

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22

DEVICES PROPOSED FOR A NEW USE  
WITH AN  
APPROVED, MARKETED DRUG  
Thursday, November 16, 2017  
9:02 a.m.

Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20903

Reported by: Michael Farkas

A P P E A R A N C E S

1 DR. RACHEL SHERMAN - PRINCIPAL DEPUTY COMMISSIONER

2 MR. JOHN WEINER - OFFICE OF COMBINATION PRODUCTS

3 MS. DIANE MALONEY - CENTER FOR BIOLOGICS, EVALUATION,  
4 AND RESEARCH

5 DR. DOUGLAS THROCKMORTON - CENTER FOR DRUG EVALUATION  
6 AND RESEARCH

7 DR. JEFF SHUREN - CENTER FOR DEVICES AND RADIOLOGICAL  
8 HEALTH

9 MS. SIYEON LEE - OFFICE OF CHIEF COUNSEL

10 DR. KHAUDEJA BANO - INTERNATIONAL SOCIETY FOR  
11 PHARMACEUTICAL ENGINEERING

12 DR. MELODIE DOMURAD - MERIC MEDICAL SYSTEMS, INC

13 DR. KIRK SEWARD - MERCATOR MEDSYSTEMS

14 MR. BRAD THOMPSON - COMBINATION PRODUCTS COALITION

15

16

17

18

19

20

21

22

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22

C O N T E N T S

	PAGE
DR. KHAUDEJA BANO	10
DR. MELODIE DOMURAD	22
DR. KIRK SEWARD	35
MR. BRAD THOMPSON	61

## 1 P R O C E E D I N G S

2 DR. SHERMAN: Good morning, everyone. Welcome  
3 to FDA's public hearing on Devices Proposed for a  
4 New Use with an Approved, Marketed Drug.

5 My name is Rachel Sherman. I am the Principal  
6 Deputy Commissioner at the Food and Drug  
7 Administration. I will serve as the presiding  
8 officer for this hearing.

9 Before we begin, I will make a few  
10 administrative announcements. Please silence all  
11 cell phones or other mobile devices, as the panel  
12 has done, as they may interfere with the audio in  
13 the room today.

14 We ask that all attendees sign in at the  
15 registration tables outside the meeting room. The  
16 restrooms are located in the lobby, past the  
17 coffee area to the right, and down the hallway.

18 The purpose of this hearing is to provide an  
19 opportunity for broad public input on a potential  
20 approach for devices referencing drugs, or DRDs,  
21 that may allow certain device sponsors to seek  
22 marketing authorization for devices labeled for

1 use with a drug that is already approved and on  
2 the market when the drug sponsor does not wish to  
3 pursue this new use.

4 FDA will use the information that it obtains  
5 during this public meeting as well as the comments  
6 that are submitted to the public docket -- and  
7 you're going to hear us say that several times  
8 because the docket is really very important, and  
9 we do study it very carefully -- those submitted  
10 by the public -- to help inform FDA's policy  
11 development in this area.

12 I would now like to ask the FDA panel to  
13 introduce itself.

14 MR. WEINER: Hi. I'm John Weiner, the  
15 Associate Director for Policy for the Office of  
16 Combination Products.

17 MS. MALONEY: Good morning. I'm Diane  
18 Maloney, Associate Director for Policy in the  
19 Center for Biologics, Evaluation, and Research.

20 DR. THROCKMORTON: Good morning. I'm the  
21 Deputy Director for Regulatory Programs in the  
22 Center for Drug Evaluation and Research.

1 DR. SHUREN: Good morning. I'm Jeff Shuren.  
2 I'm the Director of the Center for Devices and  
3 Radiological Health.

4 MS. LEE: Hi. I'm Siyeon Lee with the Office  
5 of the Chief Counsel.

6 DR. SHERMAN: Thank you. I would also like to  
7 identify the FDA press contact, Lauren Smith Dyer,  
8 who's here and waving her hand. If any members of  
9 the media are here today, please sign in. And if  
10 you have any questions or interested in speaking  
11 with the FDA about this public meeting, please  
12 contact Ms. Smith Dyer.

13 However, in keeping with the purpose of the  
14 public meeting, which is for FDA to listen to  
15 comments from the presenters, the panel members  
16 and FDA employees will not be available to make  
17 statements to the media.

18 On our agenda today, we have four speakers --  
19 so we have the luxury of time for once -- with  
20 scheduled presentation slots. In order to keep to  
21 the agenda as closely as possible, I will outline  
22 a few ground rules.

1           First, this meeting is informal. The rules of  
2 evidence do not apply. Only FDA panel members  
3 will be allowed to question a presenter. No  
4 participants may interrupt the presentation of  
5 another participant.

6           And as today's meeting is a listening meeting,  
7 the FDA panel will not be able to address  
8 questions.

9           This public meeting is subject to FDA's policy  
10 and procedures for electronic media coverage of  
11 FDA public administrative proceedings.  
12 Representatives of the electronic media may be  
13 permitted subject to certain limitations to  
14 videotape, film, or otherwise record FDA's public  
15 administrative proceedings, including the  
16 presentation of the speakers here today.

17           The meeting will be transcribed and the  
18 transcript may be accessed on the FDA website  
19 approximately 30 days after the meeting.

20           Each individual registered to speak has been  
21 given a 15-minute time slot on the agenda.  
22 Following each presentation, the FDA panel may

1 also ask clarifying questions. If a speaker ends  
2 early or the questions from the panel do not take  
3 the full allotted period, we intend to move to the  
4 next speaker. This means speakers may find  
5 themselves being called up to give their  
6 presentations before the time that is listed on  
7 the agenda.

8 We have at least three of the four speakers  
9 present.

10 For those of you who did not register to make  
11 a presentation but would like to present your  
12 comments at this meeting, you may be able to speak  
13 during the open public comment period of the  
14 meeting, which is scheduled to begin at  
15 approximately 10:45.

16 Those interested in presenting during the open  
17 public comment period at the conclusion of the  
18 presentations should sign up at the registration  
19 table outside the meeting room by 10:00 a.m. for  
20 one of the five-minute speaker slots that will be  
21 available.

22 This meeting is not your last chance to



1 comment. The docket will be open until January  
2 15th, 2018, and we strongly encourage all  
3 interested parties to submit comments to the  
4 docket by that date.

5 Please see the Federal Register notice, which  
6 is available as a handout at the registration  
7 table if you would like additional details on how  
8 to submit comments to the public docket. Once  
9 again, to emphasize, the docket is very important  
10 to us and we do appreciate the time and effort  
11 that go into the comments.

12 Before we hear from our first speaker, I'd  
13 like to provide a few additional instructions for  
14 the presenters. We request that each presenter  
15 keep to their allotted time so that we are able to  
16 keep to the schedule.

17 When you speak, you will come up to the podium  
18 here, and you will see that there is a small light  
19 on the table next to the podium which will be  
20 green when you begin. It will go to yellow when  
21 there is one minute left. And when the  
22 presentation time has ended, it will turn red.

1           So if that happens, I may ask you to conclude  
2           your remarks. I apologize in advance if I  
3           interrupt any of you, but again, we request that  
4           you keep to your allotted time.

5           Speakers can provide additional comments that  
6           go beyond what they cover by submitting comments  
7           to the docket.

8           Thank you and we will now proceed with the  
9           presentations. The first speaker is Khaudeja --  
10          and I apologize if I butcher anyone's names --  
11          Bano.

12          DR. BANO: Good morning, everyone. I'll be  
13          addressing Question number 4 from the docket  
14          related to post-market safety reporting,  
15          specifically focused on challenges related to that  
16          topic. Want to specify -- because I'm involved  
17          with so many industry forums, I want to specify  
18          this is my personal opinion. Anything I'm sharing  
19          here does not represent or reflect the opinion of  
20          any organization I work with.

21          The reason I'm standing here and talking to  
22          you is I have an interest in post-market safety,

1           mainly from a combination product perspective, but  
2           specifically this adds more complexity to that  
3           existing challenge that we see.

4           So the devices proposed for a new use with an  
5           improved or marketed drug are proposed for three  
6           reasons. The first one, either to improve or  
7           enhance the safety or effectiveness of an already  
8           marketed drug in its approved indication.

9           Second, to expand use with the approved drug  
10          for an indication for which the drug is not  
11          approved. And thirdly, any additional benefit  
12          such as increasing use of comfort or convenience.

13          In order to achieve these, there is usually  
14          either a change in dose, route, or the delivery  
15          rate of administration. The reason I reemphasize  
16          this is to highlight this will change the safety  
17          profile of the drug product.

18          The requirement or the expectation based on  
19          what has been outlined is for the product -- for  
20          the market authorization holder to plan to  
21          adequately address adverse events, including  
22          medical errors, specifically the areas of

1 identifying, capturing, reporting, and responding  
2 appropriately to adverse events associated with  
3 the drug to be used per the DRD labeling.

4 My concern here is how will a device company,  
5 an organization that's set up as a device  
6 organization prepare themselves to truly identify  
7 -- they won't be able to identify whether an  
8 adverse event happened or not, but will they be  
9 set up to identify what is causing the adverse  
10 event?

11 I have questions around capturing, and I'll  
12 address them a little later. Again, reporting, we  
13 need further clarification and understanding, and  
14 I want to highlight some of the challenges on  
15 those topics.

16 So when it comes to communicating safety  
17 information for such a product, there will  
18 obviously be device-related safety information.  
19 Then there will be drug-related safety  
20 information. I do want to specifically draw  
21 attention to the places where interaction between  
22 the drug and device will occur.

1           Where and how will that information be  
2           captured effectively enough to be communicated  
3           with all the caveats to the end product user,  
4           whether it's a healthcare professional or a  
5           consumer or a patient?

6           Now, the how. So what is the recommended most  
7           appropriate reporting approach specifically when  
8           it comes to drug-related events? Is the  
9           organization expected to follow the device  
10          reporting approach using the 30-day malfunction  
11          report, or the drug biologic pathway to report it  
12          in 15 days, or I understand it's not truly a  
13          combination product as identified right now, but  
14          is the expectation for us to follow the drug  
15          device combination pathway, or is there a fourth  
16          one?

17          From a challenge to the DRD manufacturers, the  
18          question here is who is going to capture the  
19          information and how? Is the organization going to  
20          create a new or an additional wing to specifically  
21          address the pharmacovigilance aspect because drugs  
22          do behave differently?

1           An adverse event is an adverse event. I  
2 understand. But if you look at the depth of how  
3 an event is identified, it may differ  
4 significantly between how a device organization  
5 views it versus a drug organization.

6           Going back to my question of where will this  
7 information be captured, is it going to be  
8 captured in a single entity system that's used by  
9 the device organization, or do we need two  
10 different platforms and databases to be able to  
11 handle, capture, analyze the information  
12 appropriately?

13           When it comes to reporting, is this  
14 information going to be reported to CDRH or for  
15 the drug side are we talking about sending it to  
16 CDER?

17           At a very high level, some of the key  
18 challenges -- and I know some of these have been  
19 talked about at length, there is a significant gap  
20 with missing the safety history when it comes to  
21 the drug and its behaviors.

22           When you think about a pharma organization not

1 pursuing a certain indication or a certain route  
2 of administration or a dosage, there are reasons.  
3 Maybe it's at an animal study level that there was  
4 data that prevented them. It could be safety. It  
5 could be efficacy.

6 We have to make sure -- how do we ensure that  
7 this device organization will have a thorough  
8 understanding even from an expectedness assessment  
9 of an adverse event? Will there be infrastructure  
10 and appropriate training in the organization that  
11 now has responsibility for an area that's -- that  
12 they are naïve to?

13 The data architecture questions, I understand  
14 that the EMDR update that came out has provisions  
15 for including up to 20 drug information fields in  
16 the MDR form. That's not enough. That doesn't  
17 say anything about the drug and its behaviors.

18 There are processes that are very unique to  
19 drugs, the whole causality assessment,  
20 relatedness, the attribution. Similarly, devices  
21 have their own, you know, definitions, the whole  
22 likely to cause, should it recur, we need -- what

1 is a malfunction.

2 When you mix a drug with a device, now how do  
3 you define your malfunctions? Is that going to  
4 change the approach?

5 Coding is another challenge. Suppose I have  
6 an event I'm ready to submit, whether it's to CDRH  
7 or to CDER. There is meta coding on one hand and  
8 CDRH has their own codes that they assign,  
9 specifically patient codes.

10 How are we going to address the periodic  
11 safety reporting? I have a drug manufacturer who  
12 has a certain drug profile. They maintain,  
13 monitor, and do the appropriate surveillance.

14 Going back to the initial requirement of  
15 reacting, is the device organization going to be  
16 prepared enough to react to what they find because  
17 of the drug-device interaction but also because of  
18 the changed dosage, the changed route of  
19 administration?

20 We want to learn from history to ensure we do  
21 not repeat any of the challenges and learn from  
22 it. How are we going to address corrections and



1 removals, any field actions? Is it going to be  
2 easy to discern whether it was a drug quality  
3 issue that led to certain behaviors or adverse  
4 events, a device quality issue, or a drug-device  
5 interaction issue?

6 I know those will be studied. Will studying  
7 it to the magnitude that they will be studied  
8 suffice to protect public health?

9 Some of the challenges for the reference drug  
10 manufacturers, suppose they get informed about a  
11 new adverse event that's reported to the DRD  
12 manufacturer. That information, how are they  
13 going to handle it? Are they going to -- is it  
14 adequate to update labeling based on general  
15 pharmacovigilance practices?

16 Again, how do we draw the line of off-label  
17 use or use error? If there was a product that  
18 contraindicated, or in their limitations of use,  
19 highlighted a certain use and now I have -- or we  
20 have -- a device manufacturer that's promoting  
21 that use? Granted, both are right, but if you  
22 stand in the place of a consumer or a healthcare

1 professional, it is confusing. Conflicting  
2 information may exist at the same time.

3 How are we going to inform patients and  
4 healthcare professionals about what is use error,  
5 what is off-label use, and any additional safety  
6 information along the way?

7 From a logistical point of view, if you think  
8 about field actions and corrections, people who  
9 have lived some of these, even doing it for a  
10 single product, a device recall or a drug recall,  
11 or a combination product recall, now think about  
12 this complexity where you have two entities that  
13 are not even talking to each other, trying to pull  
14 a recall.

15 We all have good intentions, but how will we  
16 logistically make it happen? Who will own the  
17 product risk profile? Is it the drug manufacturer  
18 or the DRD manufacturer?

19 My closing remarks, there is an additional  
20 global product profile that has to be maintained.  
21 The drug manufacturer owns that profile, but now  
22 this introduces an additional challenge. Do they

1 include this new route of administration or  
2 dosage? How do they communicate that globally?

3 Again, going back to the causality, if you  
4 have an adverse event from a post-market safety  
5 assessment, who is going to make the call -- who  
6 is the decision maker, whether it's a drug  
7 causality, device, or the combination effect?  
8 I'll tell you. High concentrations of alcohol in  
9 a simple on-market product can cause chelation on  
10 some of the delivery systems.

11 I understand those will be studied, but will  
12 they be studied adequately for all markets?

13 Let's say suddenly the drug is being withdrawn  
14 for no reason -- I mean, no safety reason. The  
15 manufacturer decides to discontinue the drug,  
16 marketing of that drug. Then what happens? Where  
17 do we leave our patients?

18 Another challenge is multiple reports. If the  
19 drug manufacturer gets notified, they will -- they  
20 have an obligation to report and so will the DRD  
21 manufacturer.

22 Now, you end up with potentially duplicate

1 reports with discrepant information. Hopefully  
2 it's the same information, but could have  
3 discrepant information. Who bears the burden of  
4 analyzing the post-market safety data of this  
5 combination?

6 I leave you with a big caveat, the clinical  
7 trials. There will be other speakers talking  
8 about it, but clinical trials help formulate my  
9 label.

10 If done right, we can come out with a very  
11 robust label, but the question is, who will take  
12 that burden on?

13 End of day, as I stand here as a safety  
14 physician, all that matters to me is safety. I'm  
15 all for innovation. But safety comes first.  
16 Thank you.

17 DR. SHERMAN: Thank you for your remarks.

18 Does the panel have any questions?

19 MR. WEINER: Thank you very much. I just had  
20 one question, a kind of combined issue. Regarding  
21 the kind of experience with the drug of the device  
22 manufacturer and access to information on safety

1 events, do you have any thoughts for how they  
2 might kind of enhance their understanding of the  
3 drug product and how they might ensure reports  
4 come to them to address for FDA?

5 DR. BANO: So if I can clarify, you're talking  
6 about how there can be effective communication  
7 between the drug manufacturer and the device  
8 manufacturer?

9 MR. WEINER: I guess that's a possibility, but  
10 the assumption of the DRD paradigm is that the  
11 companies don't have relationships.

12 DR. BANO: Right.

13 MR. WEINER: You know, how would you try to  
14 manage that implication?

15 DR. BANO: So to me, there will be adequate  
16 public information available. There will be  
17 literature available. There are -- clinical trial  
18 data is available. There will be comprehensive  
19 information, especially if it is a well-  
20 established drug product.

21 So you can rely on that plus the scientific  
22 know-how of the drug molecule. But will that be

1           adequate? I can't say that. It depends on the  
2           drug safety profile.

3                    Again, even with an established safety  
4           profile, my personal preference would be for some  
5           level of communication to occur between the two  
6           organizations just to make sure that there isn't  
7           something that -- it might not be a safety topic,  
8           but there isn't something that would help the DRD  
9           manufacturer make the right decision.

10                   So there is publicly available information  
11           that they can rely on. Literature would be a good  
12           source. Thank you.

13                   DR. SHERMAN: Any other questions?

14                   Thank you for your remarks.

15                   DR. BANO: Thank you.

16                   DR. SHERMAN: Our next speaker is Melodie  
17           Domurad from Merit Medical Systems.

18                   DR. DOMURAD: Good morning, and thank you for  
19           this opportunity to the Agency, the panel, and the  
20           many people who helped organize this meeting and  
21           given me the opportunity to speak to you today.

22                   I would like to address Question 7, the

1 challenges that exist at the investigational  
2 application stage and how can those challenges be  
3 addressed.

4 Devices that are going to reference drugs as a  
5 group will encompass a wide variety of products  
6 with a range of experience about the safety and  
7 effectiveness of both the drug and the device  
8 separately.

9 In some instances, however, the device may  
10 already have been cleared or approved for use  
11 without the drug. The drugs, by definition, are  
12 going to have been previously approved. And so  
13 there will be safety and effectiveness data for  
14 them alone, possibly not for that indication but  
15 conceivably having been used or published.

16 In instances where both of the medical  
17 products have demonstrated a history of being safe  
18 and effective, that knowledge should be taken into  
19 account in review of the IDE and PMA submissions.

20 I think most people would agree that well-  
21 designed Phase 3 prospective studies are critical,  
22 but they should also be realistic in scope. They

1 must be completable studies. Studies that cannot  
2 be finished, cannot be enrolled, benefit no one -  
3 including the patients. Therefore, the IDE  
4 process and the subsequent PMA should not be so  
5 burdensome that it cannot be viable.

6 And the drug referencing device response to  
7 the size or the quality of that unmet medical need  
8 should be taken into account in that review.

9 I'm going to give you a specific case in point  
10 which I think provides an illustration.

11 Hepatocellular carcinoma accounts for nearly all  
12 of the primary liver cancer, is the second most  
13 frequent cause of cancer-related death worldwide.

14 The U.S. cancer update provided by a coalition  
15 of the American Cancer Society, the Center for  
16 Disease Control, the National Cancer Institute,  
17 and the North American Association of Central  
18 Cancer Registries, published in 2016, dealing with  
19 the years 2003 through '12, indicated that while  
20 overall deaths from cancer are decreasing for  
21 hepatocellular carcinoma, death and incidence  
22 rates increased significantly between 2008 and



1           2012 and these rates are anticipated to continue  
2           rising at least through 2020. So we have an unmet  
3           need.

4           Transarterial chemoembolization has been the  
5           most common treatment for intermediate stage  
6           hepatocellular carcinoma for over 30 years. For  
7           those who are not familiar with this treatment,  
8           it's a dual action treatment. The concept,  
9           because most liver tumors are not resectable and  
10          because there is a lack of organs for transplant,  
11          a standard treatment for intermediate stage is  
12          through a transarterial catheter to deliver one or  
13          more chemotherapies mixed with an ethiodized oil,  
14          an emulsion, much like a salad dressing, followed  
15          or in conjunction with a type of embolic.

16          This allows the drug to go into the tumor, to  
17          be targeted, and then the embolic prevents  
18          backflow and also holds that chemotherapy and  
19          emulsion in the tumor.

20          However, there's also venous outflow. So even  
21          with this targeted treatment, you do get systemic  
22          exposure. This, however, has been a treatment for

1 over 30 years. The problem is, there is no  
2 consensus.

3 Different drugs and different combinations and  
4 different dosages at different treatment intervals  
5 with different follow-up imaging for different  
6 endpoints have been, if you will call it, a  
7 standard.

8 Transarterial chemoembolization is identified  
9 as a standard of care treatment for intermediate  
10 stage hepatocellular carcinoma by the American  
11 Cancer Society, the American Society of Clinical  
12 Oncology, the National Comprehensive Cancer  
13 Network, the American Association for the Study of  
14 Liver Disease, and the Society of Interventional  
15 Radiology, among others.

16 So the concept of the treatment is well known.  
17 It's been used for a long time, and it is  
18 recognized as being effective. However, no  
19 embolic, that device agent, has ever been FDA  
20 approved for the indication of chemoembolization,  
21 which means physicians have no on-label way of  
22 performing this standard of care.

1           I present to you an algorithm here for  
2           hopefully some illustration. Looking at  
3           hepatocellular carcinoma overall, it is  
4           particularly complex among cancers. As with  
5           virtually all cancers, extent, size, location  
6           plays an important role in treatment decision, but  
7           virtually no healthy patients develop  
8           hepatocellular carcinoma. It is typically the  
9           result of 30 to 40 years of insult from toxins,  
10          from -- excuse me -- from toxins, from various  
11          exposures, and primarily from viral burden load.

12          Hepatitis C is most common in the U.S., but B  
13          is also well seen. So physicians are making their  
14          treatment decisions based on not just the stage  
15          and extent of the cancer, but also the stage and  
16          the extent of the underlying liver disease that  
17          led to that cancer, as well as the cirrhosis which  
18          is a side effect which affects liver function. So  
19          they are also taking into account the existing or  
20          remaining liver function. So multifactorial, of  
21          course.

22          Resection, transplantation, and local ablation

1 are considered potentially curative. However,  
2 altogether, those three account for only about 25  
3 percent of hepatocellular carcinomas. At any  
4 given time, looking at the entire population of  
5 patients with hepatocellular carcinoma, about 50  
6 percent are receiving transarterial  
7 chemoembolization as their primary therapy, a  
8 procedure for which no product has been FDA  
9 approved.

10 However, when you take into account the fact  
11 that those patients who get resection, ablation,  
12 and transplantation frequently have recurrences  
13 overall about 70 percent of patients who have HCC  
14 over the course of their treatment lifetime will  
15 receive TACE, which must now be off-label.

16 Less than two weeks ago I did a search on  
17 PubMed , sorry, using the terms chemoembolization  
18 and hepatocellular carcinoma, which resulted in  
19 244,000 publications. All right. This is a well-  
20 known treatment for a well-known cancer.

21 However, despite a great deal of data out  
22 there, it's difficult to compare outcomes in

1 studies because of the variability in the embolic  
2 devices, the chemotherapy types, combinations,  
3 doses, treatment intervals, endpoints, and that  
4 doesn't even take into account the patient  
5 population with different stages of disease and  
6 different amounts of underlying liver disease.

7 So with no embolic device approved for  
8 chemoembolization, physicians just choose amongst  
9 the many possibilities that are out there with  
10 studies that are not easy, to compare.

11 So giving you an example of an IDE process,  
12 BioSphere Medical, which is now part of Merit  
13 Medical, sought to address this unmet need in 2009  
14 with an IDE submission to conduct a Phase 3 study  
15 that is of an embolic. But instead of just  
16 following the delivery of chemotherapy, can  
17 actually load the chemotherapy ionically so when  
18 it's delivered it stays within the tumor and you  
19 have sustained dilution. So the concept is  
20 identical with less venous outflow, so less  
21 systemic exposure.

22 This embolic device had been cleared

1 previously for use in hypervascular tumors, of  
2 which hepatocellular carcinoma is one of them,  
3 three years previously. So there is evidence,  
4 clinical evidence, safety and efficacy for the  
5 device alone.

6 The same embolic was CE marked two years prior  
7 to this IDE for this specific indication, so there  
8 is also data existing for delivery of Doxorubicin,  
9 potential adverse events, safety and efficacy.

10 And Doxorubicin itself is one of the grandparents  
11 of chemotherapy. And there's a lot of safety and  
12 effectiveness data out there.

13 And because of those 244,000 publications, a  
14 lot of it is actually for this indication,  
15 although it's not approved for this indication.

16 A pre-IDE package was sent to the Agency in  
17 June of 2009 with prompt feedback in 2000 --  
18 August of 2009, and the IDE was submitted in  
19 October 2009.

20 Over the subsequent year, there were three IDE  
21 amendments in response to three deficiency letters  
22 with five conference calls, a face-to-face

1 meeting, a multitude of emails and calls,  
2 ultimately resulting in an appeal submitted in  
3 August 2010 with conditional approval in November  
4 2010 and full approval in February of 2011, so  
5 essentially a year's process to review a device  
6 which had existing data and for a drug that had  
7 existing data and was used substantially,  
8 frequently off-label.

9 So my recommendation is that the IDE review  
10 for devices referencing drugs to conduct clinical  
11 trials should take into account the extent of  
12 existing safety and effectiveness data for  
13 products, the degree and impact of the unmet  
14 medical need -- in this case, a growing unmet  
15 medical need -- and a requirement that the data be  
16 reasonable to demonstrate safety and  
17 effectiveness.

18 Prospective, well-designed Phase 3 studies,  
19 absolutely important, but they must be feasible to  
20 accomplish. And the PMA review should take into  
21 account least burdensome provision and a balance  
22 of pre and post-market data collection.

1           The study that resulted from this IDE, by the  
2           time it was actually approved to be implemented,  
3           the so-called standard of care, which was off-  
4           label, that conventional TACE, was no longer the  
5           most commonly used method of conducting this  
6           treatment method because of data from Europe, from  
7           publications.

8           There was rapid off-label adoption. So by the  
9           time the study could be implemented, only 17  
10          percent -- and this is a published study by GABA  
11          and colleagues in 2012. A survey was conducted in  
12          2010, right, the year that the conditional  
13          approval was received.

14          And it interviewed Society of Interventional  
15          Radiology members who conducted at least 1 to 10  
16          chemoembolizations per year and a variety of  
17          medical facilities. And at that time, only 17  
18          percent of physicians were still doing only the  
19          conventional method of chemoembolization.

20                 Thank you for your attention.

21                 DR. SHERMAN: Thank you.

22                 Does the panel have any questions? Dr.



1 Shuren?

2 DR. SHUREN: You had recommended that there be  
3 an application of the least burdensome approach --

4 DR. DOMURAD: Yes, sir.

5 DR. SHUREN: -- in the PMA. And of course,  
6 those provisions, there's an explicit reference to  
7 devices in the law.

8 Do you believe that that approach should be  
9 applied to entire combination of products, not  
10 just the device, but the drug component as well?

11 DR. DOMURAD: I cannot speak to the wide  
12 range. I am sure that this panel knows far more.  
13 I am familiar only with the types of combination  
14 devices that we would do.

15 I think, honestly, it depends on the amount of  
16 information that is available at the time. So if  
17 there is a lot known about the elements, I think  
18 it should be applied. If the device is entirely  
19 new, or if the use of the drug is completely  
20 different from anything that's been seen before,  
21 that, of course, needs to be taken into account.

22 But the size of the study, the amount of data,

1 and the potential for moving some of that data  
2 collection, especially longest-term data to the  
3 post-market arena, should be considered as a  
4 possibility where the elements are relatively well  
5 understood.

6 DR. SHERMAN: Other questions? I have one.  
7 You reference -- you spoke about PMAs and IDEs.  
8 Do you -- for DRDs, do you think that there might  
9 be an occasion where an NDA or an IND would be  
10 more appropriate?

11 DR. DOMURAD: I do not work for a pharma  
12 company, so that's difficult for me to say. I  
13 think under certain -- again, this is a very wide  
14 field. I mean, if you take all of the devices  
15 that might be combined with all of the drugs that  
16 are out there, we've got a huge spectrum.

17 Do I think that there are times when the  
18 predominant treatment method -- I'm going to take  
19 something -- I'm pulling an example, all right,  
20 out of -- but if you have a vaccine, for example,  
21 that normally comes in a large vial and once you  
22 open it you have to throw it away, so an

1 individual injection syringe, the vaccine here,  
2 the biologic is going to be the predominant mode,  
3 and the syringe is going to be the device which is  
4 combined with it.

5 I think in an instance like that, clearly an  
6 IND or a BLA would be the appropriate. So where  
7 the primary effect is coming from or what the  
8 balance is, it should probably have an impact.

9 DR. SHERMAN: Thank you. Any additional  
10 questions? Thank you for your remarks?

11 DR. DOMURAD: Thank you.

12 DR. SHERMAN: Our next speaker is Kirk Seward  
13 from Mercator MedSystems.

14 DR. SEWARD: Thank you all. I want to thank  
15 the esteemed panel for facilitating this public  
16 hearing and to congratulate the Agency on working  
17 hard to confront an issue that's important both to  
18 medicine and to the development of novel therapies  
19 that utilize well-known therapeutic agents,  
20 particularly those with well-characterized safety  
21 profiles.

22 My name is Kirk Seward. I hold a bachelor's

1 and master's degree from MIT, and my Ph.D. in  
2 mechanical engineering from the University of  
3 California at Berkley. I'm the founder and  
4 president and chief science and technology officer  
5 at Mercator MedSystems.

6 We're a company that's developing drug  
7 delivery devices for local, site-specific drug  
8 delivery deep in the body. As a medical device  
9 entrepreneur, inventor, and innovator, I'm happy  
10 to be here presenting at the meeting.

11 It's clear from the written proposal and the  
12 requests for comment describing devices  
13 referencing drugs, or DRDs, that the process is  
14 intended to address the need for greater clarity  
15 and promote consistent regulatory expectations  
16 among sponsors and innovators of medically  
17 necessary therapies. The strong efforts by those  
18 who have drafted this proposal is obvious.

19 There are some points that I wish to clarify  
20 and respond to in the public comment, and in doing  
21 so, I first want to provide some background in the  
22 form of a case study example of where the DRD

1 process would clearly apply. Beyond that, I'd  
2 like to comment on how to establish risk profile  
3 in determining Class II or Class III DRD  
4 applications, on application of the evidence  
5 burden as it relates to standards of substantial  
6 evidence or reasonable assurance, and then briefly  
7 on user confusion and medication error or use  
8 error factors and on identification of generic  
9 drugs within DRD labeling.

10 Finally, I'd like to comment on how the DRD  
11 proposal relates to CDRH's regulatory science  
12 priorities in 2017.

13 First, to provide a bit of a background in a  
14 case study, at Mercator MedSystems, we manufacture  
15 the Bullfrog Micro-Infusion Device. The device is  
16 introduced into the arterial or venous circulation  
17 and advanced to a target site of interest where  
18 the balloon is inflated to push a microneedle  
19 through the vessel wall.

20 At that target site, therapeutic or diagnostic  
21 agents can be deposited into the tissues outside  
22 of the vessel wall.

1           It's important to note that this device is  
2           already 510(k) cleared based on its demonstrated  
3           safety, efficacy, and substantial equivalents to  
4           devices previously marketed under 510(k)  
5           clearance.

6           The intended use of the device is that in  
7           selective areas of peripheral and coronary  
8           vessels, it's intended for the infusion of  
9           diagnostic and therapeutic agents into the vessel  
10          wall or perivascular area or intraluminal, fairly  
11          straightforward.

12          We've been studying the device in clinical  
13          trials with a variety of legally marketed agents  
14          including the generic corticosteroid Dexamethasone  
15          sodium phosphate for injection. It's a well-known  
16          and a well-characterized injectable solution.

17          These trials are either completed or underway.  
18          With the delivery of Dexamethasone, we've been  
19          studying an anti-inflammatory use of the drug to  
20          reduce vascular inflammation after mechanical  
21          interventions to open blood vessels -- to open  
22          peripheral arteries predominantly.

1           While localized anti-inflammatory usage is  
2           commonly described within the generic labeling,  
3           and with a loose interpretation of the  
4           Dexamethasone label, the proposed use of the drug  
5           falls within the therapeutic intent of the drug  
6           and within the dosage range in the labeling, that  
7           being localized anti-inflammatory application,  
8           when read strictly against the drug label, the  
9           usage can be interpreted as falling outside of the  
10          indications for the drug since there is no  
11          specifically described perivascular route of  
12          administration nor indication for vascular anti-  
13          inflammation by local administration within the  
14          drug labeling.

15          While we've contacted generic drug  
16          manufacturers who make Dexamethasone sodium  
17          phosphate for injection, there has been a complete  
18          lack of interest from them in making labeling  
19          updates or letting us reference their drug master  
20          files.

21          This makes sense from their perspective for a  
22          number of reasons. First of all, when taken as a

1 group, these companies are not interested in  
2 adding new labeling claims to their generic drugs  
3 because it introduces new liability, which is  
4 offset by only a very limited upside since, in  
5 many cases, the generic drugs are sold for less  
6 than \$10 a vial.

7 And second, no individual general drug maker  
8 is likely to step up and change their label  
9 because of the reality of immediate substitution  
10 where other generic makers could sell into the  
11 indication without incurring the liability taken  
12 by the pioneer company.

13 Based on these behaviors from generic drug  
14 makers, we're locked into the old drug labeling  
15 but trying to innovate the use of the drug and to  
16 provide more information to users. It's clear to  
17 us that applications like this fall squarely  
18 within the intended purview of the DRD proposal.

19 Turning now to the individual questions  
20 solicited within the request for public comment,  
21 I'd like to first look at Question 1 about public  
22 health, scientific, regulatory, or legal issues



1 that should be considered.

2 In addressing the question, I contend that  
3 there are specific regulatory issues that should  
4 be considered in this approach, namely that DRDs,  
5 while described in the request for comments as  
6 most likely requiring premarket approval, or PMA  
7 applications, should not be inherently classified  
8 as Class III devices, or as Class III DRDs.

9 In the request for comments, a statement was  
10 made by the Agency that DRDs would raise different  
11 issues of safety and effectiveness since the drug  
12 aspect of the DRD would be new, but this merely  
13 qualifies DRDs as not likely to be substantially  
14 equivalent to legally marketed predicate devices.

15 And while this is true in most cases, it  
16 simply disqualifies DRDs from traditional 510(k)  
17 path. But the result of the proposal was  
18 different, that the PMA route would inherently be  
19 the appropriate device marketing application.

20 However, I contend that this isn't entirely  
21 accurate since PMAs should only apply to Class III  
22 products, which are those that support or sustain

1 human life, those that are of substantial  
2 importance in preventing impairment to human  
3 health or those that present a potential,  
4 unreasonable risk of injury.

5 In reality, there are a great many drugs that  
6 might be referenced by DRDs that have an  
7 exceedingly safe profile in humans based on years  
8 of use in millions of patients.

9 Nothing specifically inherent to DRDs should  
10 lead to an automatic classification into Class  
11 III. Alternatively, the known safety and risk  
12 profile of the drug should be considered in  
13 determining the classification of the drug or of  
14 the DRD such that DRDs are classified by risk.

15 In this regard, Class III DRDs, or those with  
16 high risk, should require general controls in PMA.  
17 Class II DRDs with moderate to high risk should  
18 require general and special controls and qualify  
19 for traditional or De Novo 510(k) pathway.

20 Meanwhile, in the case of Class I DRDs, which  
21 likely exist and are low to moderate risk, only  
22 general controls should be mandated.

1           It's extremely important that DRDs are not  
2 inherently mandated to traverse the same  
3 regulatory pathway as high-risk Class III devices  
4 but that they are regulated based on their risk  
5 profile which accounts for what is already known  
6 about commonly used drugs, for example.

7           Let us look now at Question 2, the factors in  
8 submission considerations being appropriate and  
9 what modifications should be proposed.

10           In commenting on this, we first look at the  
11 DRD proposal in which the standard of evidence for  
12 demonstrating safety and effectiveness is proposed  
13 to be the substantial evidence standard, which is  
14 the standard that applies to the new uses of drugs  
15 rather than the reasonable assurance of safety and  
16 effectiveness, which is the standard applied in  
17 the examination of devices.

18           While it may be viewed that these standards  
19 have the same intent, they appear to be  
20 implemented differently in regulatory practice.

21           At a minimum, the quantity of clinical  
22 evidence required or mandated by the standards is

1 not equivalent.

2 To demonstrate substantial evidence of safety  
3 and effectiveness requires two adequate and well-  
4 controlled clinical trials with relevant  
5 exceptions such as with label expansions.

6 However, reasonable assurance, as an  
7 evidentiary standard, has no such requirement, and  
8 can often be demonstrated with real-world evidence  
9 or non-randomized trials that compare treatment  
10 group to historical controls or performance goals.

11 Furthermore, the two standards have resulted  
12 in distinctly different types of endpoint data  
13 that are allowed in order to support regulatory  
14 approvals. For example, substantial evidence, the  
15 drug standard, requires clinical outcome measures  
16 including improvements in feel, function, or  
17 survival.

18 Again, no such requirement has been placed on  
19 devices using the reasonable assurance standard.  
20 Rather, device approvals often rely on physical or  
21 mechanical endpoints that may or may not be  
22 surrogates for feel, function, or survival.

1           As an example, if a device safely restores  
2           what would seemingly be normal anatomy, that has  
3           often been deemed enough to allow for approval.

4           To continue on this theme, there may be drugs  
5           referenced by devices that have similar intent to  
6           devices where the intent of the drug may be to  
7           preserve the device outcome. Examples of this are  
8           seen with coated pace maker leads or drug-eluting  
9           stents, which preserve the device's functionality.  
10          Or in the case of drug-coated angioplasty  
11          balloons, which preserve the vessel openness or  
12          vascular patency created by the device.

13          Each of these examples has been designated to  
14          have a device primary mode of action, therefore  
15          the drug coatings have not been held to the device  
16          evidence standards or to the drug evidence  
17          standards in their approvals.

18          The evidence standard applied to the drug  
19          component in these combination devices should not  
20          be unique to combination products that have a  
21          device primary mode of action.

22          For example, in cases where the drug can be

1           unlinked from the device, to accomplish the same  
2           effect while allowing more patient specific or  
3           anatomy specific treatments, such as different  
4           device sizing or different drug dosing, a  
5           patient's medical condition may be more  
6           appropriately addressed and the same regulatory  
7           standard should apply as if a fixed dose of drug  
8           were coated onto a fixed size device.

9           This is highly relevant since primary approval  
10          outcomes for device drug combinations, such as  
11          primary arterial patency, have not been linked to  
12          drug substantial evidence outcomes of feel,  
13          function, or survival, so a double standard should  
14          not be applied whether the drug, whether the  
15          device and the drug are applied together or  
16          separately.

17          There may be cases, of course, where the drug  
18          product -- where the drug provides therapeutic  
19          effect independent of other procedural or surgical  
20          benefit, in which case drug endpoints may more  
21          easily apply, such as the case in which better  
22          delivery of a chemotherapeutic agent for head and

1 neck cancer patients is enabled by a novel device,  
2 for example.

3 Overall, the DRD process is about unlocking  
4 innovation by device innovators that are taking  
5 older drugs with a long history of safe use and  
6 incrementally changing them.

7 In regulating DRDs, CDRH should have the same  
8 flexibility to determine the validity of endpoints  
9 and use the reasonable assurance standard. At the  
10 very least, products with similar medical intent  
11 should be afforded the same standard of evidence,  
12 including what type of endpoints are to be  
13 demonstrated.

14 Other factors also require consideration if  
15 drug standards of evidence are applied  
16 indiscriminately. If the evidence standard of  
17 substantial evidence of safety and effectiveness  
18 prevails, then does it make sense that other  
19 provisions of drug regulations would also apply to  
20 DRDs such as breakthrough designation, fast-track  
21 approval, priority review, or exclusivity  
22 provisions?

1           With specific reference to exclusivity  
2 provisions, assuming an old drug has no patents  
3 covering its use as listed in the Orange Book,  
4 what would happen if new patents describing novel  
5 methods of use of the drug are issued? Would  
6 Orange Book references inherently change in  
7 response to these new patents?

8           In response to Question 4, which addresses  
9 issues surrounding possible user confusion and  
10 medication error, use error, clearly adequate  
11 information should be provided in labeling to  
12 prevent confusion or errors. And to this end, the  
13 same level of detail should be provided as exists  
14 within current standard drug labeling.

15           This should include supplemental information  
16 for each relevant section of the drug labeling  
17 where different or new information is related to  
18 the new use, including indications in usage,  
19 contraindications, warnings and precautions,  
20 dosage and administration, adverse reactions, and  
21 clinical pharmacology.

22           In response to Question 6, addressing the case



1 when multiple versions of the drug, including  
2 generics, are marketed, identifying the challenges  
3 that exist in identifying which generic drug we're  
4 referring to, for DRDs that depend on an  
5 injectable solution, we're confident that all  
6 generics keep to the same formulation solution. As  
7 all ANDAs that reference a single NDA call out the  
8 generic name of the drug, the DRD sponsor should  
9 simply be able to reference the generic name as  
10 well.

11 If there are specific excipients that should  
12 be excluded from the DRD labeling, they should be  
13 called out in the dosage form and strength section  
14 of the drug supplemental label.

15 Clearly, the development of a DRD policy or  
16 guidance shows the forward thinking of the Agency  
17 in confronting complex regulatory issues. It  
18 should be just as clear that the CDRH regulatory  
19 science priorities should be considered with  
20 drafting any such policy or guidance.

21 In particular, the ability to leverage big  
22 data for regulatory decision-making, the

1           leveraging of real-world evidence and employing  
2           evidence synthesis across multiple domains in  
3           regulatory decision-making, and the development of  
4           methods and tools to improve and streamline  
5           clinical trial design should all be accounted for  
6           during any policymaking process.

7                     In this regard, the appropriate standards of  
8           evidence -- in other words, reasonable assurance  
9           versus substantial evidence standards -- should  
10          incorporate the guidance offered by these  
11          priorities.

12                    To summarize, it's my belief, speaking on  
13          behalf of Mercator MedSystems, a company clearly  
14          affected by DRD guidance, that DRDs can be a  
15          valuable tool in advancing medicine without  
16          unnecessary or cumbersome regulatory barriers.

17                    Risks should be assessed independently for  
18          DRDs and the De Novo 510(k) pathway should be  
19          considered with Class II DRDs. Standards of  
20          evidence should be appropriate and should allow  
21          for reasonable assurance of safety and  
22          effectiveness standards to be applied to DRDs.

1           And finally, CDRH regulatory science  
2           priorities should be strongly considered during  
3           the development of any DRD policy or guidance.

4           I thank you for your time.

5           DR. SHERMAN: Thank you for your comments.

6           Questions from the panel? Dr. Throckmorton?

7           DR. THROCKMORTON: Yeah. Can I ask for some  
8           clarification on your response to Question 6.

9           DR. SEWARD: Mm-hmm.

10          DR. THROCKMORTON: You said for DRDs that  
11          depend on an injectable solution, we are confident  
12          that generics all keep to the same solution. I  
13          don't understand what that's meant to -- because  
14          of course we know formulations change fairly  
15          frequently.

16          DR. SEWARD: Sure. ANDAs that reference an  
17          NDA, though, are -- oftentimes have exactly the  
18          same excipients. While it may be true that  
19          excipients change over time or while formulations  
20          change over time, the generics, for example, that  
21          we use and that we reference, all have exactly the  
22          same makeup. And there's four of them available

1 on the open market.

2 In cases like that, where the excipients and  
3 the formulations are the same, we should be able  
4 to reference the generic name with specific --  
5 I'll point to my third bullet here that if there  
6 are excipients that should be excluded from the  
7 DRD labeling, they should be called out in the  
8 dosage forms and strengths.

9 For example, use this drug so long as it  
10 doesn't include this excipient.

11 DR. THROCKMORTON: Thanks. And actually, that  
12 was my second question, was called out by whom?  
13 You're saying that it should be in the device  
14 label to require a specific generic product?

15 DR. SEWARD: Right. And I would actually call  
16 it the supplemental drug label, exactly. But the  
17 labeling that's provided by the device maker, in  
18 this case, the supplemental drug labeling, should  
19 include if there are caveats to that rule, that  
20 there are a number of different formulations of a  
21 drug available.

22 As that number of different formulations

1 becomes larger than one, then the drug -- then the  
2 device maker and the supplemental drug labeling  
3 should call out which formulation specifically is  
4 being referenced. Or exclude any formulations  
5 that are known to cause any safety issues.

6 MR. WEINER: I just wanted to try to maybe  
7 dumb down or kind of summarize or ask you to  
8 summarize your position on data needs.

9 So I guess the question I basically have is if  
10 you assume in a fact pattern A, is a drug company  
11 doesn't want to play --

12 DR. SEWARD: Mm-hmm.

13 MR. WEINER: -- and they're going to need to  
14 get a new label and fact pattern B is going to be  
15 labeling the device, only on the device side,  
16 should the data vary or are you saying the data  
17 should be the same regardless? Is this a legal  
18 issue or is it a scientific issue?

19 DR. SEWARD: That's a good question. It's a  
20 scientific issue.

21 The data should be supportive of the  
22 application. The data should be sensible and

1 appropriate. The data should incorporate the  
2 known usage of these, in many cases, incredibly  
3 well-known drugs, and it shouldn't be taken in a  
4 vacuum that one application of a drug, for  
5 example, in a tissue one centimeter away from  
6 where it's normally used, is a completely novel  
7 approach.

8 To that end, though, it would be the -- it  
9 should be the same data whether it's a drug maker  
10 or a device maker pursuing a claim of expanding a  
11 label for that data, for sure.

12 DR. SHERMAN: Dr. Throckmorton?

13 DR. THROCKMORTON: Thank you for your  
14 presentation. This is really helpful. And I'm  
15 going to ask another sort of fairly technical  
16 question about Question 4.

17 DR. SEWARD: Yes.

18 DR. THROCKMORTON: And this was about  
19 medication, potential confusion because it's, you  
20 know, the different products. And you said that  
21 the same level of detail should be provided as  
22 exists within a current drug label.

1           I think our interest here was to try to  
2           understand when to be concerned. So we had these  
3           two products and it was -- as one product, a DRD  
4           comes before us, when should we ask for additional  
5           testing? When should the potential for confusion  
6           raise to a level that it wouldn't be sufficient to  
7           just include the labeling information from the  
8           approved drug but, in fact, try to understand  
9           whether this combination introduced some new  
10          concern about potential confusion?

11           DR. SEWARD: If the combination introduces a  
12          new concern about potential confusion, then it  
13          should be covered in one of the aspects outlined  
14          here, whether it's the indications, how to use the  
15          drug, how to use the drug in this device, for  
16          example.

17           And I do want to be clear that the same level  
18          of detail should be provided as exists within the  
19          current standard of drug labeling, rather than the  
20          current drug labeling in the case that the drug  
21          label is 50 years old and doesn't meet the current  
22          standard.

1           That being said, most of what could be said  
2           about a drug being delivered in a new way for a  
3           new reason or at a new dosage, should be able to  
4           be covered within these sections of the  
5           supplemental labeling. And the supplemental  
6           labeling shouldn't exist in a vacuum either.

7           Supplemental labeling should be augmentative  
8           to the current labeling that's with the drug,  
9           right? So if the drug, and the vial of drug says  
10          don't use it in juvenile diabetic patients, and  
11          you don't include that in the supplemental  
12          labeling, it doesn't nullify the drug labeling  
13          that travels with the drug as well. It's -- it  
14          should be augmentative to that drug labeling.

15          DR. THROCKMORTON: Thanks.

16          DR. SHERMAN: So if I could pursue that a  
17          little further, you would envision the  
18          supplemental drug labeling, which would be if you  
19          owned and operated by the device company, to  
20          include the information specific to that  
21          particular use.

22          DR. SEWARD: Correct.



1 DR. SHERMAN: And then adverse events would be  
2 reported to the Agency and would -- if the safety  
3 profile were to change, that would be the  
4 responsibility of the device manufacturer.

5 DR. SEWARD: That's right. And the liability  
6 would be incurred to the device manufacturer for  
7 that additional labeling.

8 DR. SHERMAN: And if it were a generic and new  
9 generics came on the market, would it again be the  
10 device manufacturer's responsibility to update the  
11 supplemental --

12 DR. SEWARD: If there's any changes to those,  
13 sure.

14 DR. SHERMAN: And one last thing. That was  
15 actually very helpful. For your example, if  
16 you're willing to comment, do you believe that  
17 that is -- your primary mode of action is drug or  
18 device? If you don't want to comment, it's fine.

19 DR. SEWARD: We make a very long syringe.

20 DR. SHERMAN: Okay. Fair enough.

21 DR. SEWARD: So I don't think that it can be  
22 interpreted that it's not the drug effect that

1 we're going for. But I would point out that it's  
2 a -- the drug effect that we're going for is to  
3 maintain the device effect of balloon angioplasty,  
4 for example.

5 So it's not like we're trying to cure  
6 something by the injection of a drug. We're  
7 trying to maintain the patency of a vascular lumen  
8 that's been created by angioplasty or atherectomy,  
9 which opened it.

10 DR. SHERMAN: Okay. And would you see  
11 yourself as -- I'm sure you've thought about this  
12 -- Class III or Class II De Novo?

13 DR. SEWARD: I would consider this to very  
14 likely be Class II De Novo given the fact that  
15 it's a 510(k) cleared device, and it's a drug  
16 that's being used within its current dosage range  
17 for local administration to accomplish anti-  
18 inflammation.

19 So it's very incrementally shifting the use of  
20 the drug in that case, given the risk profile of  
21 the drug. I would assume that it's Class II.

22 DR. SHERMAN: Thank you. Any other questions

1 from --

2 MS. MALONEY: I just want to make sure I  
3 understand. If the drug company did want to play,  
4 what would be the end result in terms of the  
5 difference? Is the only difference that when  
6 they're not playing, the labeling would be in the  
7 device product? But the data and the standard of  
8 evidence would be the same in either case?

9 DR. SEWARD: No. I think that the standard of  
10 evidence -- for the standard of evidence, we're  
11 looking to what the result of the drug use is,  
12 right? Again, if we're -- and frankly, what other  
13 products the FDA has regulated using that standard  
14 of evidence. There's no greater example of that  
15 than with drug coated balloons and drug eluting  
16 stents where the drug coated balloons went down  
17 the device path because they're chemotherapeutic  
18 agent, Paclitaxel, coated onto a balloon and they  
19 met the reasonable assurance standard, not the  
20 substantial evidence standard.

21 There weren't multiple clinical trials  
22 performed with them. They -- you know, they were

1 very straightforward device studies that led to  
2 PMAs for those products.

3 If that's going to be the precedent that's set  
4 for that type of an application, then other  
5 applications should be treated the same whether,  
6 whether it's a drug device biologic or otherwise.

7 So the standard of evidence should be taken  
8 for the medicine that you're trying to accomplish  
9 or the medical therapy that you're trying to  
10 accomplish.

11 The difference -- and we're working with drug  
12 companies on more advanced applications that some  
13 of you on the panel are aware of because the drug  
14 companies have open INDs for example.

15 And in those cases, the drug company will  
16 have, within their labeling, that the drug is  
17 indicated for delivery through a catheter like  
18 ours. However, in most of those cases, that's a  
19 new chemical entity that they're developing, and  
20 so it is a different standard of evidence that's  
21 going to be applied to that new chemical entity.

22 DR. SHERMAN: No other questions?

1 Thank you for your comments.

2 DR. SEWARD: Thank you so much.

3 DR. SHERMAN: Our last speaker is Bradley  
4 Thompson from the Combination Products Coalition.

5 MR. THOMPSON: Good morning. I want to thank  
6 you for organizing this meeting, this hearing.

7 I represent a coalition. And so we've been  
8 hard at work for the last month or so since the  
9 Federal Register Notice came out. And we've done  
10 our best to put together comments today, and I'm  
11 going to try and accurately represent those  
12 orally. But we are going to be filing written  
13 comments, which will be much more detailed.

14 I was very impressed with the presentation so  
15 far because they all followed -- many of them  
16 followed your questions. If I answer any of your  
17 questions, it's going to be a coincidence, all  
18 right? I'm not going to follow the structure.  
19 I'm providing sort of more high-level  
20 observations.

21 Let me first tell you a little bit about the  
22 Coalition and how it operates because I think it's

1 very relevant to how we approach this question.

2 So the Coalition by design are those companies  
3 that are very passionate about combination  
4 products, and it includes drug, device, and  
5 biological companies, about 25 all total.

6 And we've been around for about 14 or 15  
7 years, and we have a committee structure, and we  
8 have a working group that is focused on cross-  
9 labeling, which is sort of the heart of some of  
10 what we're talking about. I recognize not  
11 exactly.

12 And we participated back in 2005 in the  
13 meeting that FDA held with DIA, and it was a very  
14 good meeting.

15 Our organizing principle, because we are so  
16 diverse, right -- we have device companies and we  
17 have drug and biologic companies. And  
18 traditionally, those companies have seen these  
19 issues from -- through a different lens at least,  
20 right?

21 So we have a very simple organizing principle  
22 in how we adopt policy positions, and that is put

1 the patient first. What is best for the patient,  
2 all right?

3 Now, if it's a safety and effectiveness issue,  
4 that's pretty simple because you use science to  
5 figure that out, right? But where it's a policy  
6 issue like this, it also includes economics. It's  
7 an unavoidable aspect of a question like this.

8 And I think to some extent, my perception of  
9 the folks who are struggling with this issue is  
10 there's an emotional component to it. And the  
11 emotional component is when a good idea walks  
12 through the door, you really want to pursue it.  
13 Anybody who cares about the patient, really wants  
14 to pursue anything that sounds like it's good for  
15 the patient.

16 But the fact is, economics exist precisely to  
17 answer the question of how do you allocate scarce  
18 resources? That's the definition of economics.  
19 And I know that because last weekend my senior in  
20 engineering came to me and said I'm struggling in  
21 economics, can you tutor me. And we sat down for  
22 a while and I had to review it all.

1           And as I was looking through all the  
2 materials, you end up drawing things like  
3 performance production frontiers and budget lines  
4 and everything. And it's all -- you know, you  
5 graph guns and butter. You graph two different  
6 things and try and show an optimization of what,  
7 from a societal standpoint, you want to accomplish  
8 in the allocation of scarce resources.

9           Well, at the end of the day, that's what we're  
10 confronted with here. We have good ideas that are  
11 coming in that may not make the cut for where we  
12 need to invest our resources. And that's not --  
13 it's economically driven to be sure. That's how -  
14 - that's the system that we have for identifying  
15 social optimal.

16           But at the end of the day, it is a tough  
17 decision. If you were a venture capitalist, you  
18 would see maybe 1000 people come through your door  
19 a year. Many of them would have very good ideas  
20 and many of them with good ideas you would have to  
21 say, sorry, I can't do it. I've got these other  
22 things that are, for various reasons, a higher



1 priority.

2 Now, when you're sitting there at the Agency  
3 and you're hearing about economics, I recognize  
4 that that may not be terribly persuasive. But at  
5 the end of the day, you guys are a gatekeeper.  
6 And I assume that if someone walks into your  
7 office and says, you know what, we tried to raise  
8 venture capital, we just couldn't do it, can you  
9 lower the bar on safety and effectiveness, you'd  
10 say no. All right? For good reason, you'd say  
11 no.

12 But it might break your heart because you  
13 might look at the idea and say that's a really  
14 good idea. I can't understand why it's not  
15 getting support.

16 It's a tough call. And it's tough on  
17 everyone. It's tough on the folks who are making  
18 the budget decisions. It's tough on the folks in  
19 your chair who are seeing the effects of it. All  
20 right.

21 So that's the basic context of my remarks. So  
22 I've been authorized to make five points.

1           Actually, I haven't gotten to any of those five  
2           points, so I'm going to do it quickly now.

3           The first point, cooperation is best. And I  
4           assume that's not a controversial statement, but  
5           I'll explain to you why I want to make this point,  
6           all right?

7           When the drug and device company are working  
8           together, they combine to know the most about the  
9           drug and the device and can really sort through  
10          the tough safety and effectiveness issues, all  
11          right? And they can do it efficiently, all right?

12          If you were to adopt a program which created a  
13          substantial alternative pathway to cooperation,  
14          you might end up discouraging cooperation, or at  
15          least not encouraging cooperation, okay? And the  
16          fact of the matter is cooperation is hard.

17          I spent a lot of time almost as a marriage  
18          counselor with drug and device companies trying to  
19          help them work together because it is hard. They  
20          have completely different cultures. Drug  
21          companies tend to be big, a little bit more  
22          bureaucratic, very slow in their thinking. Device

1 companies are constantly wanting to go fast, fast,  
2 fast. There are commercial differences between  
3 the two. There are vocabulary differences between  
4 the two. Collaboration is hard.

5 If you create a pathway that basically means  
6 that collaboration isn't needed because you create  
7 an easy way for them to go around it, you  
8 discourage something that is actually very  
9 important for companies to do, and you need to be  
10 mindful of that, in my opinion.

11 Collaboration might, in fact, be the best  
12 outcome here. And so you might be looking for  
13 policy levers to encourage cooperation. I'm not  
14 aware of any real policy levers that FDA has that  
15 are significant enough if a deal really isn't  
16 attractive to make it attractive.

17 But if it were really important, obviously we  
18 could collectively go to Congress and ask Congress  
19 to -- they're in the mood to change tax law,  
20 right? We could ask for a tax provision.

21 Let me be clear, I'm not suggesting that we  
22 want Congress to mandate cooperation, but if they

1 want to incentivize it, that would be great.

2 But the fact of the matter is you guys or we  
3 or somebody would need to go in with data and say  
4 the market isn't working, right, because you know,  
5 if my son is taking the exam -- he took it  
6 yesterday. But if he took the exam and there was  
7 a question on it, a really good idea wasn't  
8 pursued, does that mean the economic system  
9 failed, the answer would be, no, it doesn't mean  
10 that.

11 You have to go beyond that to show that  
12 there's some reason it actually should have been  
13 pursued economically, not just because it's a good  
14 idea because there's a whole lot of good ideas  
15 that are not being pursued.

16 All right, the second point. There are a lot  
17 of reasons pharmaceutical companies may not want  
18 to participate in a collaboration with a device  
19 company.

20 Back in 2005, as I mentioned, you guys held a  
21 hearing, and we testified in that, and a good  
22 colleague of mine, Danelle Miller, gave a terrific

1 presentation, and she covered like 20 different  
2 reasons. And I'm not going to repeat it all  
3 because there's a transcript that's all there,  
4 okay?

5 But just to summarize, there are scientific  
6 reasons to not collaborate. There are business  
7 reasons not to collaborate.

8 Within a drug company, you have people who are  
9 the world's leading thinkers on that particular  
10 molecule. When someone walks in the door and says  
11 I've got an idea for a different way to use that  
12 molecule, they have a pretty good intuitive sense  
13 of what will work and what won't work. It may not  
14 be based on a clinical trial. It may not be based  
15 on specific evidence. But it will be based on the  
16 fact that they've dedicated maybe 10 years of  
17 their life studying that molecule.

18 So when they say no, that's actually a pretty  
19 significant thing. And that may never come  
20 through to you, all right? And the commercial  
21 disagreement may never come through to you. There  
22 may be any number of reasons. It might be the

1 device company wanted more money than the drug  
2 company wanted to give them, or vice versa. It  
3 could be any number of things. And you won't know  
4 that context for why this didn't work.

5 The third observation I wanted to offer is  
6 we're talking about a universe of projects where  
7 the drug company has said no. It's possible, as I  
8 just said, that in some cases it's because the  
9 drug company genuinely feels that it is a risky  
10 avenue to go down, that there are public health  
11 reasons not to do it.

12 If you're in that environment, you just need  
13 to understand -- I hope this wouldn't be a common  
14 occurrence. I hope it would be very rare. But  
15 the drug company might actually oppose what you're  
16 thinking of doing. And if they oppose it, that  
17 opposition, if they're not part of the FDA  
18 process, by definition, there's no cooperation,  
19 they're not engaged with you and they're not  
20 talking to you, and it just sort of, you know, is  
21 done, the pharmaceutical company might need to  
22 make that opposition known to their -- to the

1 patients because it's their obligation to know it.

2 And so you end up debating these things in a  
3 public forum because there wasn't a private forum  
4 through which they would have been discussed  
5 previously. That's a basic conundrum of this  
6 route.

7 Fourth, and this sort of gets more to the  
8 heart of the questions that you posed to us, as  
9 we've analyzed the proposal, I want to say that  
10 the -- all of our members together believe there  
11 is a pathway here that you've identified. And  
12 that's a big statement. It may not sound like a  
13 big statement, but in my mind, it's a big  
14 statement because it means that as we've looked at  
15 all of the pieces that you're talking about  
16 putting together, to us there seems collectively,  
17 pharmaceutical, biologics, device companies, that  
18 there is an avenue here.

19 In my opinion, though, just from the tenor of  
20 the Federal Register Notice, you may be  
21 underestimating just how rare the circumstances  
22 would be when all of these pieces would fit

1 together, and I'll give you a couple of examples.

2 First, you make it clear, appropriately so,  
3 that you require the evidence of safety and  
4 effectiveness, and that you plan to respect the  
5 pharmaceutical company's ownership of the data  
6 that they've supplied to you.

7 If you truly subtract out that pharmaceutical  
8 data and say that the delta with that data removed  
9 is what the device company has to prove, that's a  
10 very substantial burden. Just look at what  
11 pharmaceutical companies pay to develop that data.

12 When you take that data out of the equation,  
13 it's going to be a very rare medical device  
14 company that can actually replace what needs to be  
15 replaced, prove what needs to be proven over  
16 again. And it'll be very important that FDA not  
17 sort of in the recesses of its mind accept certain  
18 things as proven, which actually are in reliance  
19 on the pharmaceutical company's data.

20 That's a hard thing to do, to unlearn what you  
21 feel you've learned, all right, but that is the  
22 task. And so then the demand on the device



1           company -- and again, I go back to the point  
2           because there's no cooperation in the economics of  
3           it, I assume you wouldn't lower the standard. I  
4           hope you wouldn't lower the standard any more than  
5           you would if someone came in and said we failed to  
6           raise venture capital money, will you lower the  
7           bar. You can't lower the bar, all right?

8                        So that's the first point is those data  
9           requirements are going to be very substantial.

10                      Second, there is this risk of confusion in the  
11           marketplace when the pharmaceutical company and  
12           the device company are fundamentally on a  
13           different page message-wise about what they think  
14           the public health benefits of this use are. And  
15           there's a risk of confusion in that regard.

16                      Post-market change management, that's actually  
17           an area where we have advocated that there should  
18           be a pathway that allows someone to demonstrate  
19           that they can actually manage post-market changes  
20           without cooperation. We -- as I said, we've been  
21           involved in this issue very long. We filed  
22           comments suggesting that that is, in fact, the

1 case. It's difficult to do, but it is, in fact,  
2 the case.

3 And then finally, post-market safety -- I  
4 thought Dr. Bano did a terrific presentation at  
5 the beginning of this meeting, and I'm not going  
6 to try and duplicate that. But what we're focused  
7 on is the instance where the adverse information  
8 comes first and exclusively to the drug company.

9 You really have to follow that through to  
10 figure out then what happens. The drug company's  
11 the only one to receive that. There's no  
12 obligation. There's no cooperation between them  
13 and the device company to share that adverse  
14 information with a drug company.

15 They have to review it through an appropriate  
16 prism, but they aren't involved in the device, so  
17 they don't know all the science on the device. So  
18 number one, their own decision-making, how do you  
19 do that when you're not -- when you can't go over  
20 to the device company and say, well, what's the  
21 meaning of this or can you explain that or help me  
22 understand the science behind this.

1           And there's no information being shuttled  
2           between them. Now, if you say there should be,  
3           then really what you're doing is trying to  
4           legislate cooperation because that's cooperation,  
5           right, so you can't say there should be  
6           cooperation. Nor can you say, well, FDA can step  
7           in and manage it. We can ask this one -- this  
8           question, then turn around and talk to this one.  
9           That's cooperation, too, right? And that's -- and  
10          that should be off the table.

11          So to me, the adverse events are difficult,  
12          not impossible depending on the circumstances, but  
13          very difficult.

14          The final point -- the fifth point I want to  
15          make is really about the avenue. And I thought --  
16          I loved the discussion. I thought Kirk was -- did  
17          a very nice job of presenting a very good case  
18          study for how this issue comes up.

19          The fact of the matter is, you do have to  
20          worry about fairness, all right? And it's more  
21          than fairness. There's a substance to it.

22          But the fact is, if there's no cooperation

1 between the drug and the device company, that does  
2 not mean by itself that a different pathway should  
3 be available that isn't available when there is  
4 cooperation. The cooperation isn't the salient  
5 point.

6 And I think some of you were kind of dancing  
7 around this issue. If the product has a drug  
8 primary mode of action, if it were a combination  
9 product, there's a pretty clear set of rules as to  
10 how it would be dealt with.

11 Now, you're saying this isn't a combination  
12 product. I get that. But instead, as a DRD, we  
13 want to maybe think about the PMA. Well, the fact  
14 is if the drug primary mode of action, if the  
15 issues are drug-related issues, if it's proving  
16 the safety and effectiveness of the drug because  
17 they can't use the data from the pharma company,  
18 that's a drug submission. That's an NDA.

19 It's not a 510(k). It's not a PMA. It's an  
20 NDA. And as a consequence, I appreciate that  
21 there is a distinction between the two, but you  
22 need to make sure that you're being consistent and

1 not, to use a legal term, arbitrary and  
2 capricious.

3 So in summary, we would say, look, I think  
4 this is very fruitful discussion. I'm glad we're  
5 having this discussion. I think the Agency came  
6 up with a creative and intelligent path, and I do  
7 think there is a path through the maze that you've  
8 identified, but I really think it's for a very  
9 select few.

10 DR. SHERMAN: Thank you for your comments.

11 Does the panel have questions? Mr. Weiner?

12 MR. WEINER: Thank you very much. Just one  
13 question. Since a major focus here of your  
14 presentation was on economic issues, I just want  
15 to kind of peel back on that a little bit. So if  
16 you're assuming, as you say we should be assuming,  
17 of course, that the device company is prepared to  
18 put the money forward to generate the data to get  
19 approval of new use, what is the economic issue  
20 for the drug company?

21 MR. THOMPSON: By and large, if the device  
22 company can do it all, there isn't an economic

1 issue. That's what I'm saying. There is a path  
2 forward.

3 I think folks when they read your Federal  
4 Register Notice are maybe underestimating just how  
5 much they have to prove. It's counterintuitive  
6 because to a scientist -- the stupidest thing a  
7 scientist could ever think of doing is reproving  
8 what's been proven. I'm sure to a scientist, that  
9 sounds absolutely absurd.

10 That's what we're talking about, right?  
11 Because we're talking about what was proven  
12 previously, was done through with data owned by  
13 the pharmaceutical company. If you're not using  
14 that data, you have to reprove what that data  
15 proves.

16 So if a device company can do that and  
17 navigate the other things -- that's what we're  
18 saying -- there is a pathway through here.

19 MR. WEINER: Just a follow-up to that, I think  
20 I know the answer, but just to be sure we're on  
21 the -- I'm understanding you correctly, is this  
22 analysis applicable regardless of whether there's

1 a generic approved for the drug or not, or is this  
2 only prior to ANDA approval being available?

3 MR. THOMPSON: So I asked an associate of mine  
4 to write a summary so I could sound smart of these  
5 rules, and she sent it to me this morning at 7:00  
6 a.m. and it was 20 pages long.

7 I don't have a simple question for you. There  
8 are different settings. There are drugs that have  
9 been withdrawn. There are generic drugs. There's  
10 implications of the 21st Century Cures language.  
11 It's a complicated topic. So I don't mean like --  
12 I am skirting it.

13 I was going to say I don't mean to sound like  
14 I'm skirting it, but I am skirting it. Our  
15 written comments will address that more  
16 intelligently than I could here.

17 DR. THROCKMORTON: I want to ask an economic  
18 question, too. So as I listen to you behind the  
19 tone of this is a rare thing, it's going to be  
20 challenging, people need to understand that, I  
21 also heard at least a little of a concern about an  
22 impact on overall product development. I think

1 we're all interested in, you know, in creating a  
2 pathway to foster innovative development I think  
3 is one of the specific questions we asked in the  
4 FRN.

5 Put you on the spot and ask you to say where  
6 you believe this pathway, if implemented, would  
7 take us as far as fostering innovation?

8 MR. THOMPSON: I think it would help foster  
9 innovation. I think it is well-directed at your  
10 goal of creating or identifying, I should say,  
11 because it's already there. You're not -- there's  
12 not -- we're not talking about new law --  
13 identifying a pathway for device companies to get  
14 to market without the cooperation of the pharma  
15 company, if they have the money to do it. And so  
16 I think you've done what you as an agency would  
17 need to do, which is identify the pathway, right?

18 All I'm doing I guess is sort of being clear  
19 about expectations. I think the number of  
20 companies that will be able to fund that pathway  
21 will be extraordinarily small.

22 DR. THROCKMORTON: And just to follow up a



1 little bit, we -- the concerns that we had were on  
2 both the device side and the drug side as far as  
3 development. So one concern that we've heard  
4 voiced is that this pathway might negatively  
5 influence choices drug companies could make about  
6 product development, expanded indications, that  
7 kind of thing.

8 MR. THOMPSON: Who said that? No, I'm not  
9 saying that. Let me be clear. I'm not saying  
10 that.

11 If you literally follow the pathway that you  
12 identify, it shouldn't affect the drug company at  
13 all, neither positively nor negatively, right,  
14 because the drug company can go off and keep doing  
15 what it's doing and its board can pick the  
16 programs that it wants to support. It'll channel  
17 its money into those and it'll keep optimizing its  
18 own innovation without being inhibited by this  
19 program.

20 So I personally, as I sit here today, maybe  
21 one of my members will tell me that I'm missing  
22 something, but I personally think drug companies

1 would be more or less indifferent to this if done  
2 well.

3 Now, where you could go off the rails is if  
4 you start taking their data and using it for  
5 someone else's benefit, right, because that does -  
6 - we talked about free rider problems, the generic  
7 free rider and other. That sort of free rider  
8 problem is a major economic problem.

9 So if you -- I don't mean this pejoratively --  
10 but misappropriate data from one innovator to the  
11 benefit of the other, that would be a very bad  
12 thing. But other than that, I don't see how it  
13 would negatively inhibit the pharmaceutical  
14 innovation. I may be fired tomorrow, but ...

15 DR. THROCKMORTON: I hope not. I'm going to  
16 ask you about that reliance question. So in the  
17 Federal Register Notice, we identified three  
18 general sources of information that we thought the  
19 device companies might rely on, talked about  
20 publicly available -- you know, literature,  
21 generalizable knowledge, and potentially the use  
22 of withdrawn NDAs.

1           Any pieces we're missing or do you have any  
2 concerns about those pieces as sources of  
3 information that device companies could rely on?

4           MR. THOMPSON: That's what I asked my younger  
5 colleague to research and she gave me the 20-page  
6 memo. So I respect the question. It's an  
7 important question, and I think we plan to address  
8 it. I just can't as we stand here now. Sorry.

9           DR. THROCKMORTON: Last question that I have,  
10 I promise. It has to do with the comments you  
11 made about it not always being clear why the drug  
12 company chose not to cooperate with the device  
13 company. And you sort of raised the idea that the  
14 drug company might have some authentic concern  
15 about the use of the drug in this particular way.

16           Were you suggesting that the drug company in  
17 some way or the other have an opportunity to make  
18 that concern clearer as a part of the process that  
19 we're laying out so that they would be in some way  
20 or the other made aware that this was a  
21 development that was being contemplated and they  
22 could say, boy, we've got three studies that you

1 may not know about that show that this causes  
2 cancer, whatever.

3 MR. THOMPSON: No. See, I'm really not  
4 encouraging you to draw the drug company into it.  
5 Let me clear about that. I'm actually  
6 discouraging you from drawing the drug company  
7 into it. But I am saying that that's a weakness  
8 of the process, right, because what you're  
9 describing is resources, time, effort, money, the  
10 sort of thing that the pharma company was trying  
11 to avoid when it said no to the device company.

12 So to -- instead of being drawn into it with a  
13 device company, to be drawn into it with the FDA  
14 isn't fair because you're basically forcing them  
15 to become a participant in this process when they  
16 don't want to.

17 But that's the conundrum because they may have  
18 knowledge, and some of it may just be, you know,  
19 the wisdom of people who have spent 10 years  
20 studying this molecule to -- and they understand  
21 how it behaves. You're not tapping into that.  
22 And if I were FDA, I'd be really nervous about the

1 drug company not being at the table because I know  
2 you guys are terrific at review, but reviewing  
3 isn't the same as spending 10 years of your life  
4 in a lab tinkering with a drug product and getting  
5 to know it. It's just not the same.

6 DR. THROCKMORTON: And as you pointed out, we  
7 wouldn't be able to look under the hood of the  
8 drug materials for -- you know, we wouldn't be  
9 able to rely on those data. Thanks.

10 MR. WEINER: This made me think of another  
11 question. This probably goes to your 20-page memo  
12 and what you're planning to say in writing. I'm  
13 not sure.

14 But on the issue of -- you were saying it  
15 wouldn't be appropriate to have a pathway  
16 available just because there's a lack of  
17 cooperation. Is there an economic issue there,  
18 too, or are you expecting sort of backdoors people  
19 could get better protection for less cost by using  
20 this pathway, or is that not one of the issues  
21 you're raising for the drug industry?

22 MR. THOMPSON: Can you restate it? I'm not

1           sure I followed what you asked.

2           MR. WEINER: I may be asking a question that  
3           has nothing to do with what you were saying. I  
4           had the impression what you were saying was if  
5           people have an easier pathway or a more protected  
6           pathway, whatever it might be, that should be  
7           available regardless of whether you have  
8           cooperation or not. Is that what you were driving  
9           at and, more particularly, does that mean that you  
10          could have --

11          MR. THOMPSON: Yeah.

12          MR. WEINER: -- this pathway, and therefore,  
13          the paradigm of the NDA pathway wouldn't apply to  
14          you and there might be pluses or minuses to that  
15          for that company or for their competitors?

16          MR. THOMPSON: So there's two sides of this  
17          horse to fall off on, okay, which is why I don't  
18          envy you in trying to ride the horse.

19          One side of the horse you could fall off on is  
20          making this pathway too easy. If you make it too  
21          easy, it means that companies may well not --  
22          choose not to cooperate because this is easy

1 enough we're going to not cooperate, all right?

2 That would be a bad thing because from a  
3 product development standpoint, talk about things  
4 you want to incentivize. Cooperation is something  
5 I think you want to incentivize. I don't think  
6 you want to discourage it, all right?

7 Now, the other side of the coin you could fall  
8 off on is I assume you're not going to have a gate  
9 to this thing which says come in and prove to us  
10 that the pharmaceutical company, for example, is  
11 being unreasonable in their commercial demands  
12 and, therefore, you want to go it alone.

13 You're going to have to just sort of say  
14 here's a pathway regardless of economics,  
15 regardless of anything else. It's available to  
16 all comers if you want to go it alone rather than  
17 say you have to prove that you were treated  
18 unfairly by a potential partner and that's why  
19 you're going -- so it needs to be open to all.  
20 And that creates a bit of a conundrum as to what  
21 you're truly trying to achieve.

22 DR. SHERMAN: Any additional questions?

1 Thank you for your comments.

2 As I understand it, we have no other speakers,  
3 so that is -- was a very informative, not-full  
4 morning.

5 So on behalf of the FDA panel, I would like to  
6 thank all speakers for their presentations and all  
7 the audience for their attention, whether in  
8 person or by webcast.

9 Discussing the issues for today's meeting, I  
10 also, on behalf of the panel, would like to thank  
11 the FDA staff that worked to put this meeting  
12 together.

13 We've had a productive partial morning of  
14 thoughtful, insightful comments that have provided  
15 FDA with a lot of valuable information to consider  
16 on this topic.

17 We want to encourage all our stakeholders once  
18 again to submit comments to the docket for this  
19 meeting. As a reminder, the docket is open until  
20 January 15th, 2018.

21 Our next steps will be to review all the  
22 information provided during this meeting as well



1 as the information submitted to the docket.

2 So to all attendees and speakers, have a safe  
3 trip home. The meeting is now adjourned.

4 (Whereupon, at 10:33 a.m., the meeting was  
5 adjourned.)

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20


21

22

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22

CERTIFICATE OF NOTARY PUBLIC

I, Michael Farkas, the officer before whom the foregoing proceeding was taken, do hereby certify that the proceedings were recorded by me and thereafter reduced to typewriting under my direction; that said proceedings are a true and accurate record to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.



MICHAEL FARKAS

Notary Public in and for the  
State of Maryland

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22

## CERTIFICATE OF TRANSCRIBER

I, Jessica Bodreau, do hereby certify that this transcript was prepared from audio to the best of my ability.

I am neither counsel for, related to, nor employed by any of the parties to this action, nor financially or otherwise interested in the outcome of this action.



11/20/2017

DATE

JESSICA BODREAU

<p><b>1</b>  <b>1</b> 32:15 40:21  42:20  <b>10</b> 3:4 32:15 40:6  69:16 84:19 85:3  <b>1000</b> 64:18  <b>10903</b> 1:10  <b>10:00</b> 8:19  <b>10:33</b> 89:4  <b>10:45</b> 8:15  <b>11/20/2017</b> 91:12  <b>12</b> 24:19  <b>14</b> 62:6  <b>15</b> 7:21 13:12 62:6  <b>15th</b> 9:2 88:20  <b>16</b> 1:5  <b>17</b> 32:9,17</p>	<p><b>3</b>  <b>3</b> 23:21 29:14  31:18  <b>30</b> 7:19 13:10 25:6  26:1 27:9  <b>35</b> 3:6</p>	<p>60:10 64:7  <b>account</b> 23:19  24:8 27:19 28:2  28:10 29:4 31:11  31:21 33:21  <b>accounted</b> 50:5  <b>accounts</b> 24:11  43:5  <b>accurate</b> 41:21  90:6  <b>accurately</b> 61:11  <b>achieve</b> 11:13  87:21  <b>action</b> 25:8 45:14  45:21 57:17 76:8  76:14 90:9,13  91:7,9  <b>actions</b> 17:1 18:8  <b>adding</b> 40:2  <b>additional</b> 9:7,13  10:5 11:11 13:20  18:5,19,22 35:9  55:4 57:7 87:22  <b>address</b> 7:7 11:21  12:12 13:21 16:10  16:22 21:4 22:22  29:13 36:14 79:15  83:7  <b>addressed</b> 23:3  46:6  <b>addresses</b> 48:8  <b>addressing</b> 10:13  41:2 48:22  <b>adds</b> 11:2  <b>adequate</b> 17:14  21:15 22:1 44:3  48:10  <b>adequately</b> 11:21  19:12  <b>adjourned</b> 89:3,5  <b>administration</b>  1:9 4:7 11:15 15:2  16:19 19:1 39:12  39:13 48:20 58:17</p>	<p><b>administrative</b>  4:10 7:11,15  <b>adopt</b> 62:22 66:12  <b>adoption</b> 32:8  <b>advance</b> 10:2  <b>advanced</b> 37:17  60:12  <b>advancing</b> 50:15  <b>adverse</b> 11:21  12:2,8,9 14:1,1  15:9 17:3,11 19:4  30:9 48:20 57:1  74:7,13 75:11  <b>advocated</b> 73:17  <b>affect</b> 81:12  <b>afforded</b> 47:11  <b>agency</b> 22:19  30:16 35:16 41:10  49:16 57:2 65:2  77:5 80:16  <b>agenda</b> 6:18,21  7:21 8:7  <b>agent</b> 26:19 46:22  59:18  <b>agents</b> 35:19  37:21 38:9,13  <b>ago</b> 28:16  <b>agree</b> 23:20  <b>alcohol</b> 19:8  <b>algorithm</b> 27:1  <b>allocate</b> 63:17  <b>allocation</b> 64:8  <b>allotted</b> 8:3 9:15  10:4  <b>allow</b> 4:21 45:3  50:20  <b>allowed</b> 7:3 44:13  <b>allowing</b> 46:2  <b>allows</b> 25:16 73:18  <b>alternative</b> 66:13  <b>alternatively</b>  42:11  <b>altogether</b> 28:2</p>
<p><b>2</b></p>	<p><b>4</b>  <b>4</b> 10:13 48:8 54:16  <b>40</b> 27:9</p>	<p><b>5</b>  <b>50</b> 28:5 55:21  <b>510</b> 38:2,4 41:16  42:19 50:18 58:15  76:19</p>	<p><b>administrative</b>  4:10 7:11,15  <b>adopt</b> 62:22 66:12  <b>adoption</b> 32:8  <b>advance</b> 10:2  <b>advanced</b> 37:17  60:12  <b>advancing</b> 50:15  <b>adverse</b> 11:21  12:2,8,9 14:1,1  15:9 17:3,11 19:4  30:9 48:20 57:1  74:7,13 75:11  <b>advocated</b> 73:17  <b>affect</b> 81:12  <b>afforded</b> 47:11  <b>agency</b> 22:19  30:16 35:16 41:10  49:16 57:2 65:2  77:5 80:16  <b>agenda</b> 6:18,21  7:21 8:7  <b>agent</b> 26:19 46:22  59:18  <b>agents</b> 35:19  37:21 38:9,13  <b>ago</b> 28:16  <b>agree</b> 23:20  <b>alcohol</b> 19:8  <b>algorithm</b> 27:1  <b>allocate</b> 63:17  <b>allocation</b> 64:8  <b>allotted</b> 8:3 9:15  10:4  <b>allow</b> 4:21 45:3  50:20  <b>allowed</b> 7:3 44:13  <b>allowing</b> 46:2  <b>allows</b> 25:16 73:18  <b>alternative</b> 66:13  <b>alternatively</b>  42:11  <b>altogether</b> 28:2</p>
<p><b>2</b> 43:7  <b>20</b> 15:15 69:1 79:6  83:5 85:11  <b>2000</b> 30:17  <b>2003</b> 24:19  <b>2005</b> 62:12 68:20  <b>2008</b> 24:22  <b>2009</b> 29:13 30:17  30:18,19  <b>2010</b> 31:3,4 32:12  <b>2011</b> 31:4  <b>2012</b> 25:1 32:11  <b>2016</b> 24:18  <b>2017</b> 1:5 37:12  <b>2018</b> 9:2 88:20  <b>2020</b> 25:2  <b>20903</b> 1:11  <b>21st</b> 79:10  <b>22</b> 3:5  <b>244,000</b> 28:19  30:13  <b>25</b> 28:2 62:5</p>	<p><b>6</b>  <b>6</b> 48:22 51:8  <b>61</b> 3:7</p>	<p><b>6</b>  <b>6</b> 48:22 51:8  <b>61</b> 3:7</p>	<p><b>6</b>  <b>6</b> 48:22 51:8  <b>61</b> 3:7</p>
<p><b>2</b></p>	<p><b>7</b>  <b>7</b> 22:22  <b>70</b> 28:13</p>	<p><b>7</b>  <b>7</b> 22:22  <b>70</b> 28:13</p>	<p><b>7</b>  <b>7</b> 22:22  <b>70</b> 28:13</p>
<p><b>2</b></p>	<p><b>9</b>  <b>9:02</b> 1:6</p>	<p><b>9</b>  <b>9:02</b> 1:6</p>	<p><b>9</b>  <b>9:02</b> 1:6</p>
<p><b>2</b></p>	<p><b>a</b>  <b>a.m.</b> 1:6 8:19 79:6  89:4  <b>ability</b> 49:21 90:7  91:4  <b>ablation</b> 27:22  28:11  <b>able</b> 7:7 8:12 9:15  12:7 14:10 49:9  52:3 56:3 80:20  85:7,9  <b>absolutely</b> 31:19  78:9  <b>absurd</b> 78:9  <b>accept</b> 72:17  <b>access</b> 20:22  <b>accessed</b> 7:18  <b>accomplish</b> 31:20  46:1 58:17 60:8</p>	<p><b>a</b>  <b>a.m.</b> 1:6 8:19 79:6  89:4  <b>ability</b> 49:21 90:7  91:4  <b>ablation</b> 27:22  28:11  <b>able</b> 7:7 8:12 9:15  12:7 14:10 49:9  52:3 56:3 80:20  85:7,9  <b>absolutely</b> 31:19  78:9  <b>absurd</b> 78:9  <b>accept</b> 72:17  <b>access</b> 20:22  <b>accessed</b> 7:18  <b>accomplish</b> 31:20  46:1 58:17 60:8</p>	<p><b>a</b>  <b>a.m.</b> 1:6 8:19 79:6  89:4  <b>ability</b> 49:21 90:7  91:4  <b>ablation</b> 27:22  28:11  <b>able</b> 7:7 8:12 9:15  12:7 14:10 49:9  52:3 56:3 80:20  85:7,9  <b>absolutely</b> 31:19  78:9  <b>absurd</b> 78:9  <b>accept</b> 72:17  <b>access</b> 20:22  <b>accessed</b> 7:18  <b>accomplish</b> 31:20  46:1 58:17 60:8</p>

<p><b>amendments</b> 30:21 <b>american</b> 24:15 24:17 26:10,11,13 <b>amount</b> 33:15,22 <b>amounts</b> 29:6 <b>analysis</b> 78:22 <b>analyze</b> 14:11 <b>analyzed</b> 71:9 <b>analyzing</b> 20:4 <b>anatomy</b> 45:2 46:3 <b>anda</b> 79:2 <b>andas</b> 49:7 51:16 <b>angioplasty</b> 45:10 58:3,8 <b>animal</b> 15:3 <b>announcements</b> 4:10 <b>answer</b> 61:16 63:17 68:9 78:20 <b>anti</b> 38:19 39:1,7 39:12 58:17 <b>anticipated</b> 25:1 <b>anybody</b> 63:13 <b>anyone's</b> 10:10 <b>apologize</b> 10:2,10 <b>appeal</b> 31:2 <b>appear</b> 43:19 <b>applicable</b> 78:22 <b>application</b> 23:2 33:3 37:4 39:7 41:19 53:22 54:4 60:4 <b>applications</b> 37:4 40:17 41:7 60:5 60:12 <b>applied</b> 33:9,18 43:16 45:18 46:14 46:15 47:15 50:22 60:21 <b>applies</b> 43:14 <b>apply</b> 7:2 37:1 41:21 46:7,21</p>	<p>47:19 86:13 <b>appreciate</b> 9:10 76:20 <b>approach</b> 4:20 13:7,10 16:4 33:3 33:8 41:4 54:7 62:1 <b>appropriate</b> 13:7 15:10 16:13 34:10 35:6 41:19 43:8 50:7,20 54:1 74:15 85:15 <b>appropriately</b> 12:2 14:12 46:6 72:2 <b>approval</b> 31:3,4 32:13 41:6 45:3 46:9 47:21 77:19 79:2 <b>approvals</b> 44:14 44:20 45:17 <b>approved</b> 1:4 4:4 5:1 11:8,9,11 23:10,12 26:20 28:9 29:7 30:15 32:2 55:8 79:1 <b>approximately</b> 7:19 8:15 <b>arbitrary</b> 77:1 <b>architecture</b> 15:13 <b>area</b> 4:17 5:11 15:11 38:10 73:17 <b>areas</b> 11:22 38:7 <b>arena</b> 34:3 <b>arterial</b> 37:16 46:11 <b>arteries</b> 38:22 <b>asked</b> 79:3 80:3 83:4 86:1 <b>asking</b> 86:2 <b>aspect</b> 13:21 41:12 63:7</p>	<p><b>aspects</b> 55:13 <b>assessed</b> 50:17 <b>assessment</b> 15:8 15:19 19:5 <b>assign</b> 16:8 <b>associate</b> 5:15,18 79:3 <b>associated</b> 12:2 <b>association</b> 24:17 26:13 <b>assume</b> 53:10 58:21 65:6 66:4 73:3 87:8 <b>assuming</b> 48:2 77:16,16 <b>assumption</b> 21:10 <b>assurance</b> 37:6 43:15 44:6,19 47:9 50:8,21 59:19 <b>atherectomy</b> 58:8 <b>attendees</b> 4:14 89:2 <b>attention</b> 12:21 32:20 88:7 <b>attorney</b> 90:11 <b>attractive</b> 67:16 67:16 <b>attribution</b> 15:20 <b>audience</b> 88:7 <b>audio</b> 4:12 91:3 <b>augmentative</b> 56:7,14 <b>august</b> 30:18 31:3 <b>authentic</b> 83:14 <b>authorization</b> 4:22 11:20 <b>authorized</b> 65:22 <b>automatic</b> 42:10 <b>available</b> 6:16 8:21 9:6 21:16,17 21:18 22:10 33:16 51:22 52:21 76:3 76:3 79:2 82:20</p>	<p>85:16 86:7 87:15 <b>avenue</b> 1:10 70:10 71:18 75:15 <b>avoid</b> 84:11 <b>aware</b> 60:13 67:14 83:20</p> <hr/> <p style="text-align: center;"><b>b</b></p> <hr/> <p><b>b</b> 27:12 53:14 <b>bachelor's</b> 35:22 <b>back</b> 14:6 16:14 19:3 62:12 68:20 73:1 77:15 <b>backdoors</b> 85:18 <b>backflow</b> 25:18 <b>background</b> 36:21 37:13 <b>bad</b> 82:11 87:2 <b>balance</b> 31:21 35:8 <b>balloon</b> 37:18 58:3 59:18 <b>balloons</b> 45:11 59:15,16 <b>bano</b> 2:10 3:4 10:11,12 21:5,12 21:15 22:15 74:4 <b>bar</b> 65:9 73:7,7 <b>barriers</b> 50:16 <b>based</b> 11:18 17:14 27:14 38:2 40:13 42:7 43:4 69:14 69:14,15 <b>basic</b> 65:21 71:5 <b>basically</b> 53:9 67:5 84:14 <b>bears</b> 20:3 <b>beginning</b> 74:5 <b>behalf</b> 50:13 88:5 88:10 <b>behave</b> 13:22 <b>behaves</b> 84:21 <b>behaviors</b> 14:21 15:17 17:3 40:13</p>
---	---	---	---

<p><b>belief</b> 50:12  <b>believe</b> 33:8 57:16  71:10 80:6  <b>benefit</b> 11:11 24:2  46:20 82:5,11  <b>benefits</b> 73:14  <b>berkley</b> 36:3  <b>best</b> 61:10 63:1  66:3 67:11 90:6  91:3  <b>better</b> 46:21 85:19  <b>beyond</b> 10:6 37:1  68:11  <b>big</b> 20:6 49:21  66:21 71:12,13,13  <b>biologic</b> 13:11  35:2 60:6 62:17  <b>biological</b> 62:5  <b>biologics</b> 2:3 5:19  71:17  <b>biosphere</b> 29:12  <b>bit</b> 37:13 61:21  66:21 77:15 81:1  87:20  <b>bla</b> 35:6  <b>blood</b> 38:21  <b>board</b> 81:15  <b>bodreau</b> 91:2,13  <b>body</b> 36:8  <b>book</b> 48:3,6  <b>boy</b> 83:22  <b>brad</b> 2:14 3:7  <b>bradley</b> 61:3  <b>break</b> 65:12  <b>breakthrough</b>  47:20  <b>briefly</b> 37:6  <b>broad</b> 4:19  <b>budget</b> 64:3 65:18  <b>bullet</b> 52:5  <b>bullfrog</b> 37:15  <b>burden</b> 20:3,12  27:11 37:5 72:10</p>	<p><b>burdensome</b> 24:5  31:21 33:3  <b>bureaucratic</b>  66:22  <b>business</b> 69:6  <b>butcher</b> 10:10  <b>butter</b> 64:5</p> <hr/> <p style="text-align: center;"><b>c</b></p> <hr/> <p><b>c</b> 1:22 3:1 4:1  27:12  <b>california</b> 36:3  <b>call</b> 19:5 26:6 49:7  52:15 53:3 65:16  <b>called</b> 8:5 32:3  49:13 52:7,12  <b>calls</b> 30:22 31:1  <b>cancer</b> 24:12,13  24:14,15,16,18,20  26:11,12 27:15,17  28:20 47:1 84:2  <b>cancers</b> 27:4,5  <b>capital</b> 65:8 73:6  <b>capitalist</b> 64:17  <b>capricious</b> 77:2  <b>capture</b> 13:18  14:11  <b>captured</b> 13:2  14:7,8  <b>capturing</b> 12:1,11  <b>carcinoma</b> 24:11  24:21 25:6 26:10  27:3,8 28:5,18  30:2  <b>carcinomas</b> 28:3  <b>care</b> 26:9,22 32:3  <b>carefully</b> 5:9  <b>cares</b> 63:13  <b>case</b> 24:9 31:14  36:22 37:14 42:20  45:10 46:20,21  48:22 52:18 55:20  58:20 59:8 74:1,2  75:17</p>	<p><b>cases</b> 40:5 41:15  45:22 46:17 52:2  54:2 60:15,18  70:8  <b>catheter</b> 25:12  60:17  <b>causality</b> 15:19  19:3,7  <b>cause</b> 15:22 19:9  24:13 53:5  <b>causes</b> 84:1  <b>causing</b> 12:9  <b>caveat</b> 20:6  <b>caveats</b> 13:3 52:19  <b>cder</b> 14:16 16:7  <b>cdrh</b> 14:14 16:6,8  47:7 49:18 51:1  <b>cdrh's</b> 37:11  <b>ce</b> 30:6  <b>cell</b> 4:11  <b>center</b> 2:3,5,7 5:19  5:22 6:2 24:15  <b>centimeter</b> 54:5  <b>central</b> 24:17  <b>century</b> 79:10  <b>certain</b> 4:21 7:13  15:1,1 16:12 17:3  17:19 34:13 72:17  <b>certificate</b> 90:1  91:1  <b>certify</b> 90:3 91:2  <b>chair</b> 65:19  <b>challenge</b> 11:3  13:17 16:5 18:22  19:18  <b>challenges</b> 10:15  12:14 14:18 16:21  17:9 23:1,2 49:2  <b>challenging</b> 79:20  <b>chance</b> 8:22  <b>change</b> 11:14,16  16:4 40:8 48:6  51:14,19,20 57:3  67:19 73:16</p>	<p><b>changed</b> 16:18,18  <b>changes</b> 57:12  73:19  <b>changing</b> 47:6  <b>channel</b> 81:16  <b>characterized</b>  35:20 38:16  <b>chelation</b> 19:9  <b>chemical</b> 60:19,21  <b>chemoembolizat...</b>  25:4 26:8,20 28:7  28:17 29:8 32:19  <b>chemoembolizat...</b>  32:16  <b>chemotherapeutic</b>  46:22 59:17  <b>chemotherapies</b>  25:13  <b>chemotherapy</b>  25:18 29:2,16,17  30:11  <b>chief</b> 2:9 6:5 36:4  <b>choices</b> 81:5  <b>choose</b> 29:8 86:22  <b>chose</b> 83:12  <b>circulation</b> 37:16  <b>circumstances</b>  71:21 75:12  <b>cirrhosis</b> 27:17  <b>claim</b> 54:10  <b>claims</b> 40:2  <b>clarification</b> 12:13  51:8  <b>clarify</b> 21:5 36:19  <b>clarifying</b> 8:1  <b>clarity</b> 36:14  <b>class</b> 37:3,3 41:8,8  41:21 42:10,15,17  42:20 43:3 50:19  58:12,12,14,21  <b>classification</b>  42:10,13  <b>classified</b> 41:7  42:14</p>
--	---	--	---

<p><b>clear</b> 36:11 40:16 49:18 55:17 67:21 72:2 76:9 80:18 81:9 83:11 84:5</p> <p><b>clearance</b> 38:5</p> <p><b>cleared</b> 23:10 29:22 38:2 58:15</p> <p><b>clearer</b> 83:18</p> <p><b>clearly</b> 35:5 37:1 48:10 49:15 50:13</p> <p><b>clinical</b> 20:6,8 21:17 26:11 30:4 31:10 38:12 43:21 44:4,15 48:21 50:5 59:21 69:14</p> <p><b>closely</b> 6:21</p> <p><b>closing</b> 18:19</p> <p><b>coalition</b> 2:14 24:14 61:4,7,22 62:2</p> <p><b>coated</b> 45:8,10 46:8 59:15,16,18</p> <p><b>coatings</b> 45:15</p> <p><b>codes</b> 16:8,9</p> <p><b>coding</b> 16:5,7</p> <p><b>coffee</b> 4:17</p> <p><b>coin</b> 87:7</p> <p><b>coincidence</b> 61:17</p> <p><b>collaborate</b> 69:6,7</p> <p><b>collaboration</b> 67:4 67:6,11 68:18</p> <p><b>colleague</b> 68:22 83:5</p> <p><b>colleagues</b> 32:11</p> <p><b>collection</b> 31:22 34:2</p> <p><b>collectively</b> 67:18 71:16</p> <p><b>combination</b> 2:2 2:14 5:16 11:1 13:13,15 18:11 19:7 20:5 33:9,13 45:19,20 55:9,11 61:4 62:3 76:8,11</p>	<p><b>combinations</b> 26:3 29:2 46:10</p> <p><b>combine</b> 66:8</p> <p><b>combined</b> 20:20 34:15 35:4</p> <p><b>come</b> 9:17 20:10 21:4 64:18 69:19 69:21 87:9</p> <p><b>comers</b> 87:16</p> <p><b>comes</b> 12:16 13:8 14:13,20 20:15 34:21 55:4 74:8 75:18</p> <p><b>comfort</b> 11:12</p> <p><b>coming</b> 35:7 64:11</p> <p><b>comment</b> 8:13,17 9:1 36:12,20 37:2 37:10 40:20 57:16 57:18</p> <p><b>commenting</b> 43:10</p> <p><b>comments</b> 5:5 6:15 8:12 9:3,8,11 10:5,6 41:5,9 51:5 61:1,10,13 73:22 77:10 79:15 83:10 88:1,14,18</p> <p><b>commercial</b> 67:2 69:20 87:11</p> <p><b>commissioner</b> 2:1 4:6</p> <p><b>committee</b> 62:7</p> <p><b>common</b> 25:5 27:12 70:13</p> <p><b>commonly</b> 32:5 39:2 43:6</p> <p><b>communicate</b> 19:2</p> <p><b>communicated</b> 13:2</p> <p><b>communicating</b> 12:16</p> <p><b>communication</b> 21:6 22:5</p>	<p><b>companies</b> 21:11 40:1 60:12,14 62:2,5,16,17,18 66:18,21 67:1,9 68:17 71:17 72:11 80:13,20 81:5,22 82:19 83:3 86:21</p> <p><b>company</b> 12:4 34:12 36:6 40:12 50:13 53:10 56:19 59:3 60:15 66:7 68:19 69:8 70:1,2 70:7,9,15,21 72:9 72:14 73:1,11,12 74:8,13,14,20 76:1,17 77:17,20 77:22 78:13,16 80:15 81:12,14 83:12,13,14,16 84:4,6,10,11,13 85:1 86:15 87:10</p> <p><b>company's</b> 72:5 72:19 74:10</p> <p><b>compare</b> 28:22 29:10 44:9</p> <p><b>competitors</b> 86:15</p> <p><b>completable</b> 24:1</p> <p><b>complete</b> 39:17</p> <p><b>completed</b> 38:17</p> <p><b>completely</b> 33:19 54:6 66:20</p> <p><b>complex</b> 27:4 49:17</p> <p><b>complexity</b> 11:2 18:12</p> <p><b>complicated</b> 79:11</p> <p><b>component</b> 33:10 45:19 63:10,11</p> <p><b>comprehensive</b> 21:18 26:12</p> <p><b>conceivably</b> 23:15</p> <p><b>concentrations</b> 19:8</p>	<p><b>concept</b> 25:8 26:16 29:19</p> <p><b>concern</b> 12:4 55:10,12 79:21 81:3 83:14,18</p> <p><b>concerned</b> 55:2</p> <p><b>concerns</b> 81:1 83:2</p> <p><b>conclude</b> 10:1</p> <p><b>conclusion</b> 8:17</p> <p><b>condition</b> 46:5</p> <p><b>conditional</b> 31:3 32:12</p> <p><b>conduct</b> 29:14 31:10</p> <p><b>conducted</b> 32:11 32:15</p> <p><b>conducting</b> 32:5</p> <p><b>conference</b> 30:22</p> <p><b>confident</b> 49:5 51:11</p> <p><b>conflicting</b> 18:1</p> <p><b>confront</b> 35:17</p> <p><b>confronted</b> 64:10</p> <p><b>confronting</b> 49:17</p> <p><b>confusing</b> 18:1</p> <p><b>confusion</b> 37:7 48:9,12 54:19 55:5,10,12 73:10 73:15</p> <p><b>congratulate</b> 35:16</p> <p><b>Congress</b> 67:18,18 67:22</p> <p><b>conjunction</b> 25:15</p> <p><b>consensus</b> 26:2</p> <p><b>consequence</b> 76:20</p> <p><b>consider</b> 58:13 88:15</p> <p><b>consideration</b> 47:14</p> <p><b>considerations</b> 43:8</p>
--	---	---	---

<p><b>considered</b> 28:1 34:3 41:1,4 42:12 49:19 50:19 51:2 <b>consistent</b> 36:15 76:22 <b>constantly</b> 67:1 <b>consumer</b> 13:5 17:22 <b>contact</b> 6:7,12 <b>contacted</b> 39:15 <b>contemplated</b> 83:21 <b>contend</b> 41:2,20 <b>context</b> 65:21 70:4 <b>continue</b> 25:1 45:4 <b>contraindicated</b> 17:18 <b>contraindications</b> 48:19 <b>control</b> 24:16 <b>controlled</b> 44:4 <b>controls</b> 42:16,18 42:22 44:10 <b>controversial</b> 66:4 <b>conundrum</b> 71:5 84:17 87:20 <b>convenience</b> 11:12 <b>conventional</b> 32:4 32:19 <b>cooperate</b> 83:12 86:22 87:1 <b>cooperation</b> 66:3 66:13,14,15,16 67:13,22 70:18 73:2,20 74:12 75:4,4,6,9,22 76:4 76:4 80:14 85:17 86:8 87:4 <b>coronary</b> 38:7 <b>correct</b> 56:22 <b>corrections</b> 16:22 18:8 <b>correctly</b> 78:21</p>	<p><b>corticosteroid</b> 38:14 <b>cost</b> 85:19 <b>counsel</b> 2:9 6:5 90:8,11 91:6 <b>counselor</b> 66:18 <b>counterintuitive</b> 78:5 <b>couple</b> 72:1 <b>course</b> 27:21 28:14 33:5,21 46:17 51:14 77:17 <b>cover</b> 10:6 <b>coverage</b> 7:10 <b>covered</b> 55:13 56:4 69:1 <b>covering</b> 48:3 <b>create</b> 13:20 67:5 67:6 <b>created</b> 45:12 58:8 66:12 <b>creates</b> 87:20 <b>creating</b> 80:1,10 <b>creative</b> 77:6 <b>critical</b> 23:21 <b>cross</b> 62:8 <b>cultures</b> 66:20 <b>cumbersome</b> 50:16 <b>curative</b> 28:1 <b>cure</b> 58:5 <b>cures</b> 79:10 <b>current</b> 48:14 54:22 55:19,20,21 56:8 58:16 <b>cut</b> 64:11</p>	<p>33:22 34:1,2 44:12 49:22 53:8 53:16,16,21,22 54:1,9,11 59:7 68:3 72:5,8,8,11 72:12,19 73:8 76:17 77:18 78:12 78:14,14 82:4,10 85:9 <b>databases</b> 14:10 <b>date</b> 9:4 91:13 <b>day</b> 13:10 20:13 64:9,16 65:5 <b>days</b> 7:19 13:12 <b>de</b> 42:19 50:18 58:12,14 <b>deal</b> 28:21 67:15 <b>dealing</b> 24:18 <b>dealt</b> 76:10 <b>death</b> 24:13,21 <b>deaths</b> 24:20 <b>debating</b> 71:2 <b>decides</b> 19:15 <b>decision</b> 19:6 22:9 27:6 49:22 50:3 64:17 74:18 <b>decisions</b> 27:14 65:18 <b>decreasing</b> 24:20 <b>dedicated</b> 69:16 <b>deemed</b> 45:3 <b>deep</b> 36:8 <b>deficiency</b> 30:21 <b>define</b> 16:3 <b>definition</b> 23:11 63:18 70:18 <b>definitions</b> 15:21 <b>degree</b> 31:13 36:1 <b>deliver</b> 25:12 <b>delivered</b> 29:18 56:2 <b>delivery</b> 11:14 19:10 29:16 30:8 36:7,8 38:18</p>	<p>46:22 60:17 <b>delta</b> 72:8 <b>demand</b> 72:22 <b>demands</b> 87:11 <b>demonstrate</b> 31:16 44:2 73:18 <b>demonstrated</b> 23:17 38:2 44:8 47:13 <b>demonstrating</b> 43:12 <b>depend</b> 49:4 51:11 <b>depending</b> 75:12 <b>depends</b> 22:1 33:15 <b>deposited</b> 37:21 <b>depth</b> 14:2 <b>deputy</b> 2:1 4:6 5:21 <b>described</b> 39:2,11 41:5 <b>describing</b> 36:12 48:4 84:9 <b>design</b> 50:5 62:2 <b>designated</b> 45:13 <b>designation</b> 47:20 <b>designed</b> 23:21 31:18 <b>despite</b> 28:21 <b>detail</b> 48:13 54:21 55:18 <b>detailed</b> 61:13 <b>details</b> 9:7 <b>determine</b> 47:8 <b>determining</b> 37:3 42:13 <b>develop</b> 27:7 72:11 <b>developing</b> 36:6 60:19 <b>development</b> 5:11 35:18 49:15 50:3 51:3 79:22 80:2 81:3,6 83:21 87:3</p>
	<p><b>d</b></p>		
	<p><b>d</b> 4:1 <b>dancing</b> 76:6 <b>danelle</b> 68:22 <b>data</b> 15:4,13 20:4 21:18 23:13 28:21 30:8,12 31:6,7,12 31:15,22 32:6</p>		



<p><b>device</b> 4:21 12:4,5 12:18,22 13:9,15 14:4,9 15:7 16:2 16:15,17 17:4,4 17:20 18:10 19:7 20:21 21:7 23:7,9 24:6 26:19 29:7 29:22 30:5 31:5 33:10,18 35:3 36:8 37:15,15 38:1,6,12 41:19 44:20 45:1,7,12 45:14,15,21 46:1 46:4,8,10,15 47:1 47:4 52:13,17 53:2,15,15 54:10 55:15 56:19 57:4 57:6,10,18 58:3 58:15 59:7,17 60:1,6 62:4,16 66:7,9,18,22 68:18 70:1 71:17 72:9,13,22 73:12 74:13,16,17,20 76:1 77:17,21 78:16 80:13 81:2 82:19 83:3,12 84:11,13</p> <p><b>device's</b> 45:9</p> <p><b>devices</b> 1:2 2:7 4:3 4:11,20,22 6:2 11:4 15:20 23:4 29:2 31:10 33:7 33:14 34:14 36:7 36:12 38:4 41:8 41:14 43:3,17 44:19 45:5,6,19</p> <p><b>dexamethasone</b> 38:14,18 39:4,16</p> <p><b>dia</b> 62:13</p> <p><b>diabetic</b> 56:10</p> <p><b>diagnostic</b> 37:20 38:9</p>	<p><b>diane</b> 2:3 5:17</p> <p><b>differ</b> 14:3</p> <p><b>difference</b> 59:5,5 60:11</p> <p><b>differences</b> 67:2,3</p> <p><b>different</b> 14:10 26:3,3,4,4,5,5 29:5,6 33:20 41:10,18 44:12 46:3,4 48:17 52:20,22 54:20 60:20 62:19 64:5 66:20 69:1,11 73:13 76:2 79:8</p> <p><b>differently</b> 13:22 43:20</p> <p><b>difficult</b> 28:22 34:12 74:1 75:11 75:13</p> <p><b>dilution</b> 29:19</p> <p><b>directed</b> 80:9</p> <p><b>direction</b> 90:5</p> <p><b>director</b> 5:15,18 5:21 6:2</p> <p><b>disagreement</b> 69:21</p> <p><b>discern</b> 17:2</p> <p><b>discontinue</b> 19:15</p> <p><b>discourage</b> 67:8 87:6</p> <p><b>discouraging</b> 66:14 84:6</p> <p><b>discrepant</b> 20:1,3</p> <p><b>discussed</b> 71:4</p> <p><b>discussing</b> 88:9</p> <p><b>discussion</b> 75:16 77:4,5</p> <p><b>disease</b> 24:16 26:14 27:16 29:5 29:6</p> <p><b>disqualifies</b> 41:16</p> <p><b>distinction</b> 76:21</p> <p><b>distinctly</b> 44:12</p>	<p><b>diverse</b> 62:16</p> <p><b>docket</b> 5:6,8 9:1,4 9:8,9 10:7,13 88:18,19 89:1</p> <p><b>doing</b> 18:9 32:18 36:20 70:16 75:3 78:7 80:18 81:14 81:15</p> <p><b>domains</b> 50:2</p> <p><b>domurad</b> 2:12 3:5 22:17,18 33:4,11 34:11 35:11</p> <p><b>don't</b> 82:12</p> <p><b>door</b> 63:12 64:18 69:10</p> <p><b>dosage</b> 15:2 16:18 19:2 39:6 48:20 49:13 52:8 56:3 58:16</p> <p><b>dosages</b> 26:4</p> <p><b>dose</b> 11:14 46:7</p> <p><b>doses</b> 29:3</p> <p><b>dosing</b> 46:4</p> <p><b>double</b> 46:13</p> <p><b>douglas</b> 2:5</p> <p><b>doxorubicin</b> 30:8 30:10</p> <p><b>dr</b> 2:1,5,7,10,12 2:13 3:4,5,6 4:2 5:20 6:1,6 10:12 20:17 21:5,12,15 22:13,15,16,18 32:21,22 33:2,4,5 33:11 34:6,11 35:9,11,12,14 51:5,6,7,9,10,16 52:11,15 53:12,19 54:12,12,13,17,18 55:11 56:15,16,22 57:1,5,8,12,14,19 57:20,21 58:10,13 58:22 59:9 60:22 61:2,3 74:4 77:10 79:17 80:22 82:15</p>	<p>83:9 85:6 87:22</p> <p><b>drafted</b> 36:18</p> <p><b>drafting</b> 49:20</p> <p><b>draw</b> 12:20 17:16 84:4</p> <p><b>drawing</b> 64:2 84:6</p> <p><b>drawn</b> 84:12,13</p> <p><b>drd</b> 12:3 13:17 17:11 18:18 19:20 21:10 22:8 36:22 37:3,9,10 40:18 41:12 42:14 43:11 47:3 49:8,12,15 50:14 51:3 52:7 55:3 76:12</p> <p><b>drds</b> 4:20 34:8 36:13 41:4,8,10 41:13,16 42:6,9 42:14,15,17,20 43:1 47:7,20 49:4 50:14,18,19,22 51:10</p> <p><b>dressings</b> 25:14</p> <p><b>driven</b> 64:13</p> <p><b>driving</b> 86:8</p> <p><b>drug</b> 1:4,9 2:5 4:4 4:6 5:1,2,22 11:5 11:8,9,10,17 12:3 12:19,22 13:8,11 13:14 14:5,15,21 15:15,17 16:2,11 16:12,17 17:2,4,9 18:10,17,21 19:6 19:13,15,16,19 20:21 21:3,7,20 21:22 22:2 23:7 23:11 24:6 25:16 31:6 33:10,19 36:6,7 38:19 39:4 39:5,8,10,14,15 39:19 40:7,13,14 40:15 41:11 42:12 42:13 44:15 45:6 45:8,10,15,16,18</p>
---	--	--	--

<p>45:22 46:4,7,10 46:12,14,15,17,18 46:20 47:15,19 48:2,5,14,16 49:1 49:3,8,14 52:9,16 52:18,21 53:1,2 53:10 54:4,9,22 55:8,15,15,19,20 55:20 56:2,8,9,9 56:12,13,14,18 57:17,22 58:2,6 58:15,20,21 59:3 59:11,15,15,16 60:6,11,13,15,16 62:4,17 66:7,9,18 66:20 69:8 70:1,7 70:9,15 74:8,10 74:14 76:1,7,14 76:15,16,18 77:20 79:1 81:2,5,12,14 81:22 83:11,14,15 83:16 84:4,6 85:1 85:4,8,21 <b>drugs</b> 4:20 13:21 15:19 23:4,11 26:3 31:10 34:15 36:13 37:9 40:2,5 42:5 43:6,14 45:4 47:5 54:3 79:8,9 <b>dual</b> 25:8 <b>dumb</b> 53:7 <b>duplicate</b> 19:22 74:6 <b>dyer</b> 6:7,12</p>	<p><b>economically</b> 64:13 68:13 <b>economics</b> 63:6,16 63:18,21 65:3 73:2 87:14 <b>effect</b> 19:7 27:18 35:7 46:2,19 57:22 58:2,3 <b>effective</b> 21:6 23:18 26:18 <b>effectively</b> 13:2 <b>effectiveness</b> 11:7 23:7,13 30:12 31:12,17 41:11 43:12,16 44:3 47:17 50:22 63:3 65:9 66:10 72:4 76:16 <b>effects</b> 65:19 <b>efficacy</b> 15:5 30:4 30:9 38:3 <b>efficiently</b> 66:11 <b>effort</b> 9:10 84:9 <b>efforts</b> 36:17 <b>either</b> 11:6,14 38:17 56:6 59:8 <b>electronic</b> 7:10,12 <b>elements</b> 33:17 34:4 <b>else's</b> 82:5 <b>eluting</b> 45:8 59:15 <b>emails</b> 31:1 <b>embolic</b> 25:15,17 26:19 29:1,7,15 29:22 30:6 <b>emdr</b> 15:14 <b>emotional</b> 63:10 63:11 <b>emphasize</b> 9:9 <b>employed</b> 90:8,11 91:7 <b>employee</b> 90:10 <b>employees</b> 6:16</p>	<p><b>employing</b> 50:1 <b>emulsion</b> 25:14,19 <b>enabled</b> 47:1 <b>encompass</b> 23:5 <b>encourage</b> 9:2 67:13 88:17 <b>encouraging</b> 66:15 84:4 <b>ended</b> 9:22 <b>endpoint</b> 44:12 <b>endpoints</b> 26:6 29:3 44:21 46:20 47:8,12 <b>ends</b> 8:1 <b>engaged</b> 70:19 <b>engineering</b> 2:11 36:2 63:20 <b>enhance</b> 11:7 21:2 <b>enrolled</b> 24:2 <b>ensure</b> 15:6 16:20 21:3 <b>entire</b> 28:4 33:9 <b>entirely</b> 33:18 41:20 <b>entities</b> 18:12 <b>entity</b> 14:8 60:19 60:21 <b>entrepreneur</b> 36:9 <b>environment</b> 70:12 <b>envision</b> 56:17 <b>envy</b> 86:18 <b>equation</b> 72:12 <b>equivalent</b> 41:14 44:1 <b>equivalents</b> 38:3 <b>error</b> 17:17 18:4 37:7,8 48:10,10 <b>errors</b> 11:22 48:12 <b>especially</b> 21:19 34:2 <b>essentially</b> 31:5 <b>establish</b> 37:2</p>	<p><b>established</b> 21:20 22:3 <b>esteemed</b> 35:15 <b>ethiodized</b> 25:13 <b>europe</b> 32:6 <b>evaluation</b> 2:3,5 5:19,22 <b>event</b> 12:8,10 14:1 14:1,3 15:9 16:6 17:11 19:4 <b>events</b> 11:21 12:2 13:8 17:4 21:1 30:9 57:1 75:11 <b>evidence</b> 7:2 30:3 30:4 37:4,6 43:11 43:13,22 44:2,8 44:14 45:16,16,18 46:12 47:11,15,16 47:17 50:1,2,8,9 50:20 59:8,10,10 59:14,20 60:7,20 69:15 72:3 <b>evidentiary</b> 44:7 <b>exactly</b> 51:17,21 52:16 62:11 <b>exam</b> 68:5,6 <b>examination</b> 43:17 <b>example</b> 29:11 34:19,20 36:22 43:6 44:14 45:1 45:22 47:2 51:20 52:9 54:5 55:16 57:15 58:4 59:14 60:14 87:10 <b>examples</b> 45:7,13 72:1 <b>exceedingly</b> 42:7 <b>exceptions</b> 44:5 <b>excipient</b> 52:10 <b>excipients</b> 49:11 51:18,19 52:2,6 <b>exclude</b> 53:4</p>
<b>e</b>			
<p><b>e</b> 1:22,22 3:1 4:1,1 <b>early</b> 8:2 <b>easier</b> 86:5 <b>easily</b> 46:21 <b>easy</b> 17:2 29:10 67:7 86:20,21,22 <b>economic</b> 68:8 77:14,19,22 79:17 82:8 85:17</p>			

<p><b>excluded</b> 49:12 52:6</p> <p><b>exclusively</b> 74:8</p> <p><b>exclusivity</b> 47:21 48:1</p> <p><b>excuse</b> 27:10</p> <p><b>exist</b> 18:2 23:1 42:21 49:3 56:6 63:16</p> <p><b>existing</b> 11:3 27:19 30:8 31:6,7 31:12</p> <p><b>exists</b> 48:13 54:22 55:18</p> <p><b>expand</b> 11:9</p> <p><b>expanded</b> 81:6</p> <p><b>expanding</b> 54:10</p> <p><b>expansions</b> 44:5</p> <p><b>expectation</b> 11:18 13:14</p> <p><b>expectations</b> 36:15 80:19</p> <p><b>expected</b> 13:9</p> <p><b>expectedness</b> 15:8</p> <p><b>expecting</b> 85:18</p> <p><b>experience</b> 20:21 23:6</p> <p><b>explain</b> 66:5 74:21</p> <p><b>explicit</b> 33:6</p> <p><b>exposure</b> 25:22 29:21</p> <p><b>exposures</b> 27:11</p> <p><b>extent</b> 27:5,15,16 31:11 63:8</p> <p><b>extraordinarily</b> 80:21</p> <p><b>extremely</b> 43:1</p>	<p>68:2 69:16 73:22 74:1 75:19,22 76:13</p> <p><b>factors</b> 37:8 43:7 47:14</p> <p><b>failed</b> 68:9 73:5</p> <p><b>fair</b> 57:20 84:14</p> <p><b>fairly</b> 38:10 51:14 54:15</p> <p><b>fairness</b> 75:20,21</p> <p><b>fall</b> 40:17 86:17,19 87:7</p> <p><b>falling</b> 39:9</p> <p><b>falls</b> 39:5</p> <p><b>familiar</b> 25:7 33:13</p> <p><b>far</b> 33:12 61:15 80:7 81:2</p> <p><b>farkas</b> 1:21 90:2 90:17</p> <p><b>fast</b> 47:20 67:1,1,2</p> <p><b>fda</b> 5:4,12 6:7,11 6:14,16 7:2,7,11 7:18,22 21:4 26:19 28:8 59:13 62:13 67:14 70:17 72:16 75:6 84:13 84:22 88:5,11,15</p> <p><b>fda's</b> 4:3 5:10 7:9 7:14</p> <p><b>feasible</b> 31:19</p> <p><b>february</b> 31:4</p> <p><b>federal</b> 9:5 61:9 71:20 78:3 82:17</p> <p><b>feedback</b> 30:17</p> <p><b>feel</b> 44:16,22 46:12 72:21</p> <p><b>feels</b> 70:9</p> <p><b>field</b> 17:1 18:8 34:14</p> <p><b>fields</b> 15:15</p> <p><b>fifth</b> 75:14</p> <p><b>figure</b> 63:5 74:10</p>	<p><b>filed</b> 73:21</p> <p><b>files</b> 39:20</p> <p><b>filing</b> 61:12</p> <p><b>film</b> 7:14</p> <p><b>final</b> 75:14</p> <p><b>finally</b> 37:10 51:1 74:3</p> <p><b>financially</b> 90:12 91:8</p> <p><b>find</b> 8:4 16:16</p> <p><b>fine</b> 57:18</p> <p><b>finished</b> 24:2</p> <p><b>fired</b> 82:14</p> <p><b>first</b> 7:1 9:12 10:9 11:6 20:15 36:21 37:13 39:22 40:21 43:10 61:21 63:1 66:3 72:2 73:8 74:8</p> <p><b>fit</b> 71:22</p> <p><b>five</b> 8:20 30:22 65:22 66:1</p> <p><b>fixed</b> 46:7,8</p> <p><b>flexibility</b> 47:8</p> <p><b>focus</b> 77:13</p> <p><b>focused</b> 10:15 62:8 74:6</p> <p><b>folks</b> 63:9 65:17 65:18 78:3</p> <p><b>follow</b> 13:9,14 26:5 61:18 74:9 78:19 80:22 81:11</p> <p><b>followed</b> 25:14 61:15,16 86:1</p> <p><b>following</b> 7:22 29:16</p> <p><b>food</b> 1:9 4:6</p> <p><b>forcing</b> 84:14</p> <p><b>foregoing</b> 90:3</p> <p><b>form</b> 15:16 36:22 49:13</p> <p><b>forms</b> 52:8</p> <p><b>formulate</b> 20:8</p>	<p><b>formulation</b> 49:6 53:3</p> <p><b>formulations</b> 51:14,19 52:3,20 52:22 53:4</p> <p><b>forum</b> 71:3,3</p> <p><b>forums</b> 10:17</p> <p><b>forward</b> 49:16 77:18 78:2</p> <p><b>foster</b> 80:2,8</p> <p><b>fostering</b> 80:7</p> <p><b>founder</b> 36:3</p> <p><b>four</b> 6:18 8:8 51:22</p> <p><b>fourth</b> 13:15 71:7</p> <p><b>frankly</b> 59:12</p> <p><b>free</b> 82:6,7,7</p> <p><b>frequent</b> 24:13</p> <p><b>frequently</b> 28:12 31:8 51:15</p> <p><b>frn</b> 80:4</p> <p><b>frontiers</b> 64:3</p> <p><b>fruitful</b> 77:4</p> <p><b>full</b> 8:3 31:4 88:3</p> <p><b>function</b> 27:18,20 44:16,22 46:13</p> <p><b>functionality</b> 45:9</p> <p><b>fund</b> 80:20</p> <p><b>fundamentally</b> 73:12</p> <p><b>further</b> 12:13 56:17 90:10</p> <p><b>furthermore</b> 44:11</p>
<p><b>f</b></p>			<p><b>g</b></p>
<p><b>face</b> 30:22,22</p> <p><b>facilitating</b> 35:15</p> <p><b>facilities</b> 32:17</p> <p><b>fact</b> 28:10 53:10 53:14 55:8 58:14 63:16 66:16 67:11</p>			<p><b>g</b> 4:1</p> <p><b>gaba</b> 32:10</p> <p><b>gap</b> 14:19</p> <p><b>gate</b> 87:8</p> <p><b>gatekeeper</b> 65:5</p> <p><b>general</b> 17:14 40:7 42:16,18,22 82:18</p> <p><b>generalizable</b> 82:21</p>

<p><b>generate</b> 77:18</p> <p><b>generic</b> 37:8 38:14 39:2,15 40:2,5,10 40:13 49:3,8,9 52:4,14 57:8 79:1 79:9 82:6</p> <p><b>generics</b> 49:2,6 51:12,20 57:9</p> <p><b>genuinely</b> 70:9</p> <p><b>getting</b> 65:15 85:4</p> <p><b>give</b> 8:5 24:9 70:2 72:1</p> <p><b>given</b> 7:21 22:21 28:4 58:14,20</p> <p><b>giving</b> 29:11</p> <p><b>glad</b> 77:4</p> <p><b>global</b> 18:20</p> <p><b>globally</b> 19:2</p> <p><b>go</b> 9:11,20 10:6 25:16 67:1,7,18 68:3,11 70:10 73:1 74:19 81:14 82:3 87:12,16</p> <p><b>goal</b> 80:10</p> <p><b>goals</b> 44:10</p> <p><b>goes</b> 85:11</p> <p><b>going</b> 5:7 13:18,19 14:6,7,14 16:3,10 16:14,15,22 17:1 17:13,13 18:3 19:3,5 23:4,12 24:9 34:18 35:2,3 53:13,14 54:15 58:1,2 60:3,21 61:11,12,17,18 66:2 69:2 72:13 73:9 74:5 79:13 79:19 82:15 87:1 87:8,13,19</p> <p><b>good</b> 4:2 5:17,20 6:1 10:12 18:15 22:11,18 53:19 61:5 62:14 63:11 63:14 64:10,19,20</p>	<p>65:10,14 68:7,13 68:14,21 69:12 75:17</p> <p><b>gotten</b> 66:1</p> <p><b>grandparents</b> 30:10</p> <p><b>granted</b> 17:21</p> <p><b>graph</b> 64:5,5</p> <p><b>great</b> 28:21 42:5 68:1</p> <p><b>greater</b> 36:14 59:14</p> <p><b>green</b> 9:20</p> <p><b>ground</b> 6:22</p> <p><b>group</b> 23:5 40:1 44:10 62:8</p> <p><b>growing</b> 31:14</p> <p><b>guess</b> 21:9 53:9 80:18</p> <p><b>guidance</b> 49:16,20 50:10,14 51:3</p> <p><b>guns</b> 64:5</p> <p><b>guys</b> 65:5 68:2,20 85:2</p>	<p><b>healthcare</b> 13:4 17:22 18:4</p> <p><b>healthy</b> 27:7</p> <p><b>hear</b> 5:7 9:12</p> <p><b>heard</b> 79:21 81:3</p> <p><b>hearing</b> 4:3,8,18 35:16 61:6 65:3 68:21</p> <p><b>heart</b> 62:9 65:12 71:8</p> <p><b>held</b> 45:15 62:13 68:20</p> <p><b>help</b> 5:10 20:8 22:8 66:19 74:21 80:8</p> <p><b>helped</b> 22:20</p> <p><b>helpful</b> 54:14 57:15</p> <p><b>hepatitis</b> 27:12</p> <p><b>hepatocellular</b> 24:11,21 25:6 26:10 27:3,8 28:3 28:5,18 30:2</p> <p><b>hereto</b> 90:11</p> <p><b>hi</b> 5:14 6:4</p> <p><b>high</b> 14:17 19:8 42:16,17 43:3 61:19</p> <p><b>higher</b> 64:22</p> <p><b>highlight</b> 11:16 12:14</p> <p><b>highlighted</b> 17:19</p> <p><b>highly</b> 46:9</p> <p><b>historical</b> 44:10</p> <p><b>history</b> 14:20 16:20 23:17 47:5</p> <p><b>hmm</b> 51:9 53:12</p> <p><b>hold</b> 35:22</p> <p><b>holder</b> 11:20</p> <p><b>holds</b> 25:18</p> <p><b>home</b> 89:3</p> <p><b>honestly</b> 33:15</p> <p><b>hood</b> 85:7</p>	<p><b>hope</b> 70:13,14 73:4 82:15</p> <p><b>hopefully</b> 20:1 27:2</p> <p><b>horse</b> 86:17,18,19</p> <p><b>huge</b> 34:16</p> <p><b>human</b> 42:1,2</p> <p><b>humans</b> 42:7</p> <p><b>hypervascular</b> 30:1</p>
	<b>h</b>		<b>i</b>
	<p><b>hallway</b> 4:17</p> <p><b>hampshire</b> 1:10</p> <p><b>hand</b> 6:8 16:7</p> <p><b>handle</b> 14:11 17:13</p> <p><b>handout</b> 9:6</p> <p><b>happen</b> 18:16 48:4</p> <p><b>happened</b> 12:8</p> <p><b>happens</b> 10:1 19:16 74:10</p> <p><b>happy</b> 36:9</p> <p><b>hard</b> 35:17 61:8 66:16,19 67:4 72:20</p> <p><b>hcc</b> 28:13</p> <p><b>head</b> 46:22</p> <p><b>health</b> 2:8 6:3 17:8 40:22 42:3 70:10 73:14</p>	<p><b>ide</b> 23:19 24:3 29:11,14 30:7,16 30:18,20 31:9 32:1</p> <p><b>idea</b> 63:11 65:13 65:14 68:7,14 69:11 83:13</p> <p><b>ideas</b> 64:10,19,20 68:14</p> <p><b>identical</b> 29:20</p> <p><b>identification</b> 37:8</p> <p><b>identified</b> 13:13 14:3 26:8 71:11 77:8 82:17</p> <p><b>identify</b> 6:7 12:6,7 12:9 80:17 81:12</p> <p><b>identifying</b> 12:1 49:2,3 64:14 80:10,13</p> <p><b>ides</b> 34:7</p> <p><b>ii</b> 37:3 42:17 50:19 58:12,14,21</p> <p><b>iii</b> 37:3 41:8,8,21 42:11,15 43:3 58:12</p> <p><b>illustration</b> 24:10 27:2</p> <p><b>imaging</b> 26:5</p> <p><b>immediate</b> 40:9</p> <p><b>impact</b> 31:13 35:8 79:22</p> <p><b>impairment</b> 42:2</p>	

<p><b>implemented</b> 32:2 32:9 43:20 80:6</p> <p><b>implication</b> 21:14</p> <p><b>implications</b> 79:10</p> <p><b>importance</b> 42:2</p> <p><b>important</b> 5:8 9:9 27:6 31:19 35:17 38:1 43:1 67:9,17 72:16 83:7</p> <p><b>impossible</b> 75:12</p> <p><b>impressed</b> 61:14</p> <p><b>impression</b> 86:4</p> <p><b>improve</b> 11:6 50:4</p> <p><b>improved</b> 11:5</p> <p><b>improvements</b> 44:16</p> <p><b>incentivize</b> 68:1 87:4,5</p> <p><b>incidence</b> 24:21</p> <p><b>include</b> 19:1 48:15 52:10,19 55:7 56:11,20</p> <p><b>includes</b> 62:4 63:6</p> <p><b>including</b> 7:15 11:21 15:15 24:3 38:14 44:16 47:12 48:18 49:1</p> <p><b>incorporate</b> 50:10 54:1</p> <p><b>increased</b> 24:22</p> <p><b>increasing</b> 11:12</p> <p><b>incredibly</b> 54:2</p> <p><b>incrementally</b> 47:6 58:19</p> <p><b>incurred</b> 57:6</p> <p><b>incurring</b> 40:11</p> <p><b>ind</b> 34:9 35:6</p> <p><b>independent</b> 46:19</p> <p><b>independently</b> 50:17</p> <p><b>indicated</b> 24:19 60:17</p>	<p><b>indication</b> 11:8,10 15:1 23:14 26:20 30:7,14,15 39:12 40:11</p> <p><b>indications</b> 39:10 48:18 55:14 81:6</p> <p><b>indifferent</b> 82:1</p> <p><b>indiscriminately</b> 47:16</p> <p><b>individual</b> 7:20 35:1 40:7,19</p> <p><b>inds</b> 60:14</p> <p><b>industry</b> 10:17 85:21</p> <p><b>inflammation</b> 38:20 39:13 58:18</p> <p><b>inflammatory</b> 38:19 39:1,7</p> <p><b>inflated</b> 37:18</p> <p><b>influence</b> 81:5</p> <p><b>inform</b> 5:10 18:3</p> <p><b>informal</b> 7:1</p> <p><b>information</b> 5:4 12:17,18,20 13:1 13:19 14:7,11,14 15:15 17:12 18:2 18:6 20:1,2,3,22 21:16,19 22:10 33:16 40:16 48:11 48:15,17 55:7 56:20 74:7,14 75:1 82:18 83:3 88:15,22 89:1</p> <p><b>informative</b> 88:3</p> <p><b>informed</b> 17:10</p> <p><b>infrastructure</b> 15:9</p> <p><b>infusion</b> 37:15 38:8</p> <p><b>inherent</b> 42:9</p> <p><b>inherently</b> 41:7,18 43:2 48:6</p> <p><b>inhibit</b> 82:13</p>	<p><b>inhibited</b> 81:18</p> <p><b>initial</b> 16:14</p> <p><b>injectable</b> 38:16 49:5 51:11</p> <p><b>injection</b> 35:1 38:15 39:17 58:6</p> <p><b>injury</b> 42:4</p> <p><b>innovate</b> 40:15</p> <p><b>innovation</b> 20:15 47:4 80:7,9 81:18 82:14</p> <p><b>innovative</b> 80:2</p> <p><b>innovator</b> 36:9 82:10</p> <p><b>innovators</b> 36:16 47:4</p> <p><b>input</b> 4:19</p> <p><b>insightful</b> 88:14</p> <p><b>instance</b> 35:5 74:7</p> <p><b>instances</b> 23:9,16</p> <p><b>institute</b> 24:16</p> <p><b>instructions</b> 9:13</p> <p><b>insult</b> 27:9</p> <p><b>intelligent</b> 77:6</p> <p><b>intelligently</b> 79:16</p> <p><b>intend</b> 8:3</p> <p><b>intended</b> 36:14 38:6,8 40:18</p> <p><b>intent</b> 39:5 43:19 45:5,6 47:10</p> <p><b>intentions</b> 18:15</p> <p><b>interaction</b> 12:21 16:17 17:5</p> <p><b>interest</b> 10:22 37:17 39:18 55:1</p> <p><b>interested</b> 6:10 8:16 9:3 40:1 80:1 90:12 91:8</p> <p><b>interfere</b> 4:12</p> <p><b>intermediate</b> 25:5 25:11 26:9</p> <p><b>international</b> 2:10</p> <p><b>interpretation</b> 39:3</p>	<p><b>interpreted</b> 39:9 57:22</p> <p><b>interrupt</b> 7:4 10:3</p> <p><b>intervals</b> 26:4 29:3</p> <p><b>interventional</b> 26:14 32:14</p> <p><b>interventions</b> 38:21</p> <p><b>interviewed</b> 32:14</p> <p><b>intraluminal</b> 38:10</p> <p><b>introduce</b> 5:13</p> <p><b>introduced</b> 37:16 55:9</p> <p><b>introduces</b> 18:22 40:3 55:11</p> <p><b>intuitive</b> 69:12</p> <p><b>inventor</b> 36:9</p> <p><b>invest</b> 64:12</p> <p><b>investigational</b> 23:1</p> <p><b>involved</b> 10:16 73:21 74:16</p> <p><b>ionically</b> 29:17</p> <p><b>issue</b> 17:3,4,5 20:20 35:17 53:18 53:18,20 63:3,6,9 73:21 75:18 76:7 77:19 78:1 85:14 85:17</p> <p><b>issued</b> 48:5</p> <p><b>issues</b> 40:22 41:3 41:11 48:9 49:17 53:5 62:19 66:10 76:15,15 77:14 85:20 88:9</p> <p><b>it'll</b> 72:16 81:16 81:17</p> <p><b>i'm</b> 78:8</p>
<b>j</b>			
		<p><b>january</b> 9:1 88:20</p> <p><b>jeff</b> 2:7 6:1</p>	

<p><b>jessica</b> 91:2,13  <b>job</b> 75:17  <b>john</b> 2:2 5:14  <b>june</b> 30:17  <b>juvenile</b> 56:10</p>	<p>49:14 52:14,16                      53:14 54:11,22                      55:21  <b>labeled</b> 4:22  <b>labeling</b> 12:3                      17:14 37:9 39:2,6                      39:14,18 40:2,14                      48:11,14,16 49:12                      52:7,17,18 53:2                      53:15 55:7,19,20                      56:5,6,7,8,12,12                      56:14,18 57:7                      59:6 60:16 62:9  <b>lack</b> 25:10 39:18                      85:16  <b>language</b> 79:10  <b>large</b> 34:21 77:21  <b>larger</b> 53:1  <b>lauren</b> 6:7  <b>law</b> 33:7 67:19                      80:12  <b>laying</b> 83:19  <b>lead</b> 42:10  <b>leading</b> 69:9  <b>leads</b> 45:8  <b>learn</b> 16:20,21  <b>learned</b> 72:21  <b>leave</b> 19:17 20:6  <b>led</b> 17:3 27:17                      60:1  <b>lee</b> 2:9 6:4,4  <b>left</b> 9:21  <b>legal</b> 40:22 53:17                      77:1  <b>legally</b> 38:13                      41:14  <b>legislate</b> 75:4  <b>length</b> 14:19  <b>lens</b> 62:19  <b>letters</b> 30:21  <b>letting</b> 39:19  <b>level</b> 14:17 15:3                      22:5 48:13 54:21                      55:6,17 61:19</p>	<p><b>leverage</b> 49:21  <b>leveraging</b> 50:1  <b>levers</b> 67:13,14  <b>liability</b> 40:3,11                      57:5  <b>life</b> 42:1 69:17                      85:3  <b>lifetime</b> 28:14  <b>light</b> 9:18  <b>limitations</b> 7:13                      17:18  <b>limited</b> 40:4  <b>line</b> 17:16  <b>lines</b> 64:3  <b>linked</b> 46:11  <b>listed</b> 8:6 48:3  <b>listen</b> 6:14 79:18  <b>listening</b> 7:6  <b>literally</b> 81:11  <b>literature</b> 21:17                      22:11 82:20  <b>little</b> 12:12 56:17                      61:21 66:21 77:15                      79:21 81:1  <b>lived</b> 18:9  <b>liver</b> 24:12 25:9                      26:14 27:16,18,20                      29:6  <b>load</b> 27:11 29:17  <b>lobby</b> 4:16  <b>local</b> 27:22 36:7                      39:13 58:17  <b>localized</b> 39:1,7  <b>located</b> 4:16  <b>location</b> 27:5  <b>locked</b> 40:14  <b>logistical</b> 18:7  <b>logistically</b> 18:16  <b>long</b> 26:17 47:5                      52:9 57:19 73:21                      79:6  <b>longer</b> 32:4  <b>longest</b> 34:2</p>	<p><b>look</b> 14:2 40:21                      43:7,10 65:13                      72:10 77:3 85:7  <b>looked</b> 71:14  <b>looking</b> 27:2 28:4                      59:11 64:1 67:12  <b>loose</b> 39:3  <b>lot</b> 30:11,14 33:17                      66:17 68:14,16                      88:15  <b>loved</b> 75:16  <b>low</b> 42:21  <b>lower</b> 65:9 73:3,4                      73:6,7  <b>lumen</b> 58:7  <b>luxury</b> 6:19</p>
<b>k</b>			
<p><b>k</b> 38:2,4 41:16                      42:19 50:18 58:15                      76:19  <b>keep</b> 6:20 9:15,16                      10:4 49:6 51:12                      81:14,17  <b>keeping</b> 6:13  <b>key</b> 14:17  <b>khaudeja</b> 2:10 3:4                      10:9  <b>kind</b> 20:20,21                      21:2 53:7 76:6                      77:15 81:7  <b>kirk</b> 2:13 3:6                      35:12,22 75:16  <b>know</b> 14:18 15:21                      17:6 21:13,22                      51:14 54:20 59:22                      63:19 64:4 65:7                      66:8 68:4 70:3,20                      71:1 74:17 78:20                      80:1 82:20 84:1                      84:18 85:1,5,8  <b>knowledge</b> 23:18                      82:21 84:18 90:7  <b>known</b> 26:16                      28:20,20 33:17                      35:19 38:15 42:11                      43:5 53:5 54:2,3                      70:22  <b>knows</b> 33:12</p>			
<b>l</b>			
<p><b>lab</b> 85:4  <b>label</b> 17:16 18:5                      20:9,11 26:21                      28:15 31:8 32:4,8                      39:4,8 40:8 44:5</p>			
		<p style="text-align: center;"><b>m</b></p> <p><b>magnitude</b> 17:7  <b>maintain</b> 16:12                      58:3,7  <b>maintained</b> 18:20  <b>major</b> 77:13 82:8  <b>maker</b> 19:6 40:7                      45:8 52:17 53:2                      54:9,10  <b>makers</b> 40:10,14  <b>makeup</b> 51:22  <b>making</b> 27:13                      39:18 49:22 50:3                      65:17 74:18 86:20  <b>malfunction</b> 13:10                      16:1  <b>malfunctions</b> 16:3  <b>maloney</b> 2:3 5:17                      5:18 59:2  <b>manage</b> 21:14                      73:19 75:7  <b>management</b>                      73:16  <b>mandate</b> 67:22  <b>mandated</b> 42:22                      43:2,22  <b>manufacture</b>                      37:14</p>	

<b>manufacturer</b> 16:11 17:12,20 18:17,18,21 19:15 19:19,21 20:22 21:7,8 22:9 57:4,6	<b>measures</b> 44:15 <b>mechanical</b> 36:2 38:20 44:21 <b>media</b> 6:9,17 7:10 7:12 <b>medical</b> 2:12 11:22 22:17 23:16 24:7 29:12,13 31:14,15 32:17 36:8 46:5 47:10 60:9 72:13 <b>medically</b> 36:16 <b>medication</b> 37:7 48:10 54:19 <b>medicine</b> 35:18 50:15 60:8 <b>medsystems</b> 2:13 35:13 36:5 37:14 50:13	<b>meta</b> 16:7 <b>method</b> 32:5,6,19 34:18 <b>methods</b> 48:5 50:4 <b>michael</b> 1:21 90:2 90:17 <b>micro</b> 37:15 <b>microneedle</b> 37:18 <b>miller</b> 68:22 <b>millions</b> 42:8 <b>mind</b> 71:13 72:17 <b>mindful</b> 67:10 <b>mine</b> 68:22 79:3 <b>minimum</b> 43:21 <b>minuses</b> 86:14 <b>minute</b> 7:21 8:20 9:21 <b>misappropriate</b> 82:10 <b>missing</b> 14:20 81:21 83:1 <b>mit</b> 36:1 <b>mix</b> 16:2 <b>mixed</b> 25:13 <b>mm</b> 51:9 53:12 <b>mobile</b> 4:11 <b>mode</b> 35:2 45:14 45:21 57:17 76:8 76:14 <b>moderate</b> 42:17 42:21 <b>modifications</b> 43:9 <b>molecule</b> 21:22 69:10,12,17 84:20 <b>money</b> 70:1 73:6 77:18 80:15 81:17 84:9 <b>monitor</b> 16:13 <b>month</b> 61:8 <b>mood</b> 67:19 <b>morning</b> 4:2 5:17 5:20 6:1 10:12 22:18 61:5 79:5	88:4,13 <b>move</b> 8:3 <b>moving</b> 34:1 <b>multifactorial</b> 27:20 <b>multiple</b> 19:18 49:1 50:2 59:21 <b>multitude</b> 31:1
<b>manufacturer's</b> 57:10 <b>manufacturers</b> 13:17 17:10 39:16 <b>marked</b> 30:6 <b>market</b> 5:2 10:14 10:22 11:20 19:4 19:9 20:4 31:22 34:3 52:1 57:9 68:4 73:16,19 74:3 80:14 <b>marketed</b> 1:4 4:4 11:5,8 38:4,13 41:14 49:2 <b>marketing</b> 4:22 19:16 41:19 <b>marketplace</b> 73:11 <b>markets</b> 19:12 <b>marriage</b> 66:17 <b>maryland</b> 90:19 <b>master</b> 39:19 <b>master's</b> 36:1 <b>materials</b> 64:2 85:8 <b>matter</b> 66:16 68:2 75:19 <b>matters</b> 20:14 <b>maze</b> 77:7 <b>md</b> 1:11 <b>mdr</b> 15:16 <b>mean</b> 19:14 34:14 68:8,9 76:2 79:11 79:13 82:9 86:9 <b>meaning</b> 74:21 <b>means</b> 8:4 26:21 67:5 71:14 86:21 <b>meant</b> 51:13	<b>meet</b> 55:21 <b>meeting</b> 4:15 5:5 6:11,14 7:1,6,6,9 7:17,19 8:12,14 8:19,22 22:20 31:1 36:10 61:6 62:13,14 74:5 88:9,11,19,22 89:3,4 <b>melodie</b> 2:12 3:5 22:16 <b>members</b> 6:8,15 7:2 32:15 71:10 81:21 <b>memo</b> 83:6 85:11 <b>mentioned</b> 68:20 <b>mercator</b> 2:13 35:13 36:5 37:14 50:13 <b>merely</b> 41:12 <b>meric</b> 2:12 <b>merit</b> 22:17 29:12 <b>message</b> 73:13 <b>met</b> 59:19	<b>millions</b> 42:8 <b>mind</b> 71:13 72:17 <b>mindful</b> 67:10 <b>mine</b> 68:22 79:3 <b>minimum</b> 43:21 <b>minuses</b> 86:14 <b>minute</b> 7:21 8:20 9:21 <b>misappropriate</b> 82:10 <b>missing</b> 14:20 81:21 83:1 <b>mit</b> 36:1 <b>mix</b> 16:2 <b>mixed</b> 25:13 <b>mm</b> 51:9 53:12 <b>mobile</b> 4:11 <b>mode</b> 35:2 45:14 45:21 57:17 76:8 76:14 <b>moderate</b> 42:17 42:21 <b>modifications</b> 43:9 <b>molecule</b> 21:22 69:10,12,17 84:20 <b>money</b> 70:1 73:6 77:18 80:15 81:17 84:9 <b>monitor</b> 16:13 <b>month</b> 61:8 <b>mood</b> 67:19 <b>morning</b> 4:2 5:17 5:20 6:1 10:12 22:18 61:5 79:5	<b>n</b> <b>n</b> 1:22 3:1,1 4:1 <b>name</b> 4:5 35:22 49:8,9 52:4 <b>names</b> 10:10 <b>national</b> 24:16 26:12 <b>navigate</b> 78:17 <b>naïve</b> 15:12 <b>nda</b> 34:9 49:7 51:17 76:18,20 86:13 <b>ndas</b> 82:22 <b>nearly</b> 24:11 <b>necessary</b> 36:17 <b>neck</b> 47:1 <b>need</b> 12:13 14:9 15:22 24:7 25:3 29:13 31:14,15 36:14 53:13 64:12 67:9 68:3 70:12 70:21 76:22 79:20 80:17 <b>needed</b> 67:6 <b>needs</b> 33:21 53:8 72:14,15 87:19 <b>negatively</b> 81:4,13 82:13 <b>neither</b> 81:13 90:7 91:6 <b>nervous</b> 84:22 <b>network</b> 26:13 <b>never</b> 69:19,21 <b>new</b> 1:2,10 4:4 5:3 11:4 13:20 17:11 19:1 33:19 40:2,3

<p>41:12 43:14 48:4 48:7,17,18 53:14 55:9,12 56:2,3,3 57:8 60:19,21 77:19 80:12 <b>nice</b> 75:17 <b>non</b> 44:9 <b>normal</b> 45:2 <b>normally</b> 34:21 54:6 <b>north</b> 24:17 <b>notary</b> 90:1,18 <b>note</b> 38:1 <b>notice</b> 9:5 61:9 71:20 78:4 82:17 <b>notified</b> 19:19 <b>novel</b> 35:18 47:1 48:4 54:6 <b>november</b> 1:5 31:3 <b>novo</b> 42:19 50:18 58:12,14 <b>nullify</b> 56:12 <b>number</b> 10:13 39:22 52:20,22 69:22 70:3 74:18 80:19</p>	<p><b>offered</b> 50:10 <b>office</b> 2:2,9 5:15 6:4 65:7 <b>officer</b> 4:8 36:4 90:2 <b>offset</b> 40:4 <b>oftentimes</b> 51:17 <b>oil</b> 25:13 <b>okay</b> 57:20 58:10 66:15 69:4 86:17 <b>old</b> 40:14 48:2 55:21 <b>older</b> 47:5 <b>once</b> 6:19 9:8 34:21 88:17 <b>oncology</b> 26:12 <b>open</b> 8:13,16 9:1 34:22 38:21,21 52:1 60:14 87:19 88:19 <b>opened</b> 58:9 <b>openness</b> 45:11 <b>operated</b> 56:19 <b>operates</b> 61:22 <b>opinion</b> 10:18,19 67:10 71:19 <b>opportunity</b> 4:19 22:19,21 83:17 <b>oppose</b> 70:15,16 <b>opposition</b> 70:17 70:22 <b>optimal</b> 64:15 <b>optimization</b> 64:6 <b>optimizing</b> 81:17 <b>orally</b> 61:12 <b>orange</b> 48:3,6 <b>order</b> 6:20 11:13 44:13 <b>organization</b> 10:20 12:5,6 13:9 13:19 14:4,5,9,22 15:7,10 16:15 <b>organizations</b> 22:6</p>	<p><b>organize</b> 22:20 <b>organizing</b> 61:6 62:15,21 <b>organs</b> 25:10 <b>outcome</b> 44:15 45:7 67:12 90:12 91:8 <b>outcomes</b> 28:22 46:10,12 <b>outflow</b> 25:20 29:20 <b>outline</b> 6:21 <b>outlined</b> 11:19 55:13 <b>outside</b> 4:15 8:19 37:21 39:9 <b>overall</b> 24:20 27:3 28:13 47:3 79:22 <b>owned</b> 56:19 78:12 <b>ownership</b> 72:5 <b>owns</b> 18:21</p>	<p><b>participants</b> 7:4 <b>participate</b> 68:18 <b>participated</b> 62:12 <b>particular</b> 49:21 56:21 69:9 83:15 <b>particularly</b> 27:4 35:20 86:9 <b>parties</b> 9:3 90:9 90:11 91:7 <b>partner</b> 87:18 <b>passionate</b> 62:3 <b>patency</b> 45:12 46:11 58:7 <b>patents</b> 48:2,4,7 <b>path</b> 41:17 59:17 77:6,7 78:1 <b>pathway</b> 13:11,15 42:19 43:3 50:18 66:13 67:5 71:11 73:18 76:2 78:18 80:2,6,13,17,20 81:4,11 85:15,20 86:5,6,12,13,20 87:14 <b>patient</b> 13:5 16:9 29:4 46:2 63:1,1 63:13,15 <b>patient's</b> 46:5 <b>patients</b> 18:3 19:17 24:3 27:7 28:5,11,13 42:8 47:1 56:10 71:1 <b>pattern</b> 53:10,14 <b>pay</b> 72:11 <b>peel</b> 77:15 <b>pejoratively</b> 82:9 <b>people</b> 18:8 22:20 23:20 64:18 69:8 79:20 84:19 85:18 86:5 <b>percent</b> 28:3,6,13 32:10,18</p>
<b>o</b>		<b>p</b>	
<p><b>o</b> 3:1 4:1 <b>obligation</b> 19:20 71:1 74:12 <b>observation</b> 70:5 <b>observations</b> 61:20 <b>obtains</b> 5:4 <b>obvious</b> 36:18 <b>obviously</b> 12:18 67:17 <b>occasion</b> 34:9 <b>occur</b> 12:22 22:5 <b>occurrence</b> 70:14 <b>october</b> 30:19 <b>offer</b> 70:5</p>		<p><b>pace</b> 45:8 <b>package</b> 30:16 <b>paclitaxel</b> 59:18 <b>page</b> 3:3 73:13 83:5 85:11 <b>pages</b> 79:6 <b>panel</b> 4:11 5:12 6:15 7:2,7,22 8:2 20:18 22:19 32:22 33:12 35:15 51:6 60:13 77:11 88:5 88:10 <b>paradigm</b> 21:10 86:13 <b>part</b> 29:12 70:17 83:18 <b>partial</b> 88:13 <b>participant</b> 7:5 84:15</p>	



<p><b>perception</b> 63:8</p> <p><b>performance</b> 44:10 64:3</p> <p><b>performed</b> 59:22</p> <p><b>performing</b> 26:22</p> <p><b>period</b> 8:3,13,17</p> <p><b>periodic</b> 16:10</p> <p><b>peripheral</b> 38:7 38:22</p> <p><b>perivascular</b> 38:10 39:11</p> <p><b>permitted</b> 7:13</p> <p><b>person</b> 88:8</p> <p><b>personal</b> 10:18 22:4</p> <p><b>personally</b> 81:20 81:22</p> <p><b>perspective</b> 11:1 39:21</p> <p><b>persuasive</b> 65:4</p> <p><b>ph.d.</b> 36:1</p> <p><b>pharma</b> 14:22 34:11 76:17 80:14 84:10</p> <p><b>pharmaceutical</b> 2:11 68:17 70:21 71:17 72:5,7,11 72:19 73:11 78:13 82:13 87:10</p> <p><b>pharmacology</b> 48:21</p> <p><b>pharmacovigila...</b> 13:21 17:15</p> <p><b>phase</b> 23:21 29:14 31:18</p> <p><b>phones</b> 4:11</p> <p><b>phosphate</b> 38:15 39:17</p> <p><b>physical</b> 44:20</p> <p><b>physician</b> 20:14</p> <p><b>physicians</b> 26:21 27:13 29:8 32:18</p> <p><b>pick</b> 81:15</p>	<p><b>pieces</b> 71:15,22 83:1,2</p> <p><b>pioneer</b> 40:12</p> <p><b>place</b> 17:22</p> <p><b>placed</b> 44:18</p> <p><b>places</b> 12:21</p> <p><b>plan</b> 11:20 72:4 83:7</p> <p><b>planning</b> 85:12</p> <p><b>platforms</b> 14:10</p> <p><b>play</b> 53:11 59:3</p> <p><b>playing</b> 59:6</p> <p><b>plays</b> 27:6</p> <p><b>please</b> 4:10 6:9,11 9:5</p> <p><b>plus</b> 21:21</p> <p><b>pluses</b> 86:14</p> <p><b>pma</b> 23:19 24:4 31:20 33:5 41:6 41:18 42:16 76:13 76:19</p> <p><b>pmas</b> 34:7 41:21 60:2</p> <p><b>podium</b> 9:17,19</p> <p><b>point</b> 18:7 24:9 52:5 58:1 66:3,5 68:16 73:1,8 75:14,14 76:5</p> <p><b>pointed</b> 85:6</p> <p><b>points</b> 36:19 65:22 66:2</p> <p><b>policy</b> 5:10,15,18 7:9 49:15,20 51:3 62:22 63:5 67:13 67:14</p> <p><b>policymaking</b> 50:6</p> <p><b>population</b> 28:4 29:5</p> <p><b>posed</b> 71:8</p> <p><b>position</b> 53:8</p> <p><b>positions</b> 62:22</p> <p><b>positively</b> 81:13</p>	<p><b>possibilities</b> 29:9</p> <p><b>possibility</b> 21:9 34:4</p> <p><b>possible</b> 6:21 48:9 70:7</p> <p><b>possibly</b> 23:14</p> <p><b>post</b> 10:14,22 19:4 20:4 31:22 34:3 73:16,19 74:3</p> <p><b>potential</b> 4:19 30:9 34:1 42:3 54:19 55:5,10,12 87:18</p> <p><b>potentially</b> 19:22 28:1 82:21</p> <p><b>practice</b> 43:20</p> <p><b>practices</b> 17:15</p> <p><b>pre</b> 30:16 31:22</p> <p><b>precautions</b> 48:19</p> <p><b>precedent</b> 60:3</p> <p><b>precisely</b> 63:16</p> <p><b>predicate</b> 41:14</p> <p><b>predominant</b> 34:18 35:2</p> <p><b>predominantly</b> 38:22</p> <p><b>preference</b> 22:4</p> <p><b>premarket</b> 41:6</p> <p><b>prepare</b> 12:6</p> <p><b>prepared</b> 16:16 77:17 91:3</p> <p><b>present</b> 8:9,11 27:1 42:3</p> <p><b>presentation</b> 6:20 7:4,16,22 8:11 9:22 54:14 61:14 69:1 74:4 77:14</p> <p><b>presentations</b> 8:6 8:18 10:9 88:6</p> <p><b>presenter</b> 7:3 9:14</p> <p><b>presenters</b> 6:15 9:14</p> <p><b>presenting</b> 8:16 36:10 75:17</p>	<p><b>preserve</b> 45:7,9,11</p> <p><b>president</b> 36:4</p> <p><b>presiding</b> 4:7</p> <p><b>press</b> 6:7</p> <p><b>pretty</b> 63:4 69:12 69:18 76:9</p> <p><b>prevails</b> 47:18</p> <p><b>prevent</b> 48:12</p> <p><b>prevented</b> 15:4</p> <p><b>preventing</b> 42:2</p> <p><b>prevents</b> 25:17</p> <p><b>previously</b> 23:12 30:1,3 38:4 71:5 78:12</p> <p><b>primarily</b> 27:11</p> <p><b>primary</b> 24:12 28:7 35:7 45:14 45:21 46:9,11 57:17 76:8,14</p> <p><b>principal</b> 2:1 4:5</p> <p><b>principle</b> 62:15,21</p> <p><b>prior</b> 30:6 79:2</p> <p><b>priorities</b> 37:12 49:19 50:11 51:2</p> <p><b>priority</b> 47:21 65:1</p> <p><b>prism</b> 74:16</p> <p><b>private</b> 71:3</p> <p><b>probably</b> 35:8 85:11</p> <p><b>problem</b> 26:1 82:8 82:8</p> <p><b>problems</b> 82:6</p> <p><b>procedural</b> 46:19</p> <p><b>procedure</b> 28:8</p> <p><b>procedures</b> 7:10</p> <p><b>proceed</b> 10:8</p> <p><b>proceeding</b> 90:3</p> <p><b>proceedings</b> 7:11 7:15 90:4,6</p> <p><b>process</b> 24:4 29:11 31:5 36:13 37:1 47:3 50:6 70:18 83:18 84:8,15</p>
--	---	---	---

<p><b>processes</b> 15:18</p> <p><b>product</b> 11:1,17 11:19 12:17 13:3 13:13 17:17 18:10 18:11,17,20 19:9 21:3,20 28:8 46:18 52:14 55:3 59:7 76:7,9,12 79:22 81:6 85:4 87:3</p> <p><b>production</b> 64:3</p> <p><b>productive</b> 88:13</p> <p><b>products</b> 2:2,14 5:16 23:5,17 31:13 33:9 41:22 45:20 47:10 54:20 55:3 59:13 60:2 61:4 62:4</p> <p><b>professional</b> 13:4 18:1</p> <p><b>professionals</b> 18:4</p> <p><b>profile</b> 11:17 16:12 18:17,20,21 22:2,4 37:2 42:7 42:12 43:5 57:3 58:20</p> <p><b>profiles</b> 35:21</p> <p><b>program</b> 66:12 81:19</p> <p><b>programs</b> 5:21 81:16</p> <p><b>projects</b> 70:6</p> <p><b>promise</b> 83:10</p> <p><b>promote</b> 36:15</p> <p><b>promoting</b> 17:20</p> <p><b>prompt</b> 30:17</p> <p><b>proposal</b> 36:11,18 37:11 40:18 41:17 43:11 71:9</p> <p><b>proposed</b> 1:2 4:3 11:4,5 39:4 43:9 43:12</p> <p><b>prospective</b> 23:21 31:18</p>	<p><b>protect</b> 17:8</p> <p><b>protected</b> 86:5</p> <p><b>protection</b> 85:19</p> <p><b>prove</b> 72:9,15 78:5 87:9,17</p> <p><b>proven</b> 72:15,18 78:8,11</p> <p><b>proves</b> 78:15</p> <p><b>provide</b> 4:18 9:13 10:5 36:21 37:13 40:16</p> <p><b>provided</b> 24:14 48:11,13 52:17 54:21 55:18 88:14 88:22</p> <p><b>provides</b> 24:10 46:18</p> <p><b>providing</b> 61:19</p> <p><b>proving</b> 76:15</p> <p><b>provision</b> 31:21 67:20</p> <p><b>provisions</b> 15:14 33:6 47:19,22 48:2</p> <p><b>public</b> 4:3,19 5:5,6 5:10 6:11,14 7:9 7:11,14 8:13,17 9:8 17:8 21:16 35:15 36:20 40:20 40:21 70:10 71:3 73:14 90:1,18</p> <p><b>publications</b> 28:19 30:13 32:7</p> <p><b>publicly</b> 22:10 82:20</p> <p><b>published</b> 23:15 24:18 32:10</p> <p><b>pubmed</b> 28:17</p> <p><b>pull</b> 18:13</p> <p><b>pulling</b> 34:19</p> <p><b>purpose</b> 4:18 6:13</p> <p><b>pursue</b> 5:3 56:16 63:12,14</p>	<p><b>pursued</b> 68:8,13 68:15</p> <p><b>pursuing</b> 15:1 54:10</p> <p><b>purview</b> 40:18</p> <p><b>push</b> 37:18</p> <p><b>put</b> 61:10 62:22 77:18 80:5 88:11</p> <p><b>putting</b> 71:16</p> <p style="text-align: center;"><b>q</b></p> <p><b>qualifies</b> 41:13</p> <p><b>qualify</b> 42:18</p> <p><b>quality</b> 17:2,4 24:7</p> <p><b>quantity</b> 43:21</p> <p><b>question</b> 7:3 10:13 13:18 14:6 20:11 20:20 22:22 40:21 41:2 43:7 48:8,22 51:8 52:12 53:9 53:19 54:16,16 62:1 63:7,17 68:7 75:8 77:13 79:7 79:18 82:16 83:6 83:7,9 85:11 86:2</p> <p><b>questions</b> 6:10 7:8 8:1,2 12:11 15:13 20:18 22:13 32:22 34:6 35:10 40:19 51:6 58:22 60:22 61:16,17 71:8 77:11 80:3 87:22</p> <p><b>quickly</b> 66:2</p> <p style="text-align: center;"><b>r</b></p> <p><b>r</b> 1:22 4:1</p> <p><b>rachel</b> 2:1 4:5</p> <p><b>radiological</b> 2:7 6:3</p> <p><b>radiology</b> 26:15 32:15</p> <p><b>rails</b> 82:3</p> <p><b>raise</b> 41:10 55:6 65:7 73:6</p>	<p><b>raised</b> 83:13</p> <p><b>raising</b> 85:21</p> <p><b>randomized</b> 44:9</p> <p><b>range</b> 23:6 33:12 39:6 58:16</p> <p><b>rapid</b> 32:8</p> <p><b>rare</b> 70:14 71:21 72:13 79:19</p> <p><b>rate</b> 11:15</p> <p><b>rates</b> 24:22 25:1</p> <p><b>react</b> 16:16</p> <p><b>reacting</b> 16:15</p> <p><b>reactions</b> 48:20</p> <p><b>read</b> 39:8 78:3</p> <p><b>ready</b> 16:6</p> <p><b>real</b> 44:8 50:1 67:14</p> <p><b>realistic</b> 23:22</p> <p><b>reality</b> 40:9 42:5</p> <p><b>really</b> 5:8 54:14 63:12,13 65:13 66:9 67:15,17 68:7 74:9 75:3,15 77:8 84:3,22</p> <p><b>reason</b> 10:21 11:15 19:14,14 56:3 65:10 68:12</p> <p><b>reasonable</b> 31:16 37:6 43:15 44:6 44:19 47:9 50:8 50:21 59:19</p> <p><b>reasons</b> 11:6 15:2 39:22 64:22 68:17 69:2,6,7,22 70:11</p> <p><b>recall</b> 18:10,10,11 18:14</p> <p><b>receive</b> 28:15 74:11</p> <p><b>received</b> 32:13</p> <p><b>receiving</b> 28:6</p> <p><b>recesses</b> 72:17</p> <p><b>recognize</b> 62:10 65:3</p>
--	--	--	--

<p><b>recognized</b> 26:18  <b>recommendation</b> 31:9  <b>recommended</b> 13:6 33:2  <b>record</b> 7:14 90:6  <b>recorded</b> 90:4  <b>recur</b> 15:22  <b>recurrences</b> 28:12  <b>red</b> 9:22  <b>reduce</b> 38:20  <b>reduced</b> 90:5  <b>reemphasize</b> 11:15  <b>reference</b> 17:9 23:4 33:6 34:7 39:19 48:1 49:7,9 51:16,21 52:4  <b>referenced</b> 42:6 45:5 53:4  <b>references</b> 48:6  <b>referencing</b> 4:20 24:6 31:10 36:13  <b>referring</b> 49:4  <b>reflect</b> 10:19  <b>regard</b> 42:15 50:7 73:15  <b>regarding</b> 20:20  <b>regardless</b> 53:17 78:22 86:7 87:14 87:15  <b>register</b> 8:10 9:5 61:9 71:20 78:4 82:17  <b>registered</b> 7:20  <b>registration</b> 4:15 8:18 9:6  <b>registries</b> 24:18  <b>regulated</b> 43:4 59:13  <b>regulating</b> 47:7  <b>regulations</b> 47:19  <b>regulatory</b> 5:21 36:15 37:11 40:22</p>	<p>41:3 43:3,20  44:13 46:6 49:17 49:18,22 50:3,16 51:1  <b>related</b> 10:14,15 12:18,19 13:8 24:13 48:17 76:15 90:8 91:6  <b>relatedness</b> 15:20  <b>relates</b> 37:5,11  <b>relationships</b> 21:11  <b>relative</b> 90:10  <b>relatively</b> 34:4  <b>relevant</b> 44:4 46:9 48:16 62:1  <b>reliance</b> 72:18 82:16  <b>rely</b> 21:21 22:11 44:20 82:19 83:3 85:9  <b>remaining</b> 27:20  <b>remarks</b> 10:2 18:19 20:17 22:14 35:10 65:21  <b>reminder</b> 88:19  <b>removals</b> 17:1  <b>removed</b> 72:8  <b>repeat</b> 16:21 69:2  <b>replace</b> 72:14  <b>replaced</b> 72:15  <b>report</b> 13:11,11 19:20  <b>reported</b> 1:21 14:14 17:11 57:2  <b>reporting</b> 10:14 12:1,12 13:7,10 14:13 16:11  <b>reports</b> 19:18 20:1 21:3  <b>represent</b> 10:19 61:7,11  <b>representatives</b> 7:12</p>	<p><b>reprove</b> 78:14  <b>reproving</b> 78:7  <b>request</b> 9:14 10:3 40:20 41:5,9  <b>requests</b> 36:12  <b>require</b> 42:16,18 47:14 52:14 72:3  <b>required</b> 43:22  <b>requirement</b> 11:18 16:14 31:15 44:7,18  <b>requirements</b> 73:9  <b>requires</b> 44:3,15  <b>requiring</b> 41:6  <b>research</b> 2:4,6 5:19,22 83:5  <b>resectable</b> 25:9  <b>resection</b> 27:22 28:11  <b>resources</b> 63:18 64:8,12 84:9  <b>respect</b> 72:4 83:6  <b>respond</b> 36:20  <b>responding</b> 12:1  <b>response</b> 24:6 30:21 48:7,8,22 51:8  <b>responsibility</b> 15:11 57:4,10  <b>restate</b> 85:22  <b>restores</b> 45:1  <b>restrooms</b> 4:16  <b>result</b> 27:9 41:17 59:4,11  <b>resulted</b> 28:18 32:1 44:11  <b>resulting</b> 31:2  <b>review</b> 23:19 24:8 31:5,9,20 47:21 63:22 74:15 85:2 88:21  <b>reviewing</b> 85:2  <b>ride</b> 86:18</p>	<p><b>rider</b> 82:6,7,7  <b>right</b> 4:17 13:13 17:21 20:10 21:12 22:9 28:19 32:12 34:19 52:15 56:9 57:5 59:12 61:18 62:16,20 63:2,5 65:10,20 66:6,11 66:11 67:20 68:4 68:16 69:20 72:21 73:7 75:5,9,20 78:10 80:17 81:13 82:5 84:8 87:1,6  <b>rising</b> 25:2  <b>risk</b> 18:17 37:2 42:4,11,14,16,17 42:21 43:3,4 58:20 73:10,15  <b>risks</b> 50:17  <b>risky</b> 70:9  <b>robust</b> 20:11  <b>role</b> 27:6  <b>room</b> 4:13,15 8:19  <b>route</b> 11:14 15:1 16:18 19:1 39:11 41:18 71:6  <b>rule</b> 52:19  <b>rules</b> 6:22 7:1 76:9 79:5</p>
<b>s</b>			
<p><b>s</b> 1:22 3:1 4:1  <b>safe</b> 23:17 42:7 47:5 89:2  <b>safely</b> 45:1  <b>safety</b> 10:14,22 11:7,16 12:16,18 12:19 14:20 15:4 16:11 18:5 19:4 19:14 20:4,13,14 20:15,22 22:2,3,7 23:6,13 30:4,9,11 31:12,16 35:20 38:3 41:11 42:11 43:12,15 44:2</p>			

47:17 50:21 53:5 57:2 63:3 65:9 66:10 72:3 74:3 76:16 <b>salad</b> 25:14 <b>salient</b> 76:4 <b>sat</b> 63:21 <b>saying</b> 52:13 53:16 76:11 78:1 78:18 81:9,9 84:7 85:14 86:3,4 <b>says</b> 56:9 65:7 69:10 87:9 <b>scarce</b> 63:17 64:8 <b>schedule</b> 9:16 <b>scheduled</b> 6:20 8:14 <b>science</b> 36:4 37:11 49:19 51:1 63:4 74:17,22 <b>scientific</b> 21:21 40:22 53:18,20 69:5 <b>scientist</b> 78:6,7,8 <b>scope</b> 23:22 <b>search</b> 28:16 <b>second</b> 11:9 24:12 40:7 52:12 68:16 73:10 <b>section</b> 48:16 49:13 <b>sections</b> 56:4 <b>see</b> 9:5,18 11:3 58:10 64:18 82:12 84:3 <b>seeing</b> 65:19 <b>seek</b> 4:21 <b>seemingly</b> 45:2 <b>seen</b> 27:13 33:20 45:8 62:18 <b>select</b> 77:9 <b>selective</b> 38:7 <b>sell</b> 40:10	<b>sending</b> 14:15 <b>senior</b> 63:19 <b>sense</b> 39:21 47:18 69:12 <b>sensible</b> 53:22 <b>sent</b> 30:16 79:5 <b>separately</b> 23:8 46:16 <b>serve</b> 4:7 <b>set</b> 12:5,9 60:3 76:9 <b>settings</b> 79:8 <b>seward</b> 2:13 3:6 35:12,14,22 51:9 51:16 52:15 53:12 53:19 54:17 55:11 56:22 57:5,12,19 57:21 58:13 59:9 61:2 <b>share</b> 74:13 <b>sharing</b> 10:18 <b>sherman</b> 2:1 4:2,5 6:6 20:17 22:13 22:16 32:21 34:6 35:9,12 51:5 54:12 56:16 57:1 57:8,14,20 58:10 58:22 60:22 61:3 77:10 87:22 <b>shifting</b> 58:19 <b>show</b> 64:6 68:11 84:1 <b>shows</b> 49:16 <b>shuren</b> 2:7 6:1,1 33:1,2,5 <b>shuttled</b> 75:1 <b>side</b> 14:15 27:18 53:15 81:2,2 86:19 87:7 <b>sides</b> 86:16 <b>sign</b> 4:14 6:9 8:18 <b>significant</b> 14:19 67:15 69:19	<b>significantly</b> 14:4 24:22 <b>silence</b> 4:10 <b>silver</b> 1:11 <b>similar</b> 45:5 47:10 <b>similarly</b> 15:20 <b>simple</b> 19:9 62:21 63:4 79:7 <b>simply</b> 41:16 49:9 <b>single</b> 14:8 18:10 49:7 <b>sir</b> 33:4 <b>sit</b> 81:20 <b>site</b> 36:7 37:17,20 <b>sitting</b> 65:2 <b>siyeon</b> 2:9 6:4 <b>size</b> 24:7 27:5 33:22 46:8 <b>sizing</b> 46:4 <b>skills</b> 90:7 <b>skirting</b> 79:12,14 79:14 <b>slot</b> 7:21 <b>slots</b> 6:20 8:20 <b>slow</b> 66:22 <b>small</b> 9:18 80:21 <b>smart</b> 79:4 <b>smith</b> 6:7,12 <b>social</b> 64:15 <b>societal</b> 64:7 <b>society</b> 2:10 24:15 26:11,11,14 32:14 <b>sodium</b> 38:15 39:16 <b>sold</b> 40:5 <b>solicited</b> 40:20 <b>solution</b> 38:16 49:5,6 51:11,12 <b>somebody</b> 68:3 <b>son</b> 68:5 <b>sorry</b> 28:17 64:21 83:8 <b>sort</b> 54:15 61:19 62:9 66:9 70:20	71:7 72:17 80:18 82:7 83:13 84:10 85:18 87:13 <b>sought</b> 29:13 <b>sound</b> 71:12 79:4 79:13 <b>sounds</b> 63:14 78:9 <b>source</b> 22:12 <b>sources</b> 82:18 83:2 <b>speak</b> 7:20 8:12 9:17 22:21 33:11 <b>speaker</b> 8:1,4,20 9:12 10:9 22:16 35:12 61:3 <b>speakers</b> 6:18 7:16 8:4,8 10:5 20:7 88:2,6 89:2 <b>speaking</b> 6:10 50:12 <b>special</b> 42:18 <b>specific</b> 24:9 30:7 36:7 41:3 46:2,3 48:1 49:11 52:4 52:14 56:20 69:15 80:3 <b>specifically</b> 10:15 11:2,22 12:20 13:7,20 16:9 39:11 42:9 53:3 <b>specify</b> 10:16,17 <b>spectrum</b> 34:16 <b>spending</b> 85:3 <b>spent</b> 66:17 84:19 <b>spoke</b> 34:7 <b>sponsor</b> 5:2 49:8 <b>sponsors</b> 4:21 36:16 <b>spot</b> 80:5 <b>spring</b> 1:11 <b>squarely</b> 40:17 <b>staff</b> 88:11 <b>stage</b> 23:2 25:5,11 26:10 27:14,15
--	---	---	---

<b>stages</b> 29:5 <b>stakeholders</b> 88:17 <b>stand</b> 17:22 20:13 83:8 <b>standard</b> 25:11 26:7,9,22 32:3 43:11,13,14,16 44:7,15,19 45:18 46:7,13 47:9,11 47:16 48:14 55:19 55:22 59:7,9,10 59:13,19,20 60:7 60:20 73:3,4 <b>standards</b> 37:5 43:18,22 44:11 45:16,17 47:15 50:7,9,19,22 <b>standing</b> 10:21 <b>standpoint</b> 64:7 87:3 <b>start</b> 82:4 <b>state</b> 90:19 <b>statement</b> 41:9 66:4 71:12,13,14 <b>statements</b> 6:17 <b>stays</b> 29:18 <b>stents</b> 45:9 59:16 <b>step</b> 40:8 75:6 <b>steps</b> 88:21 <b>straightforward</b> 38:11 60:1 <b>streamline</b> 50:4 <b>strength</b> 49:13 <b>strengths</b> 52:8 <b>strictly</b> 39:8 <b>strong</b> 36:17 <b>strongly</b> 9:2 51:2 <b>structure</b> 61:18 62:7 <b>struggling</b> 63:9,20 <b>studied</b> 17:6,7 19:11,12	<b>studies</b> 23:21 24:1 24:1 29:1,10 31:18 60:1 83:22 <b>study</b> 5:9 15:3 26:13 29:14 32:1 32:9,10 33:22 36:22 37:14 75:18 <b>studying</b> 17:6 38:12,19 69:17 84:20 <b>stupidest</b> 78:6 <b>subject</b> 7:9,13 <b>submission</b> 29:14 43:8 76:18 <b>submissions</b> 23:19 <b>submit</b> 9:3,8 16:6 88:18 <b>submitted</b> 5:6,9 30:18 31:2 89:1 <b>submitting</b> 10:6 <b>subsequent</b> 24:4 30:20 <b>substance</b> 75:21 <b>substantial</b> 37:5 38:3 42:1 43:13 44:2,14 46:12 47:17 50:9 59:20 66:13 72:10 73:9 <b>substantially</b> 31:7 41:13 <b>substitution</b> 40:9 <b>subtract</b> 72:7 <b>suddenly</b> 19:13 <b>suffice</b> 17:8 <b>sufficient</b> 55:6 <b>suggesting</b> 67:21 73:22 83:16 <b>summarize</b> 50:12 53:7,8 69:5 <b>summary</b> 77:3 79:4 <b>supplemental</b> 48:15 49:14 52:16 52:18 53:2 56:5,5	56:7,11,18 57:11 <b>supplied</b> 72:6 <b>support</b> 41:22 44:13 65:15 81:16 <b>supportive</b> 53:21 <b>suppose</b> 16:5 17:10 <b>sure</b> 15:6 22:6 33:12 51:16 54:11 57:13 58:11 59:2 64:13 76:22 78:8 78:20 85:13 86:1 <b>surgical</b> 46:19 <b>surrogates</b> 44:22 <b>surrounding</b> 48:9 <b>surveillance</b> 16:13 <b>survey</b> 32:11 <b>survival</b> 44:17,22 46:13 <b>sustain</b> 41:22 <b>sustained</b> 29:19 <b>synthesis</b> 50:2 <b>syringe</b> 35:1,3 57:19 <b>system</b> 14:8 64:14 68:8 <b>systemic</b> 25:21 29:21 <b>systems</b> 2:12 19:10 22:17	<b>talk</b> 75:8 87:3 <b>talked</b> 14:19 82:6 82:19 <b>talking</b> 10:21 14:15 18:13 20:7 21:5 62:10 70:6 70:20 71:15 78:10 78:11 80:12 <b>tapping</b> 84:21 <b>target</b> 37:17,20 <b>targeted</b> 25:17,21 <b>task</b> 72:22 <b>tax</b> 67:19,20 <b>technical</b> 54:15 <b>technology</b> 36:4 <b>tell</b> 19:8 61:21 81:21 <b>tend</b> 66:21 <b>tenor</b> 71:19 <b>term</b> 34:2 77:1 <b>terms</b> 28:17 59:4 <b>terribly</b> 65:4 <b>terrific</b> 68:22 74:4 85:2 <b>testified</b> 68:21 <b>testing</b> 55:5 <b>thank</b> 6:6 10:8 20:16,17,19 22:12 22:14,15,18 32:20 32:21 35:9,10,11 35:14,14 51:4,5 54:13 58:22 61:1 61:2,5 77:10,12 88:1,6,10 <b>thanks</b> 52:11 56:15 85:9 <b>theme</b> 45:4 <b>therapeutic</b> 35:19 37:20 38:9 39:5 46:18 <b>therapies</b> 35:18 36:17 <b>therapy</b> 28:7 60:9
			<b>t</b>
		<b>t</b> 3:1,1 <b>table</b> 8:19 9:7,19 75:10 85:1 <b>tables</b> 4:15 <b>tace</b> 28:15 32:4 <b>take</b> 8:2 20:11 28:10 29:4 31:11 31:20 34:14,18 72:12 80:7 <b>taken</b> 23:18 24:8 33:21 39:22 40:11 54:3 60:7 90:3,9	

<p><b>thing</b> 57:14 69:19 72:20 78:6 79:19 81:7 82:12 84:10 87:2,9 <b>things</b> 64:2,6,22 70:3 71:2 72:18 78:17 87:3 <b>think</b> 14:22 18:7 18:11 23:20 24:10 33:15,17 34:8,13 34:17 35:5 55:1 57:21 59:9 61:22 63:8 73:13 76:6 76:13 77:3,5,7,8 78:3,7,19 79:22 80:2,8,9,16,19 81:22 83:7 85:10 87:5,5 <b>thinkers</b> 69:9 <b>thinking</b> 49:16 66:22 70:16 <b>third</b> 52:5 70:5 <b>thirdly</b> 11:11 <b>thompson</b> 2:14 3:7 61:4,5 77:21 79:3 80:8 81:8 83:4 84:3 85:22 86:11,16 <b>thorough</b> 15:7 <b>thought</b> 58:11 74:4 75:15,16 82:18 <b>thoughtful</b> 88:14 <b>thoughts</b> 21:1 <b>three</b> 8:8 11:5 28:2 30:3,20,21 82:17 83:22 <b>throckmorton</b> 2:5 5:20 51:6,7,10 52:11 54:12,13,18 56:15 79:17 80:22 82:15 83:9 85:6 <b>throw</b> 34:22</p>	<p><b>thursday</b> 1:5 <b>time</b> 6:19 7:21 8:6 9:10,15,22 10:4 18:2 26:17 28:4 32:2,9,17 33:16 51:4,19,20 66:17 84:9 <b>times</b> 5:7 34:17 <b>tinkering</b> 85:4 <b>tissue</b> 54:5 <b>tissues</b> 37:21 <b>today</b> 4:13 6:9,18 7:16 22:21 61:10 81:20 <b>today's</b> 7:6 88:9 <b>tomorrow</b> 82:14 <b>tone</b> 79:19 <b>tool</b> 50:15 <b>tools</b> 50:4 <b>topic</b> 10:16 22:7 79:11 88:16 <b>topics</b> 12:15 <b>total</b> 62:5 <b>tough</b> 64:16 65:16 65:16,17,18 66:10 <b>toxins</b> 27:9,10 <b>track</b> 47:20 <b>traditional</b> 41:16 42:19 <b>traditionally</b> 62:18 <b>training</b> 15:10 <b>transarterial</b> 25:4 25:12 26:8 28:6 <b>transcribed</b> 7:17 <b>transcriber</b> 91:1 <b>transcript</b> 7:18 69:3 91:3 <b>transplant</b> 25:10 <b>transplantation</b> 27:22 28:12 <b>travels</b> 56:13 <b>traverse</b> 43:2</p>	<p><b>treated</b> 60:5 87:17 <b>treatment</b> 25:5,7,8 25:11,21,22 26:4 26:9,16 27:6,14 28:14,20 29:3 32:6 34:18 44:9 <b>treatments</b> 46:3 <b>trial</b> 21:17 50:5 69:14 <b>trials</b> 20:7,8 31:11 38:13,17 44:4,9 59:21 <b>tried</b> 65:7 <b>trip</b> 89:3 <b>true</b> 41:15 51:18 90:6 <b>truly</b> 12:6 13:12 72:7 87:21 <b>try</b> 21:13 53:6 55:1,8 61:11 64:6 74:6 <b>trying</b> 18:13 40:15 58:5,7 60:8,9 66:18 75:3 84:10 86:18 87:21 <b>tumor</b> 25:16,19 29:18 <b>tumors</b> 25:9 30:1 <b>turn</b> 9:22 75:8 <b>turning</b> 40:19 <b>tutor</b> 63:21 <b>two</b> 14:9 18:12 22:5 28:16 30:6 44:3,11 55:3 64:5 67:3,4 76:21 86:16 <b>type</b> 25:15 47:12 60:4 <b>types</b> 29:2 33:13 44:12 <b>typewriting</b> 90:5 <b>typically</b> 27:8</p>	<p><b>u</b> <b>u.s.</b> 24:14 27:12 <b>ultimately</b> 31:2 <b>unavoidable</b> 63:7 <b>underestimating</b> 71:21 78:4 <b>underlying</b> 27:16 29:6 <b>understand</b> 13:12 14:2 15:13 19:11 51:13 55:2,8 59:3 65:14 70:13 74:22 79:20 84:20 88:2 <b>understanding</b> 12:13 15:8 21:2 78:21 <b>understood</b> 34:5 <b>underway</b> 38:17 <b>unfairly</b> 87:18 <b>unique</b> 15:18 45:20 <b>universe</b> 70:6 <b>university</b> 36:2 <b>unlearn</b> 72:20 <b>unlinked</b> 46:1 <b>unlocking</b> 47:3 <b>unmet</b> 24:7 25:2 29:13 31:13,14 <b>unnecessary</b> 50:16 <b>unreasonable</b> 42:4 87:11 <b>update</b> 15:14 17:14 24:14 57:10 <b>updates</b> 39:19 <b>upside</b> 40:4 <b>usage</b> 39:1,9 48:18 54:2 <b>use</b> 1:2 4:4 5:1,3,4 11:4,9,12 17:17 17:17,18,19,21 18:4,5 23:10 30:1 33:19 37:7 38:6 38:19 39:4 40:15</p>
---	---	--	---

42:8 47:5,9 48:3,5 48:10,18 51:21 52:9 55:14,15 56:10,21 58:19 59:11 63:4 69:11 73:14 76:17 77:1 77:19 82:21 83:15	<b>viewed</b> 43:18 <b>views</b> 14:5 <b>viral</b> 27:11 <b>virtually</b> 27:5,7 <b>vocabulary</b> 67:3 <b>voiced</b> 81:4	78:19 85:10 86:2 86:12 <b>welcome</b> 4:2 <b>went</b> 59:16 <b>wide</b> 23:5 33:11 34:13
<b>user</b> 13:3 37:7 48:9 <b>users</b> 40:16 <b>uses</b> 43:14 <b>usually</b> 11:13 <b>utilize</b> 35:19	<b>w</b>	<b>willing</b> 57:16 <b>wing</b> 13:20 <b>wisdom</b> 84:19 <b>wise</b> 73:13 <b>wish</b> 5:2 36:19 <b>withdrawn</b> 19:13 79:9 82:22 <b>words</b> 50:8 <b>work</b> 10:20 34:11 61:8 66:19 69:13 69:13 70:4 <b>worked</b> 88:11 <b>working</b> 35:16 60:11 62:8 66:7 68:4 <b>world</b> 44:8 50:1 <b>world's</b> 69:9 <b>worldwide</b> 24:13 <b>worry</b> 75:20 <b>write</b> 79:4 <b>writing</b> 85:12 <b>written</b> 36:11 61:12 79:15
<b>v</b>	<b>walks</b> 63:11 65:6 69:10 <b>wall</b> 37:19,22 38:10 <b>want</b> 10:16,17 12:14,20 16:20 35:14 36:21 53:11 55:17 57:18 59:2 59:3 61:5 63:12 64:7 66:5 67:22 68:1,17 71:9 75:14 76:13 77:14 79:17 84:16 87:4 87:5,6,12,16 88:17 <b>wanted</b> 53:6 70:1 70:2,5 <b>wanting</b> 67:1 <b>wants</b> 63:13 81:16 <b>warnings</b> 48:19 <b>waving</b> 6:8 <b>way</b> 18:6 26:21 56:2 67:7 69:11 83:15,17,19 <b>we've</b> 34:16 38:12 38:18 39:15 61:7 61:9 62:6 71:9,14 73:20 81:3 83:22 88:13 <b>weakness</b> 84:7 <b>webcast</b> 88:8 <b>website</b> 7:18 <b>weekend</b> 63:19 <b>weeks</b> 28:16 <b>weiner</b> 2:2 5:14,14 20:19 21:9,13 53:6,13 77:11,12	<b>y</b>
<b>vaccine</b> 34:20 35:1 <b>vacuum</b> 54:4 56:6 <b>validity</b> 47:8 <b>valuable</b> 50:15 88:15 <b>variability</b> 29:1 <b>variety</b> 23:5 32:16 38:13 <b>various</b> 27:10 64:22 <b>vary</b> 53:16 <b>vascular</b> 38:20 39:12 45:12 58:7 <b>venous</b> 25:20 29:20 37:16 <b>venture</b> 64:17 65:8 73:6 <b>versa</b> 70:2 <b>versions</b> 49:1 <b>versus</b> 14:5 50:9 <b>vessel</b> 37:19,22 38:9 45:11 <b>vessels</b> 38:8,21 <b>viable</b> 24:5 <b>vial</b> 34:21 40:6 56:9 <b>vice</b> 70:2 <b>videotape</b> 7:14 <b>view</b> 18:7		<b>yeah</b> 51:7 86:11 <b>year</b> 30:20 32:12 32:16 64:19 <b>year's</b> 31:5 <b>years</b> 24:19 25:6 26:1 27:9 30:3,6 42:7 55:21 62:7 69:16 84:19 85:3 <b>yellow</b> 9:20 <b>yesterday</b> 68:6 <b>younger</b> 83:4