in the family we have allergy problems,
1715 honey. We got him to an allergist. Between the cream that worked
1716 for me that my pharmacist knew, between the steroid creams,
1717 between the antihistamines that they gave him we were able to
1718 control that situation. We still have issues there. But for
1719 a child under the age of two, there were no -- some of that might
1720 have been on-label, but most of that treatment was off-label,
1721 so I appreciated Ms. Charo saying that we ought to take a look
1722 at that because I think those are the two hot button areas. But
1723 that doesn't mean we should exclude others.

1724 I was very curious, too, about this whole agent concept that
1725 is going on where you can't go and tell the 300 other doctors,
1726 Dr. Van Hare. Could you speak on that briefly and I have only
1727 got a minute left of this time period.

1728 Dr. Van Hare. Yes. It has to do with how CME or Continuing
1729 Medical Education is defined. CME is actually a safe harbor.

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1730 If I am speaking at a conference that is sponsored by an
1731 accredited CME provider, like the Heart Rhythm Society or the
1732 American College of Cardiology or some other group, I can say
1733 whatever I want and I can talk about off-label indications as
1734 much as I want. If I am actually speaking at a conference that
1735 is actually sponsored by the pharmaceutical company or the
1736 manufacturer, then I basically am an agent, or considered an
1737 agent.

1738 Mr. Griffith. So if on the podium somebody asks you about
1739 a catheter to be used in a child that might be off-label, you
1740 could then be deemed and the company could be deemed that you
1741 are their agent and then be in trouble under the current rules
1742 of the FDA. Is that correct?

1743 Dr. Van Hare. That is my understanding.

1744 Mr. Griffith. That is my understanding also. All right,
1745 Ms. Klasmeier, my friend and colleague from New Jersey, Mr. Lance,
1746 did a great job of going through the intellectual. Let us
1747 translate that into human regular English. That means that if
1748 you bring that example to the courts, FDA is most likely going
1749 to lose, wouldn't you agree?

1750 Ms. Klasmeier. I would agree and I would go one further.
1751 FDA did lose that case. That was the Washington Legal Foundation
1752 decision in 1998 and the upshot of that is that the court found
1753 it unconstitutional for the government to purport to restrict
1754 the identity of the speakers that could participate in those kinds

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1755 of continuing education events that Dr. Van Hare described.

1756 Mr. Griffith. Thank you very much. I yield back to my
1757 colleague. Thank you.

1758 Mr. Bucshon. I yield back.

1759 Mr. Burgess. The gentleman had a unanimous consent request
1760 and I sought counsel from the other side of the dais, so without
1761 objection so ordered if that unanimous consent request still
1762 stands.

1763 Mr. Griffith. It goes and I apologize. I just saw my time
1764 taken away.

1765 Mr. Burgess. Very well. The chair recognizes the
1766 gentlelady from Florida, Ms. Castor, for 5 minutes for questions.

1767 Ms. Castor. Well, thank you very much, Mr. Chairman, for
1768 calling this hearing. I think allowing drug companies and
1769 manufacturers to market their drugs and devices for unapproved
1770 uses would be very dangerous for American families, American
1771 consumers. It would reduce the incentive for them to go through
1772 FDA's approval process and reduce the incentive to go through
1773 clinical trials that really just test whether or not a product
1774 is safe and it is effective. FDA's approval process right now
1775 is the gold standard for safety and efficacy.

1776 The FDA Commissioner, Dr. Gottlieb, has said the most
1777 important incentive to developing useful information remains the
1778 ability for companies to market drugs based on what can be proven
1779 scientifically. Now this is not a hard and fast rule because

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1780 I have learned today and reviewing your testimony, there are safe
1781 harbors, but nevertheless, Professor Charo, some contend that
1782 we must revisit this regulation of off-label promotion because
1783 the trend in the courts is that restrictions on off-label
1784 promotion run afoul of the First Amendment. I think this is a
1785 stretch. Does the First Amendment limit FDA's responsibility
1786 for scientific review? Does it limit FDA from restricting
1787 promotion of unapproved uses? If not, what avenues do medical
1788 product manufacturers have to communicate about such uses?

1789 Ms. Charo. Well, we have seen some cases that have touched
1790 on these things from the fringes, but you don't actually get cases
1791 that touch on it directly. For example, in one case that is
1792 frequently cited for the suggestion that the Constitution
1793 prevents the FDA from restricting truthful speech, at issue at
1794 the time was not truthful speech, but simply off-label speech
1795 and the FDA premised its entire case on the fact that the speaker
1796 had been discussing an off-label use and never really talked to
1797 the issue about whether or not the speaker's comments had been
1798 true.

1799 The problem here has simply been that it is really and I
1800 hope that Mr. Griffith's staff is still around for this, the
1801 problem is that no company is going to have all the information
1802 about all the studies that are being done at that time including
1803 those that have negative results because of various rules about
1804 confidentiality of information. The FDA may be in possession

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1805 of all the information, but not necessarily every company. So
1806 even with the best of intentions to be conveying what they believe
1807 to be truthful and contextualized information, there is the risk
1808 that that actually is missing large areas of data that would
1809 suggest that the studies they are discussing are not, in fact,
1810 going to be indicative of a truly safe and effective drug at the
1811 end of the day. This is why there really is a substantial public
1812 interest which is one of the key elements in the restriction of
1813 speech to the current system.

1814 And the alternatives that have been presented,
1815 unfortunately, I believe offer risks to public health that dwarf
1816 their benefits which is why the second rung, the second prong
1817 of these tests which have to do with whether or not the government
1818 can find an alternative way of achieving its goals I think show
1819 that really the current system is probably the best way, tweaking,
1820 yes, but the removal of many of these restrictions, I don't believe
1821 is necessary in order to meet the Constitution test.

1822 Ms. Castor. And there seems to be debate on whether
1823 the Griffith proposal would restrict scientific exchange under
1824 the safe harbor. What is your view of this and the Griffith
1825 discussion draft?

1826 Ms. Charo. You know, I think that the text does attempt
1827 does attempt to isolate what is non-promotional and protect that
1828 while continuing the prohibit promotional language. I think that
1829 the difficulty here is that the very notion of what is promotional

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1830 is actually somewhat ambiguous. We now know, for example, that
1831 it is possible to tweak how various results come up on the
1832 internet, whether or not it is the first, second, or third thing
1833 you see on the page. If there is a tweaking algorithm, does that
1834 constitute promotional if all it does is raise your particular
1835 data to the front of the page? These are the kinds of subtle
1836 questions that can both make the language ambiguous despite our
1837 efforts and also from my perspective, suggest that it is better
1838 to have the flexible tools of guidances that can be negotiated
1839 over time with the constantly-changing nature of communication
1840 rather than the somewhat more rigid tools of regulation and
1841 legislation, let alone having courts do it 17 years after the
1842 fact and leave everybody uncertain for that long period in
1843 between.

1844 Ms. Castor. Dr. Kesselheim, do you have a comment on this
1845 topic as well?

1846 Dr. Kesselheim. I mean I also agree that the way that this
1847 discussion draft is written provides substantial leeway for
1848 companies to interpret these various provisions in ways that are
1849 favorable to their particular advertising strategy.

1850 Ms. Castor. And at the cost to public safety.

1851 Dr. Kesselheim. And at the cost to public safety.

1852 Ms. Castor. Thank you. I yield back. I am out of time.

1853 Mr. Burgess. The gentleman yields back. The chair thanks
1854 the gentlelady. The chair recognizes the gentleman from Georgia,

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1855 Mr. Carter, 5 minutes for questions, please.

1856 Mr. Carter. Thank you, Mr. Chairman. And thank all of you
1857 for being here. Certainly, an important subject.

1858 Dr. Khachatourian, you are a pharmacist, as am I. And I
1859 can tell you that after 30 years of practicing pharmacy, certainly
1860 side effects are -- we call them side effects. And you know,
1861 it has always been interesting to me why we call them side effects
1862 because essentially they are effects of the drug, but they are
1863 not what we want it to do, so we kind of label them as side effects.

1864 I noticed in your statement, in your testimony, in your
1865 written testimony that you feel like the Pharmaceutical
1866 Information Exchange would be helpful and useful and there is
1867 some debate on whether it should be evidenced based or whether
1868 it should be information based. And I noticed that you said that
1869 it should be based on information only, well, not only, but
1870 basically. Can you kind of elaborate on that?

1871 Ms. Khachatourian. Absolutely, thank you. So when we
1872 think about evidence, there are established criteria for evidence
1873 as far as what constitutes a clinical trial and the acceptable
1874 level of evidence for FDA approval. When I talk about
1875 information, information may include financial models, may
1876 include other information that does not quite meet the level of
1877 evidence that one might traditionally think. So when we talk
1878 about information, if I am able to discuss with my clinical
1879 colleagues at a manufacturer what models might be available, what

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1880 sub-populations were studied and what level of information might
1881 be available that can help me to make more effective decisions,
1882 that is what I mean by information.

1883 And again, I will reference the multi-stakeholder forum
1884 where we discuss developing criteria that will set the foundation
1885 for what that information might entail and what level of quality
1886 of information could be deemed acceptable.

1887 Mr. Carter. You also mentioned in your testimony that a
1888 very proactive pharmaceutical information exchange would lead
1889 cost savings. It could lead to cost savings for patients. So
1890 in that respect, how can we assure that the cost savings are going
1891 to be passed on to the patients if we don't have transparency
1892 within the prescription benefit managers and the other middle
1893 men that are included so often in these scenarios?

1894 Ms. Khachatourian. Sure. While cost is an aspect of
1895 evolving and emerging therapies and treatments that are coming,
1896 cost is an aspect that needs to be discussed. However, with the
1897 exchange of information it makes us more effective in the use
1898 of the funds that we have available to make benefit decisions.

1899 So when we are structuring a benefit based on value, that is
1900 what value will be conveyed to both us as the payer as well as
1901 the patient. So ultimately from a cost discussion, that is, in
1902 turn, outside of the transparency which is a little bit of a
1903 different discussion.

1904 Mr. Carter. I am not sure I understand how it can be a little

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1905 bit of a different discussion. Because I believe truly that it
1906 can have cost savings to the patient if we have transparency within
1907 the system and I don't see how it can be if we don't have
1908 transparency.

1909 Ms. Khachatourian. So I absolutely acknowledge
1910 transparency is an important factor. However, the information
1911 exchange between a payer, as well as the manufacturer, will help
1912 us to make better decisions and with a limited pool of money that
1913 we are able to allocate to benefit design. We try to make the
1914 most cost-effective decisions on behalf of those patients that
1915 we serve, so in turn, the cost savings are passed to the patient
1916 as the ultimate user of our benefit design.

1917 Mr. Carter. Okay. I will move on. Dr. Van Hare -- and
1918 thank you very much for being here, Dr. Khachatourian.

1919 Dr. Van Hare, I have seen in my practice over the years,
1920 particularly with prescription drugs, a lot of off-label uses,
1921 if you will, in pediatric patients. And I just want to get your
1922 feeling on the value of that? Because I have seen it first hand
1923 that it has been very valuable.

1924 Dr. Van Hare. Yes, well, so I would say it is essential,
1925 in fact, for most of what we do, particularly in the pediatric
1926 cardiology area. But I mean I do think we have reservations about
1927 it. When people make decisions based on information they get
1928 from like one other colleague who used it once on some patient,
1929 that is very, very sort of limited. But I would say that certainly

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1930 we have to do it. We have no choice but to do off-label
1931 prescribing in a lot of situations. And we would prefer to have
1932 the best possible information.

1933 We also use what is known about the use of these medications
1934 in other age groups, particularly adults, or other particular
1935 conditions and basically extend to these particular
1936 populations. That may or may not be valid as some other members
1937 of the panel here have talked about. But absent better data,
1938 it is all we actually have.

1939 Mr. Carter. Great. Thank you all very much for your
1940 participation here today. A very important subject I can tell
1941 you. Many years of practice in pharmacy, we have used many drugs
1942 that were not indicated or at least not approved for certain
1943 therapies that have been very, very beneficial to patients.

1944 Thank you, Mr. Chairman. I yield back.

1945 Mr. Burgess. The chair thanks the gentleman, the gentleman
1946 yields back. The chair recognizes the gentleman from California,
1947 Ms. Eshoo, 5 minutes for questions, please.

1948 Ms. Eshoo. Thank you, Mr. Chairman. And thank you to all
1949 of the witnesses. I also want to thank our colleagues who are
1950 offering the drafts and to Mr. Griffith, I especially appreciate
1951 your openness to suggestions and I think that that is very
1952 important.

1953 Over all the years I have been in Congress, this is my 25th
1954 year, and have worked with medical device manufacturers, worked

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1955 with the biotechnology industry, done legislation that has
1956 reformed how medical devices are approved, passed legislation
1957 signed into law but I can't remember which President relative
1958 to pediatric medications and improved that system for children.

1959 This issue, the issues that are being discussed here today, no
1960 one has ever raised with me. So this is the first time I am hearing
1961 about it. But it is good. It is a discussion, but it still says
1962 something to me that no one has contacted me about this. So I
1963 don't think it is exactly a burning issue.

1964 Number two, it is my understanding that what is being offered
1965 by our two colleagues today were supposed to be a part of the
1966 overall approval for the FDA, but were pulled because they were
1967 controversial. I can hear today where the controversy is coming
1968 from. That is legitimate and I am glad that it wasn't in the
1969 larger bill, because they really didn't belong there. This cake
1970 has not been baked yet.

1971 Now it is my understanding that in one of the discussion
1972 drafts, that there is no clear list of what qualifies as scientific
1973 information. Now that is foundational to me, scientific
1974 information. Not who is gabbing and saying what from a given
1975 industry. That is always interesting and those discussions take
1976 place. But we are dealing with over 200 million people in our
1977 country and these words are going to walk into their life. This
1978 is a huge responsibility. They don't know that we are here today.
1979 They don't know any of our names, but we have the public interest

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1980 in the safety and the efficacy of what takes place on their behalf.

1981 To Ms. House, I am not sure, are you in favor of the two
1982 discussion drafts? Yes or no?

1983 Ms. House. We have not taken a formal position on either.

1984 Ms. Eshoo. That is fine.

1985 Ms. House. Neither of them are perfect.

1986 Ms. Eshoo. Yes, well, but I couldn't tell from your
1987 testimony whether you were for or against or where you were.

1988 Ms. Charo, thank you for your testimony. I think that you
1989 have set down the importance of where the information comes from
1990 and that it can't be haphazard. There has to be a final kind
1991 of resting place that has all of the information for people in
1992 our country that can be used.

1993 I don't think anyone has really made the case here to take
1994 it outside of the FDA. Maybe I am missing something, but I haven't
1995 heard that.

1996 To Ms. Khachatourian, I love the I-A-N. I share either your
1997 husband's heritage or yours. When you spoke about hep C, how
1998 many patients were excluded from treatment?

1999 Ms. Khachatourian. So while I can't speak for all payers
2000 and all --

2001 Ms. Eshoo. No, but you used that as an example, hep C.
2002 So we know, it is a company I am very familiar with in my district.
2003 I have worked with them. They have presented a cure which we
2004 are not accustomed to. It is expensive. But who was left out

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2005 according to your testimony?

2006 Ms. Khachatourian. Sure. So in the initial approval, we
2007 approved treatments according to the label. So for the first
2008 time in hepatitis C, we saw the criteria, the approval criteria
2009 change multiple times. So initially it excluded patients that
2010 might have cirrhosis. It initially excluded patients that
2011 according to the FDA label --

2012 Ms. Eshoo. How do these drafts fix that?

2013 Ms. Khachatourian. So with the drafts, we could understand
2014 that there would be evidence published that would add additional
2015 clinical evidence to indicate effectiveness of treatment in those
2016 sub-populations although at the time of the initial approval,
2017 that evidence was not available for decision making.

2018 So in my medical space --

2019 Ms. Eshoo. You are saying people were excluded, but you
2020 don't know how many?

2021 Ms. Khachatourian. I can't speak to the exact number
2022 globally. However, within our population, Medicare is who
2023 defines our coverage criteria. So when we submit our criteria
2024 to CMS for approval, it has to be according to the Part D coverage,
2025 what is listed in the FDA-approved label. So we cannot cover
2026 off-label unless it is within the oncology space. When we are
2027 talking about a Part D indication.

2028 Ms. Eshoo. I still don't know who has been injured in this
2029 according to your testimony. That is why I am asking you and

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2030 I still don't know. But I appreciate your trying.

2031 Thank you, Mr. Chairman.

2032 Ms. Khachatourian. If we expand the discussion to
2033 commercial payer outside of Part D, the additional patients that
2034 were denied treatment.

2035 Ms. Eshoo. But you don't know how many.

2036 Ms. Khachatourian. I don't coverage commercial insurance,
2037 however, that is something I would be happy to look into for you.

2038 Ms. Eshoo. Thank you.

2039 Mr. Burgess. The gentlelady yields back. The chair thanks
2040 the gentleman. The chair recognizes the gentleman from Virginia,
2041 Mr. Griffith, 5 minutes for questions, please.

2042 Mr. Griffith. Thank you very much. I appreciate it. Ms.
2043 Klasmeier, we have had some discussions and I know this is not
2044 the Judiciary Committee, but this is where the law touches
2045 everything. And so as we consider legislation in this area, just
2046 so the committee knows as a whole and that I am better educated,
2047 what points should we be taking away from the various judicial
2048 cases in considering First Amendment challenges to the FDA's
2049 regulations? And what should we be looking out for? So that
2050 is Part A and Part B. What should we be looking out for to make
2051 sure that we get it right and that we do it where it is
2052 constitutional as we draft this?

2053 Ms. Klasmeier. Thank you very much for the question,
2054 Congressman. I think a very important take away from the case

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2055 law is the need for clarity and that point arises out of the
2056 intersection of the Fifth Amendment case law and the First
2057 Amendment case law. I think there is a lot of discussion about
2058 the First Amendment, but the due process laws requires clarity
2059 and precision, requires rules that give regulated entities clear
2060 notice on an a priori basis of what conduct is prohibited versus
2061 permitted.

2062 Mr. Griffith. And let me, I don't want to cut the rest of
2063 the answer off, but let me interrupt up there because that is
2064 one of my pet peeves. So many times people think that means we
2065 have to define every word in the bill, but if there is no definition
2066 in the bill, then the courts use the normal usage of the English
2067 language or if it is a term of art, the term of art in this case
2068 from the medical community. Is that not correct?

2069 Ms. Klasmeier. It is absolutely correct, sir. And just
2070 to augment your observation, there was a conversation earlier
2071 this morning about the definition of claim and promotion and where
2072 do we draw the line. And I understand why there may be some
2073 misunderstanding around that, but I have to say as a practitioner
2074 in this area and I also have to say I suffer from a little bit
2075 of an existential crisis because the news that this is not a hot
2076 button issue or something that needs to be resolved makes me
2077 question what I have spent the last 20 years of my life doing.
2078 But that is an aside.

2079 Mr. Griffith. Not worry, her phones will be lit up before

2080 the day is done, I am sure.

2081 Ms. Khachatourian. But there is among those of us who
2082 practice in this area day in and day out a very well understood
2083 line between promotional speech and non-promotional speech. So
2084 I think the legislative measures that we have been talking about
2085 this morning would just under foundational interpretive
2086 principles be examined against those background legal norms.
2087 So there is a very rich body of administrative precedent from
2088 FDA in addition to case law and the statutory foundation of the
2089 measures that you are talking about. We know what these words
2090 mean. So I agree to the extent that you are saying we ought not
2091 to feel overly anxious about those two or three words. I think
2092 folks who are battle tested in this area know the difference
2093 between promotional speech and non-promotional speech and can
2094 advise clients accordingly.

2095 Mr. Griffith. And I kind of got you off track there for
2096 a second. You were talking about the First and the Fifth. I
2097 am going to let you go back to is there anything else on that
2098 you wanted to touch base on that I distracted --

2099 Ms. Khachatourian. Many things, but I will try to limit
2100 it to a big ticket item which is it is increasingly obvious from
2101 the case law which goes back to at least to 1976 that it is very
2102 hard for the government to defend any speech regulation that
2103 affects accurate communication regarding lawful activity. I
2104 think we tend to get hung up on the kind of Central Hudson test

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2105 and prongs and that sort of thing. But just to sort of bring
2106 it down to its essence, if the government wants to restrain
2107 accurate speech about conduct that is permitted and off-label
2108 use is not only permitted in almost all cases, it is by federal
2109 law, it is also the standard of care in many instances, it has
2110 really got an uphill battle.

2111 I think there is probably a way for all of these very
2112 challenging and complex policy considerations to be balanced in
2113 a smart way that takes account of the First Amendment backdrop
2114 and I think the measures that we are talking about today have
2115 done an admirable job of strengthening that balance. But there
2116 is a little bit of a thumb on the scale, if you like, as a result
2117 of years and years of case law going back to at least 1976 against
2118 anything that would purport to prohibit speech that is about --
2119 accurate speech about lawful activity.

2120 Mr. Griffith. And while I wasn't as concerned about the
2121 freedom of speech per se, although it is very important to me,
2122 when I put in that clause that they have to put in the contradictory
2123 information, as well, and the contextual information, that
2124 actually shores that up from a free speech standpoint as well
2125 because we are saying you have to present, if you are going to
2126 present, you have to present both sides of the data. Isn't that
2127 accurate?

2128 Ms. Khachatourian. Absolutely accurate, yes, sir.

2129 Mr. Griffith. I appreciate that. And it does make me worry

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2130 and I know it is not their field of expertise either, but you
2131 indicated there was a late '90s case that clarified some of this.

2132 I think the bill clarifies it more, but I am just curious why
2133 the FDA keeps going down this pathway when they have lost a number
2134 of cases over the years, if not in this circle of the three-ring
2135 circus, in another circle of that same circus under the same tent.

2136 Ms. Khachatourian. Yes, well, it is concerning because you
2137 have not only the cases that we have been talking about here,
2138 Caronia and Amarin and Pacira, but also on the dietary supplement
2139 side of the house, a great many cases from the D.C. Circuit, a
2140 lot of other sources of precedent that draw into question the
2141 constitutionality of the current scheme. That said, I think
2142 there are a lot of undeveloped arguments that we have been, in
2143 industry, waiting with bated breath for FDA to articulate and
2144 there was a memoranda that FDA lodged in one of its administrative
2145 dockets in January, right before the inauguration that purported
2146 to explain for all the world to see how the agency thought through
2147 these constitutional issues and it was a little more than a
2148 defense of the status quo.

2149 I think there is a lot of room for optimism in the coming
2150 months, particularly with the involvement of this subcommittee
2151 and the Congress, generally, that FDA will do a better job of
2152 explaining and including stakeholders in a conversation about
2153 the constitutionality and constitutional issues associated with
2154 this current regulatory scheme.

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2155 Mr. Griffith. I appreciate it and yield back. Thank you,
2156 Mr. Chairman.

2157 Mr. Burgess. The chair thanks the gentleman. The chair
2158 thanks Ms. Khachatourian for her optimism. We always welcome
2159 optimism on this subcommittee.

2160 The chair now recognizes the gentleman from Maryland, Mr.
2161 Sarbanes, 5 minutes for questions.

2162 Mr. Sarbanes. Thank you, Mr. Chairman. I want to thank
2163 the panel. This is a really complicated issue I am finding.
2164 I sat here through the entire testimony. And certainly the
2165 ability and the internet is kind of at the center of this now
2166 for people to get hold of information about beneficial off-label
2167 use of drugs and medical devices much more readily than obviously
2168 they ever could before, is creating some pressure to figure out
2169 a way to make that opportunity more available to people. The
2170 fast distribution of information can also allow for the fast
2171 distribution of bad information and lead to poor decision making.

2172 But I understand that Congressmen Griffith, Guthrie, and others
2173 are trying to respond to pressure and often it comes from patients
2174 that are seeking a solution.

2175 What I am concerned about is that you could solve the way
2176 they are proposing for this pressure, or you could solve perhaps
2177 by building more capacity inside the FDA. So what I am interested
2178 in hearing about, I don't want us to take a short cut. I don't
2179 want the reason we are reaching for the proposed solution here

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2180 to be that we have overlooked the opportunity to build more
2181 capacity in FDA as a way of solving for this, and perhaps solving
2182 for in a way that protects public safety better than taking the
2183 alternative route.

2184 So I wonder, Ms. Charo, maybe you could begin here. Speak
2185 to that issue. How do we explore fully the opportunity to build
2186 capacity in FDA to respond to the pressure we are talking about?
2187 Can that be done? If so, what are the ways in which it can be
2188 done, etcetera?

2189 Ms. Charo. Well, first, I am going to second what has been
2190 said by others here which is that FDA, just in terms of sure
2191 personnel, would certainly benefit from having more people able
2192 to act on data as it is coming in and everything would move more
2193 rapidly with no question. But we shouldn't restrict ourselves
2194 only to FDA. I mean one of the things we have been struggling
2195 with here is that there are areas in which the incentive systems
2196 that currently exist are inadequate for driving the research that
2197 we all agree would be ideal to figure out what really works and
2198 what does not. Pediatrics, rare diseases are two very good
2199 examples.

2200 Now we have some new tools. Congress have given things like
2201 priority reviews and extended patent periods as incentives, but
2202 we have yet to completely explore the full range of tools.
2203 Antibiotics is another example where the Infectious Disease
2204 Society of America has been pointing out for years we could use

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2205 rewards, milestone rewards. We have not talked about NIHI
2206 funding for direction of studies that would look at things like
2207 off-label uses that are hinted at already and that need to be
2208 confirmed.

2209 In other words, we need not restrict ourselves to only one
2210 tool which is to pull the industry slowly to do the research under
2211 the threat of not being able to market. But we could bring to
2212 bear a combination of tools to get the information developed more
2213 rapidly. And ideally, then everybody would benefit because we
2214 would have a wider range of applications, but we would have more
2215 confidence that they have been tested in a way that is
2216 comprehensive and objective and has been vetted by independent
2217 eyes.

2218 Mr. Sarbanes. I appreciate that. I mean I worry a little
2219 bit that I don't completely trust the industries we are talking
2220 about here to restrain themselves if they get -- if there is an
2221 avenue for aggressively pursuing a particular product's appeal
2222 out there in ways that may compromise public safety and I worry
2223 about a bunch of camels starting to get their noses under the
2224 tent. So I understand the desire to try to accommodate people's
2225 interest in pursuing this, but if there are other ways we can
2226 respond to that, without sacrificing some of these concerns about
2227 public safety, then I think that we ought to pursue those and
2228 explore some of the additional tools that you have suggested
2229 perhaps. With that, I yield back. Thank you.

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2230 Mr. Burgess. The gentleman yields back. The chair thanks
2231 the gentleman. The chair recognizes the gentleman from Florida,
2232 Mr. Bilirakis, 5 minutes for questions.

2233 Mr. Bilirakis. Thank you, Mr. Chairman. I thank the panel
2234 as well. I have a question for Ms. House. Again, thank you for
2235 your testimony. Throughout my time on the Energy and Commerce
2236 Committee, I have been involved with the rare disease community.

2237 There are about 30 million Americans, and there are 7,000 rare
2238 diseases, 30 million Americans have a rare disease which includes
2239 pediatric cancers. And I understand there are about 500 FDA
2240 approved treatments. Correct me if I am wrong.

2241 Do you think that many of these 30 million Americans are
2242 taking medications off-label? For Ms. House, please.

2243 Ms. House. Yes. Yes, I do. I do. In my written comments,
2244 I have referenced in particular Lupus and if you look at the FDA
2245 site right now, there are only four drugs that are approved for
2246 Lupus. And the approvals of those go back into the mid-1900s.

2247 So when you look at the drugs, aspirin was approved first in
2248 1948, followed by steroids, and there was no drug listed. There
2249 was an anti-malarial that was approved in 1955. And finally,
2250 a new drug approved in 2011. So if you are a patient living
2251 with Lupus, you are likely not getting aspirin as a therapeutic
2252 option for your particular disease. And certainly when you look
2253 at cancer, there is a reason why there is such a high rate of
2254 pediatrics in cancer clinical trials and it is because they don't

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2255 have a lot of other options available to them.

2256 Mr. Bilirakis. Thank you, so there are other examples out
2257 there. So a large percentage of the 30 million are taking
2258 medication off-label.

2259 Ms. House. Arthritis is another good sample. If you look
2260 at the label of methotrexate, for example, you will see that the
2261 label doesn't reflect the broad use of that particular product
2262 and you can probably speak to that better than I could.

2263 Mr. Bilirakis. Thank you. I am here with a young Floridian
2264 from the Miami area who told me about how she came down with ITP,
2265 a condition where her body destroyed her platelets. And I have
2266 conversed with her over a long period of time on these particular
2267 issues. I have sponsored the Open Act and we are working
2268 together.

2269 She had to become an expert. She became an expert on ITP
2270 and she really became her own doctor and found a treatment, really
2271 extraordinary. She was able to find a drug that could treat her
2272 condition. The drug was FDA approved for non-Hodgkin lymphoma
2273 and rheumatoid arthritis, but not for ITP.

2274 After a long conversation with her physician, we were able
2275 to pursue that course, the off-label treatment and it was very
2276 successful. She comes to D.C. on a regular basis as an advocate
2277 for cures and treatments for rare diseases.

2278 Ms. House, does it make sense to withhold information from
2279 physicians and not share truthful medical information that could

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2280 say a person's life? And who should be in charge of a patient's
2281 treatment? The patient working with her physician or again, a
2282 bureaucrat? If you could answer that question, I would
2283 appreciate that.

2284 Ms. House. Well, you know, we have spent 35 years trying
2285 to assist patients to become equal participants and empower
2286 participants in their care, so I am going to answer that as the
2287 patient needs to be quarterback of their care, working with their
2288 particular physician.

2289 I will say that it is incredibly important though that the
2290 information that is provided, both to patients and to physicians,
2291 is fair balanced. I worked in the pharmaceutical industry for
2292 a period of time, so I also understand the bright white lines
2293 between what is promotional and what is non-promotional and we
2294 are not talking about shipping patients or physicians glossy
2295 pieces of information on off-label uses or other additional
2296 information, but we have to provide for them and whether that
2297 is, I do agree that there are alternative solutions, whether it
2298 is through the FDA, whether it is through a professional society,
2299 whether it is through a third party peer reviewed entity, we have
2300 to get to a point where we are providing that data set to people
2301 who are making decisions, including patients who are making more
2302 and more of their care decisions as you have referenced.

2303 Mr. Bilirakis. Thank you. Agreed. Dr. Van Hare, in your
2304 practice, you deal with children and adults who suffer from a

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2305 heart condition such as the congenital heart and some are
2306 congenital heart in nature. I sponsored a bill to reauthorize
2307 a congenital heart program and it went through this committee
2308 and hopefully on the floor as soon as possible.

2309 If you have a child who comes to the hospital with a heart
2310 condition, you might need to do a surgical procedure. How common
2311 is it for medical devices to be approved for use in children?

2312 Mr. Bilirakis. Well, as I understand, most medical devices,
2313 at least that I use in the cardiology sphere are not specific
2314 to children or adults. They are more specific to actual specific
2315 arrhythmias. And as I talked about in my oral testimony, a lot
2316 of what we take care of, the devices, in fact, are not labeled
2317 for those particular sort of conditions.

2318 I will say that you sort of raise the issue of surgery for
2319 congenital heart disease. We often think about surgery as
2320 basically correcting a problem. But those patients need to have
2321 a cardiologist for the rest of their life and one of the biggest
2322 problems if they develop heart rhythm issues and those heart
2323 rhythm issues are often very, very difficult to take care of and
2324 so we are reaching for whatever we can find to treat those things
2325 most effectively. And we use technology and we use devices that
2326 have been approved for other indications for this particular
2327 situation.

2328 I just want to emphasize that we keep talking about
2329 pediatrics as sort of being an important issue and I am a proud

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2330 pediatrician and I believe that. But I think pediatrics is a
2331 special case of a larger issue which is there are a lot of patients
2332 that devices and drugs have been developed for other indications.
2333 We have to find a way to take care of our patients. I think
2334 pediatric diseases, but also rare diseases, and anything that
2335 is kind of on a cutting edge of what we are doing medically to
2336 treat things are going to fall into this discussion.

2337 Mr. Bilirakis. Thank you very much. I yield back, Mr.
2338 Chairman.

2339 Mr. Burgess. The chair thanks the gentleman. The
2340 gentleman yields back. The chair recognizes the gentleman from
2341 New York, Mr. Engel, 5 minutes for questions, please?

2342 Mr. Engel. Thank you very much, Mr. Chairman. I have long
2343 been an advocate for those suffering from rare diseases. I was
2344 an author of the ALS Registry Act and the two most recent Muscular
2345 Dystrophy Care Act reauthorizations and I know how much relief
2346 and encouragement new therapies can bring to rare disease
2347 patients. And I think I speak for everyone on this subcommittee
2348 when I say that all of us want to do what we can to bring effective
2349 and potentially life-saving treatments to patients as quickly
2350 as possible, but it is absolutely critical that we ensure our
2351 actions do not compromise patient safety.

2352 Efficiency is a worthwhile goal that we all share, but as
2353 we strive to hasten the delivery of new treatments, safety and
2354 effectiveness must always be paramount and that is why this

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2355 hearing is so important. Any action by this committee needs to
2356 take into account the input of expert witnesses who can speak
2357 to the potential implications of our actions. And that is what
2358 we have, Mr. Chairman, in our panel. And so I want to thank
2359 today's witnesses for being here and sharing your insights.

2360 Let me start with Ms. Charo. During your testimony, you
2361 noted that "approval of a drug for labeled" -- I am quoting you
2362 -- "indication does not mean it will be safe and effective for
2363 off-label uses." And that "additional studies are needed to
2364 explore them."

2365 Now it would seem to me that if a manufacturer wished to
2366 communicate about an off-label use for a product that manufacturer
2367 must already have reason to believe that this product is safe
2368 and effective for the given off-label use. So if there is already
2369 evidence supporting an off-label use, can you explain why
2370 additional studies would be necessary?

2371 Ms. Charo. Of course. And I think other people on this
2372 panel are even more expert than I in research trial design, but
2373 the reality is that evidence comes in many forms and often it
2374 is based on small numbers of people with very homogenous kinds
2375 of situations. But in the real world, you need larger numbers
2376 of people with a wider variety of background conditions and
2377 complexities in order to detect both the areas in which it will
2378 or will not be effective. It might depend upon co-morbidity,
2379 and also to detect some of the less common kinds of side effects

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2380 or adverse events. And those things are relevant to
2381 deciding whether or not the benefit that some people get will
2382 be sufficient to outweigh the kinds of risks or failures to work
2383 for other people.

2384 So initial evidence often can look extremely promising.
2385 Pre-clinical evidence, particularly we have cured cancer in mice
2386 countless times, but also early human evidence is often very,
2387 very promising and then when we move into larger trials with more
2388 complicated and more diverse populations we discover that,
2389 unfortunately, it was misleading. And it is just a matter of
2390 basic statistics as well as medicine. That is why there is such
2391 an emphasis on properly-controlled trials of sufficient size and
2392 statistical power and the ability, too, to look at the possibility
2393 of inherent biases and how you structure the trials. It is very
2394 easy to structure trials in a way that subtly lead to one
2395 conclusion or another without even intending to do so. That is
2396 the value of the independent expert eyes that the agency brings.

2397 Mr. Engel. Thank you very much. Dr. Kesselheim, you also
2398 touched on the need for additional studies in your testimony.

2399 So I would like to ask you the same question. If there is already
2400 evidence supporting an off-label use, can you explain why
2401 additional studies would be necessary?

2402 Dr. Kesselheim. Sure. I mean if there is evidence
2403 supporting an off-label use and there are certainly plenty of
2404 ways that that evidence can already be communicated under the

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2405 current rules. I think the rules are fairly clear about what
2406 types of communications are, where there are opportunities to
2407 communicate that information. And if there are additional
2408 studies and again, I think the importance is what is the nature
2409 of that evidence. How is that evidence defined? What are the
2410 statistical methods that were used in testing? How is the
2411 population defined? And these are details that, you know,
2412 average physicians don't know a lot, don't have a lot of training
2413 in and don't know a lot about it and these are the details that
2414 the FDA has expertise in. And so if there are nuances that might
2415 not be caught in initial examination of the information,
2416 additional studies that are necessary, then the numerous dozens
2417 of experts at the FDA with training in various different fields
2418 can identify that and pick up on that and determine whether or
2419 not what might initially be seen in the data, turns out to be
2420 legitimate.

2421 Mr. Engel. Thank you. Ms. Charo, I have one final question
2422 for you. It is my understanding that in January the FDA released
2423 draft guidance regarding which manufacturer communications are
2424 consistent with the FDA required labeling in which are not. And
2425 I understand also that this guidance has not yet been finalized.

2426 So do you feel that draft guidance strikes the right balance
2427 between enabling potentially helpful communications to take place
2428 and protecting patient safety and why shouldn't we legislate in
2429 this space to provide even greater clarity for manufacturers?

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2430 Ms. Charo. I do think the FDA is moving in the right
2431 direction. I agree that draft guidances would be better off if
2432 they were finalized guidances, although it is worth noting that
2433 a tremendous amount is already done through draft guidances at
2434 the FDA without any Fifth Amendment due process questions being
2435 raised about it.

2436 The thing that I think is most important about what the FDA
2437 has been doing is its insistence that actual knowledge about how
2438 your product is being used can be in some instances considered
2439 to be evidence that you actually intended for the product to be
2440 used that way. I think a lot of the debate has been around that
2441 phenomenon. But we have seen that phenomenon in other contexts.

2442 We have seen it in areas having to do with constructive knowledge
2443 in tort law where if you know something is about to happen and
2444 you actually go ahead and do all the things that are necessary
2445 for it to come about, you are actually going to be considered
2446 to have intended that to happen in many cases.

2447 On the other hand, we have seen in the area of gun law, a
2448 lot of resistance to the idea that actual knowledge constitute
2449 intent. I do think that is an area where we have to have some
2450 more discussion to clarify, but I also think that it is risky
2451 to simply allow for an expansion of communication while
2452 simultaneously saying but now that I have communicated more, the
2453 fact that I know that it is having an effect doesn't mean that
2454 I intended that particular outcome. I think to have both of those

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2455 things at once I think is particularly risky. Choosing one or
2456 the other at least would be the right direction.

2457 Mr. Engel. Thank you very much. Thank you, Mr. Chairman.

2458 Mr. Burgess. The gentleman yields back. The chair thanks
2459 the gentleman. Does the gentleman from Texas have a unanimous
2460 consent request?

2461 Mr. Green. Yes, Mr. Chairman, I have a consent request.

2462 Mr. Burgess. I will yield to the chairman for a unanimous
2463 consent request.

2464 Mr. Green. I move that we have statements in the record
2465 from the American Health Insurance Plans, the Campaign for
2466 Sustainable Drug Pricing, and also Public Citizen Action be placed
2467 into the record.

2468 Mr. Burgess. Without objection, so ordered. Seeing no
2469 other members wishing to ask questions, I once again want to thank
2470 our witnesses for being here today.

2471 Pursuant to committee rules I remind members they have ten
2472 business days to submit additional questions for the record.
2473 I ask the witnesses to submit their responses within ten business
2474 days upon receipt of those questions. And without objection,
2475 the subcommittee stands adjourned.

2476 [Whereupon, at 12:37 p.m., the subcommittee was adjourned.]

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