

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

U.S. FOOD AND DRUG ADMINISTRATION

PUBLIC MEETING ON THE RECOMMENDATIONS FOR  
PRESCRIPTION DRUG USER FEE ACT (PDUFA) REAUTHORIZATION

Tuesday, September 28, 2021

9:00 a.m.

JOB No. : 4808420

Page 2		Page 4	
1	A P P E A R A N C E S	1	
2	ANDREW CHRIS	2	Lunch 94
3	CARTIER ESHAM	3	
4	LUCY VERESHCHANGA	4	Public Stakeholder Perspectives 96
5	PETER STEIN	5	Michael Abrams, Public Citizen Senior
6	GRAHAM TOMPSON	6	Health Researcher 96
7	THERESA MULLIN	7	Cynthia Bens, Personalized Medicine
8	TERRY TOIGO	8	Coalition Senior Vice President,
9	CAROL REHKOPF	9	Public Policy 103
10	MARY ANN SLACK	10	Annie Kennedy, EveryLife Foundation
11	JOSHUA BARTON	11	for Rare Diseases Chief of Policy
12	MICHAEL ABRAHAMS	12	and Advocacy 110
13	CYNTHIA BENS	13	Ed Neilan, National Organization for
14	ANNIE KENNEDY	14	Rare Diseases Chief Medical and
15	ED NEILAN	15	Scientific Officer 117
16	ROBERT FALB	16	
17	BRAD JORDAN	17	Public Comments 124
18	PAUL MELMEYER	18	
19	JERRY S ROTH	19	
20	DRU WEST	20	
21	KIM WITCZAK	21	
22	DIANA ZUCKERMAN	22	
23		23	
24		24	
25		25	
Page 3		Page 5	
1	C O N T E N T S	1	P R O C E E D I N G S
2	PAGE	2	MR. THOMPSON: Apologies for one second, we're
3	PDUFA Background and Overview 5	3	having so -- I'm sure you can tell that there was some
4	Andrew Kish, Center for Drug Evaluation	4	issues with the audio. We're going to see if we can
5	and Research, FDA Director, Office of	5	get that back.
6	Program and Strategic Analysis	6	All right. Well, looks like we're having some
7		7	issues with the audio there. What we're going to do is
8	CBER Review Support Proposed Enhancements 10	8	end up posting a full video of Janet's remarks -- Dr.
9		9	Woodcock's remarks to the website, so you'll be able to
10	Pre-Market Review Proposed Enhancements 25	10	see them there. Apologies for that.
11		11	And let's move on to Andrew Kish, who will be
12	Break 43	12	providing the background of the PDUFA program where we
13		13	are in the reauthorization process, and quick overview
14	Regulatory Decision Tools Proposed 43	14	of the proposed enhancements. And, hopefully, it will
15	Enhancements	15	be done in a more crystal clear audio fashion.
16		16	
17	Post-Market Safety Proposed Enhancements 54	17	PDUFA Background and Overview
18		18	
19	Chemistry, Manufacturing, and Controls	19	MR. KISH: Thank you, Graham. Good morning,
20	Proposed Enhancements 63	20	everyone. Sorry about the technical challenge there.
21		21	There's -- have any problems hearing me please --
22	Digital Health and Informatics Proposed	22	please let me know. We aren't going to minimize folks
23	Enhancements 74	23	on video. Make sure everyone has enough bandwidth to
24		24	hear us and see us during the presentation today.
25	Finance and Hiring Proposed Enhancements 85	25	So, I'm going to give a really quick

Page 6

1 background on PDUFA and the reauthorization process.  
 2 And those of you who were -- had been following this  
 3 since it started, which is last summer with our initial  
 4 kickoff meeting, some of this going to look very  
 5 familiar.  
 6 We will go ahead and go to the next slide. We  
 7 can jump to the next one. Okay. So, just really brief  
 8 background on the history of PDUFA. PDUFA is the  
 9 oldest user fee program at FDA. And it started in 1992  
 10 and it has evolved quite a bit. It came about  
 11 initially, really just to add funds for premarket  
 12 review. And this was really helping with a substantial  
 13 backlog we had at that time where we could set  
 14 additional funds that would allow us to hire staff, to  
 15 have capacity, to set predictable timelines, to make  
 16 decisions on applications.  
 17 As we move into PDUFA II, they were added  
 18 goals and shortening of review times. And then as we  
 19 got into PDUFA III and PDUFA IV, really start to see  
 20 the program move into the post-market area,  
 21 particularly in PDUFA IV where there's a focus on  
 22 modernizing post-market safety system.  
 23 PDUFA V introduced the small increase to the  
 24 base funding review enhancements to increase  
 25 communications and sponsors, the program, the folks are

Page 7

1 familiar with the program and strengthened regulatory  
 2 science and post-market safety.  
 3 As we moved into VI, which is what we're  
 4 currently in right now, there's a focus on modernizing  
 5 the user fee structure, on enhancing HR and financial  
 6 management, creating a new capacity planning capability  
 7 and enhancing our use of regulatory tools via benefit-  
 8 risk, patient-focused drug development, complex,  
 9 innovative trial designs, model informed drug  
 10 development, and a number of other enhancements,  
 11 including exploring RWE in regulatory decision-making.  
 12 That's the very brief background of PDUFA.  
 13 And as folks know today we're presenting the  
 14 recommendations for enhancements to PDUFA VII.  
 15 You can go to the next slide. A little bit on  
 16 the timeline. Graham did touch on this on his opening  
 17 remarks. But, as we started this process last summer  
 18 with the public announcement of the initial meeting --  
 19 the public meeting to kick off the negotiation process.  
 20 We then engaged in technical negotiations  
 21 between industry and FDA, starting in September that  
 22 ran through February and this also included a parallel  
 23 process where we held -- FDA held meetings with  
 24 stakeholders who signed up for the stakeholder  
 25 engagement process.

Page 8

1 And then through March of this year, and  
 2 September, there's the clearance process for -- on the  
 3 government side, which includes FDA, HHS, and OMB  
 4 finalization of the package, including briefing the two  
 5 congressional committees responsible for heavily  
 6 reviewing this proposed legislation package. And then  
 7 where we are today -- the final public meeting.  
 8 Today's public meeting, as Graham mentioned,  
 9 is for us to share proposed enhancements and to hear  
 10 your feedback through the public comment period. And  
 11 as also noted, the public docket is open, we encourage  
 12 you to submit your comments through the docket. That  
 13 will remain open through nearly the end of October.  
 14 After we reviewed the dockets comments and  
 15 feedback from this public reading, we will then make  
 16 any changes as necessary to the proposed commitment  
 17 letter, and then we have a statutory deadline to  
 18 transmit that to Congress by January 15th of next year.  
 19 And from January 15th to September 30 of 2022, it is  
 20 with Congress for consideration and anticipated passage  
 21 of reauthorization. As currently noted -- as  
 22 previously noted, the current PDUFA program will sunset  
 23 in September 30, 2022.  
 24 You can jump to the next slide. And here's  
 25 the statute prepared (inaudible) that we are at that

Page 9

1 fourth step public review of recommendations, as I  
 2 mentioned on the previous slide.  
 3 We can go to the next slide. So, give a  
 4 really quick overview of really the recommendation  
 5 sections, then we'll have lead negotiators for those  
 6 sections in FDA, present an overview of the highlights  
 7 of those particular sections and then have our industry  
 8 colleagues from pharma and bio provide their input and  
 9 thoughts after the presentation of each section.  
 10 Okay. So, there are a number of areas of  
 11 proposed enhancements. And the commitment letter, I'm  
 12 sure those of you, who have looked through it are  
 13 familiar with this. Also those of you who have  
 14 followed our public meeting minutes that we posted  
 15 throughout the entire negotiation process. And I'm not  
 16 sure if you heard it in Janet's opening remarks, but  
 17 there is over 100 meeting minutes posted during the  
 18 process.  
 19 We have structured the presentation today that  
 20 closely follow how those meeting minutes were posted in  
 21 the groups, so you can follow those topic areas if you  
 22 have a particular interest. That includes CBER review  
 23 support. So that's heavily focused on enhancing CBER's  
 24 capacity, particularly around cell and gene therapies.  
 25 Pre-market, sort of introducing new approaches

<p style="text-align: right;">Page 10</p> <p>1 to improve the human drug review process, including new 2 pilot programs. Regulatory decision tools; post- 3 market; a new area for PDUFA -- chemistry and 4 manufacturing controls, particularly around 5 facilitating manufacturing readiness and use of 6 innovative manufacturing technologies. And also 7 partially new introduction to PDUFA is digital health - 8 - digital health and informatics variant. We'll have 9 Mary Ann Slack provide the overview; and finance; and 10 then hiring and retention.</p> <p>11 So we have a lot to cover. And I will go 12 ahead and turn it over to Chris Joneckis from CBER, who 13 will be presenting the CBER Review Support.</p> <p>14 MR. THOMPSON: While we're transitioning, I'd 15 just like to let people know that, yes, we will be 16 making these slides available after the meeting along 17 with the recording and the transcript of the meeting. 18 Thanks very much.</p> <p>19 And Chris, it looks like your slides are 20 loaded. So we'll turn it over to you and our -- we can 21 move the slides yourself or you can request control if 22 you'd prefer.</p> <p>23 24 CBER Review Support Proposed Enhancements 25</p>	<p style="text-align: right;">Page 12</p> <p>1 So, during negotiations, industry and CBER 2 both recognized that there was need for an additional 3 support for the cell and gene therapy program. And in 4 discussing this, we determined that there needs to be a 5 more comprehensive approach to address what CBER wanted 6 to achieve, and of course, what industry wanted to 7 achieve and felt was necessary to have a very strong 8 and sustained cell and gene therapy program.</p> <p>9 Slide please. So, one of the major outcomes 10 of this -- of PDUFA in this field is that there was a 11 significant increase in staff capacity and capabilities 12 in CBER to support that regulation and review of the 13 cell and gene therapy products. There is a substantial 14 number of staff to support the cell and gene therapy 15 review in the order of approximately 160 additional 16 staff that will be joining over the course of the PDUFA 17 VII.</p> <p>18 The majority will be involved in, of course, 19 the cell and gene therapy review and regulation and 20 they'll be in our office -- OTAT -- Office of Tissues 21 and Advanced Therapies and other review offices that 22 directly support that review.</p> <p>23 There will be a limited -- very limited number 24 of staff that will support other related functions 25 related to things of hiring, communication and such, as</p>
<p style="text-align: right;">Page 11</p> <p>1 MR. JONECKIS: Good morning, Graham. Can 2 everyone hear me?</p> <p>3 MR. THOMPSON: Yes, we can.</p> <p>4 MR. JONECKIS: Great, thank you. Good 5 morning. My name is Chris Joneckis. As the slide 6 indicates I was the lead for the CBER Review Support 7 Group and I also served as the CBER lead for user fees, 8 including PDUFA.</p> <p>9 So, I think everyone is well aware that there 10 has been a substantial and sustained increase in 11 activity in the cell and gene therapy arena, especially 12 over the past few years. And this has clearly been 13 reflected in increased numbers of meetings, IND 14 submissions, BLA submissions and evidence that, you 15 know, as more additional products are approved, there's 16 a maturing field, so there's additional post approval 17 work and activity.</p> <p>18 As an aside, this actually increase continues 19 to be maintained throughout COVID as well. This 20 increased demand has far exceeded the staff numbers and 21 staff capacity that CBER felt was needed to provide for 22 the -- support for the cell and gene therapy program to 23 the ability that we would prefer, especially to support 24 and grow the cell and gene therapy program as we would 25 like.</p>	<p style="text-align: right;">Page 13</p> <p>1 well some regulation policy, and so on and so forth 2 that is necessary to provide both a direct and indirect 3 support for the review of cell and gene therapy 4 products.</p> <p>5 This staff capacity will clearly allow us to 6 meet these increasing challenges and demand in this 7 evolving and rapidly growing field such that we can 8 spend additional time when existing reviews, meetings, 9 growing the program, and also there's other indirect 10 activities to provide additional regulatory support and 11 outreach. Things such as, you know, webinars, doing 12 additional recorded training, to facilitate both 13 industry and stakeholder education and interactions, 14 which again occurs both nationally and internationally, 15 additional policy developments and such.</p> <p>16 In the field of cell and gene therapy, I 17 think, it's important to understand that there's a wide 18 variety of industry -- industries that are 19 representative. They are of all sizes from small to 20 large and well established industries, and a lot of 21 newer industries as well who perhaps don't have as much 22 regulatory expertise -- those who are well established 23 and therefore we need to provide support across the 24 board.</p> <p>25 So with that increase in amounts of staff that</p>

<p style="text-align: right;">Page 14</p> <p>1 we would have, it's important -- it was felt important  2 by both CBER and the industry negotiators that we  3 provide support to integrate and onboard that large  4 number of new staff. And so, to that end, there are --  5 some of the PDUFA funding will be used to look at  6 integration and onboarding, making sure we have an  7 appropriate change management program, as well doing an  8 assessment of the office, OTAT, for example, and other  9 structures within CBER to see what -- how it was the  10 best way to efficiently organize those. And also some  11 additional funding to provide an assessment of the  12 program, how we communicate, and so on and so forth.  13 A key part is to make sure that we have --  14 facilitate an enhanced communications. So, we will  15 continue the interactions that we've had with our other  16 stakeholders continue, for example, public-private  17 partnerships, national and international venues. Also,  18 internal outreach as well through the wide variety of  19 cell and gene therapy applicants that we have.  20 We're also taking some of that money to do an  21 internal assessment as well to -- as part of the CBER  22 modernization program to evaluate, streamline and  23 harmonize our various cell and gene therapy processes  24 and procedures, how we interact with people, how we  25 communicate, in an attempt to enhance the regulatory</p>	<p style="text-align: right;">Page 16</p> <p>1 have been starting a lot of the assessments, initiating  2 changes, how we're going to be doing hiring with the  3 limited resources that we have available. And so we've  4 been making quite a bit of progress on that.  5 As part of the field, CBER and industry both  6 agreed on a series of meetings to explore the  7 challenges cell and gene therapies and how we can meet  8 them. This is a continuation of a lot of the meetings  9 that we've had over the years with stakeholders that  10 have been funded, in part, by base funding as well as  11 PDUFA funding.  12 So, some of the major ones that we have agreed  13 to and are described in the PDUFA commitment letter  14 would be a patient focused drug development meeting in  15 which we can better understand patient perspectives on  16 gene therapy studies and products.  17 That things -- so we would explore areas like  18 patient and caregiver's level of understanding and  19 expectations regarding the benefits and risks of their  20 cellular and gene therapies, which would be their  21 involvement in the clinical study design and execution,  22 exploring patient experience and patient preference  23 data, looking at existing tools or considering the need  24 to develop new ones, and so on.  25 Another area is looking at novel approaches.</p>
<p style="text-align: right;">Page 15</p> <p>1 actions and reduce that burden, basically to take a  2 look at our optimization of our efficiency as well.  3 A peer part of this is to enhance regulatory  4 consistency and additional -- hopefully, provide  5 additional review standards, reduce any kind of  6 regulatory burden, optimize our efficiency, and so on.  7 Again, this has to occur in the context of a rapidly  8 developing and evolving field, so it's very challenging  9 to do so. Also, we will continue again our external  10 collaborations to participate in various public-private  11 partnerships, internal interactions, and so on.  12 We will also continue to have those  13 discussions, as the Agency is having discussions on the  14 use of existing approaches and evaluating potential new  15 approaches. So discussions on surrogate endpoints,  16 real-world evidence, complex innovative designs,  17 natural history studies, for example, in the clinical  18 area, as well as exploring new approaches for how we  19 can obtain efficiency and safety information.  20 And especially in the cell and gene therapy  21 area, it's important to look at that for rare and  22 ultra-rare diseases, because there are a lot of those  23 disease populations that are looking at cell and gene  24 therapy as a potential therapeutic core.  25 We have not been waiting for PDUFA VII, we</p>	<p style="text-align: right;">Page 17</p> <p>1 What types of various novel approaches can be used to  2 determine efficacy and safety data. Again, there is a  3 large emphasis on small or ultra-rare populations in  4 the cell and gene therapy field. So, we have been  5 looking at different ways of how we can challenge that  6 and we'll explore those in stakeholder meetings with  7 industry academics, patient group, so on.  8 Part of the novel approaches as in this  9 rapidly evolving field, we are faced with many  10 challenges, and so we'll be looking at trying to take a  11 more Q&amp;A approach to keep documents updated to reflect  12 some of our current thinking on challenges -- common  13 challenges that lot of individuals in this area face.  14 We also, therefore, also look at exploring approaches  15 to capturing that post approval safety and efficacy  16 data for both the cell and gene therapy product.  17 Another area in which we'll be having more  18 public discussions will be in the expedited programs  19 area. I think most people are probably aware in this  20 field of the RMAT program, the regenerative medicines  21 advanced therapies programs.  22 We are going to be -- have been looking at  23 reviewing and updating our experience gained from that  24 since its passage several years ago, and we'll be  25 having additional discussions on how we can use --</p>

<p style="text-align: right;">Page 18</p> <p>1 potential use, real-world evidence, accelerated  2 approval. And then in particular for cell and gene  3 therapy is making sure that CMC areas are ready for  4 applications. This has been again particularly  5 challenging for cell and gene therapy products, because  6 they're really new and novel manufacturing approaches  7 and challenges that have to be overcome.  8 And the last area in the support for public  9 meetings will be in leveraging knowledge. This was of  10 great interest to our Industry partners, and they  11 wanted to understand how is it possible that they can  12 access nonproprietary knowledge in multiple areas. We  13 will continue our advancement of standards, for  14 example, in various areas that we have been emphasizing  15 over the past few years. And how can manufacturers and  16 other Industry individuals can leverage internal prior  17 knowledge and public knowledges in multiple areas --  18 preclinical, clinical, and CMCs.  19 So, all of these activities that we've  20 discussed involve public-private partnerships,  21 involvement of all stakeholders in various public  22 meetings. And the information gained from these types  23 of meetings can be used to inform subsequent thinking  24 and development of guidances.  25 And, of course, as you will hear later today,</p>	<p style="text-align: right;">Page 20</p> <p>1 fees. So, basically new INDs, BLAs, and so on, will be  2 included in those user fees.  3 The third bullet point here, allergenic  4 extract products licensed before October 1, 2022 and  5 standardize allergenic extract product submitted  6 pursuant to a notification to the applicant from the  7 secretary regarding the existence of a potency test  8 that measures the allergenic activity of an allergenic  9 extract product licensed by the applicant before  10 October 1, 2022, would remain excluded from PDUFA.  11 So, what that that says basically is that, for  12 existing allergenic products that already have been --  13 have applications submitted, if you will, they will  14 continue to be regulated as non-PDUFA products. And  15 also have the ability, occasionally we will standardize  16 allergenic extract products, which means that we issue  17 a specific potency standard and all the other  18 allergenic products out there have to determine their  19 potency relative to that product. Those will not be  20 different products and therefore no fees will accrue --  21 will accrue.  22 Of course, with these newer allergenic  23 products, again, that are mostly targeted at food  24 allergies, all the performance goals, procedures  25 commitments, will apply to allergenic products that</p>
<p style="text-align: right;">Page 19</p> <p>1 all the sections of PDUFA also do support the cell --  2 the cell and gene therapy program as they support other  3 CBER products as well that are considered (inaudible)  4 products of course.  5 Now turning to Allergenic, next slide please  6 Graham. The other major part in this area of support  7 for CBER biologics is the incorporation of new  8 allergenic extract products into the PDUFA program and  9 the PDUFA resources will provide that additional  10 capability to review these products under the PDUFA  11 paradigm.  12 Since PDUFA's inception, the allergenic  13 extract products have previously been excluded in the  14 statute. It's important to recognize that the most of  15 our new allergenic products that are under development  16 are targeted food allergies, such as the recent  17 approvals for peanut allergy treatments.  18 So allergies to foods are increasing,  19 especially among children, and so it's very timely that  20 getting the PDUFA resources to support this program  21 will be very beneficial both to CBER, to industry and  22 to the patients that are targeted for these allergenic  23 extract products.  24 So, basically, with the start of PDUFA VII on  25 October 1st, they will generally be included in user</p>	<p style="text-align: right;">Page 21</p> <p>1 include too -- excuse me, that includes the PDUFA  2 products as well. And these PDUFA resources for these  3 newer products will allow for a more timely review of  4 these INDs, BLA submissions, post approval submissions  5 that were previously reviewed on a resource dependent  6 basis, as well.  7 And I think this overall approach to  8 allergenic products strikes a really good balance in  9 the regulation of allergenics and meets both the needs  10 of CBER's and industry and the various patients that  11 have these products.  12 So, with that, thank you for your attention  13 this morning.  14 MR. THOMPSON: Thanks very much, Chris. Now  15 we are going to turn it over to Cartier and Lucy from  16 Industry to give some Industry comments.  17 MS. ESHAM: All right. Good morning,  18 everybody. I'll do my audio check. Is this coming in  19 clear?  20 MR. THOMPSON: I can hear you loud and clear.  21 MS. ESHAM: Great, thank you. And thank you  22 Chris for that great overview. And I'm just going to  23 underscore a couple of things for the audience.  24 Again, Chris did an excellent job covering the  25 points of the agreement. But I think it's important to</p>

<p style="text-align: right;">Page 22</p> <p>1 note and underline that there was significant alignment  2 going into these negotiations that there was -- that  3 there was a need to focus on CBER's resources given the  4 high -- the present high -- increased volume and demand  5 being put on CBER and that, that we sort of projected  6 and predicted that will be needed over the course of  7 the next PDUFA cycle.</p> <p>8 And so, again, I think the agreement reflects  9 appropriately the significant need that we wanted to  10 resolve. And with, in the commitment, there is going  11 to be -- the ability of CBER to bring on a significant  12 number of staff to address that increased volume and  13 demand. And we did want to make sure they could get  14 that as soon as possible. So, we do expect the  15 onboarding -- a majority of the onboarding to be  16 happening in the first year or two.</p> <p>17 Given that, as Chris mentioned, you know, we  18 discussed a lot about the importance of ensuring that  19 with that onboarding, there was resources provided for  20 CBER to make sure that they could do change management  21 and onboard those new staff in a way that will continue  22 CBER to be able to maintain a culture of scientific  23 engagement and optimal -- optimal scientific dialogue.</p> <p>24 Additionally, there was a lot of discussion to  25 make sure that CBER had the resources they need to best</p>	<p style="text-align: right;">Page 24</p> <p>1 that we have effective and efficient review processes  2 over the course of the next PDUFA cycle.</p> <p>3 And, lastly, I'll just note that we also had  4 some discussions that, there are oftentimes if there  5 are frequently asked questions that everybody is asking  6 the same question maybe through meeting requests. And  7 so there is a commitment to publish a frequently asked  8 question document that could be put out a little bit  9 faster than traditional guidance with the hope that,  10 that not only provides key information to sponsors of  11 applications, but also create maybe a faster process to  12 understand current thinking, perhaps in the future,  13 maybe in a more iterative manner.</p> <p>14 So, with that, I'm going to turn it over to my  15 colleague Lucy for additional comments.</p> <p>16 MS. VERESHCHANGA: Good morning, everyone.  17 Lucy Vereshchanga, PhRMA. And I'll start with  18 emphasizing the overall importance of PDUFA for  19 biopharmaceutical innovation and for patients. So --  20 and we believe that PDUFA VII includes all this  21 critical provisions that will advance innovations for  22 patients.</p> <p>23 And I wouldn't repeat all the great things  24 that were just said about cell and gene therapy  25 provisions, but I would just -- building on Cartier's</p>
<p style="text-align: right;">Page 23</p> <p>1 enable bio and pharmaceutical companies to continue to  2 modernize how they're approaching drug development,  3 including for cell and gene therapies. And so, we  4 wanted to make sure that there were resources and  5 ability to advance regulatory -- to better understand  6 regulatory thinking, advanced regulatory thinking, and  7 create a shared understanding about how to utilize  8 things such as patient perspective data, real-world  9 evidence, innovative clinical trial designs. And as  10 Chris mentioned, to be able to be engaging with key  11 stakeholders and scientific leaders throughout our  12 community to even explore new ways to assess benefit  13 and risks in cell and gene therapies.</p> <p>14 This also included -- as Chris mentioned,  15 there will be appropriate focus on the unique needs of  16 small and ultra-rare diseases that is of particular  17 input for many of our cell and gene therapy,  18 treatments.</p> <p>19 And lastly, I just want to underscore there's  20 also going to be some engagement and dialogue and  21 guidance on things like CMC readiness. And how can we  22 think about leveraging prior knowledge across  23 therapeutic areas for non-clinical, clinical knowledge,  24 CMC knowledge. And I think all of that will really  25 serve well to continue to advance the field and ensure</p>	<p style="text-align: right;">Page 25</p> <p>1 comment, I'll just emphasize the importance of the  2 patient centric approach to drug development,  3 specifically for cell and gene therapies. And the  4 importance of public process for gathering patient  5 input for cell and gene therapists. We heard about  6 dedicated meetings for patient-focused drug development  7 disease areas, and also would echo what Cartier said  8 about the importance of external collaborations.</p> <p>9 It will help to advance thinking in using  10 novel approaches and obtaining safety and efficacy  11 information, for example, from real-world data  12 evidence, nature history (ph) studies and other novel  13 approaches. I'll stop here.</p> <p>14 MR. THOMPSON: All right. Thank you both very  15 much. We will now move forward with an overview of the  16 proposed enhancements for Pre-market Review. And could  17 we have the slides please.</p> <p>18 Our FDA presented for this topic will be Peter  19 Stein, our Industry speakers again, we'll be Lucy  20 Cartier. After this session, we'll be taking a break.  21 Peter, you have 25 minutes and you can start whenever  22 you're ready.</p> <p>23</p> <p>24 Pre-Market Review Proposed Enhancements  25</p>

<p style="text-align: right;">Page 26</p> <p>1 MR. STEIN: Great, Graham, thank you very 2 much, and good morning, everybody. I served as the 3 lead for the Pre-Market PDUFA VII review. And I will 4 share with you some of the enhancements and new 5 programs that I think will enhance the efficiency and 6 provide areas for innovation in how we -- how we do 7 pre-market review of drug applications.</p> <p>8 I think you'll see that some of these programs 9 really are geared to target areas -- of important 10 growth areas like rare disease and real-world evidence 11 that I think these programs will support and 12 facilitate.</p> <p>13 Next slide. So, what I'll do is, I'll walk 14 through the programs that are part of the PDUFA VII 15 commitment and talk about their role and importance. 16 So, let me start with the enhancements for post- 17 marketing requirements. Of course, when we complete a 18 review and a drug has to be approved, there may still 19 be some issues that require some additional 20 clarification, additional data generation after 21 approval, these are then -- can be put into post- 22 marketing requirements.</p> <p>23 Of course, the very detailed assessment plans 24 are specified in a protocol that may be after approval, 25 but the key elements -- the key design elements of the</p>	<p style="text-align: right;">Page 28</p> <p>1 has been called the real-time oncology review. And out 2 of that same -- out of that program, we've developed an 3 applications that will be across divisions and offices, 4 and this is called the split time -- Split Real-Time 5 Application Review or STAR as the acronym.</p> <p>6 The idea here -- the intent here is that for 7 particular drugs, where there's a supplement that 8 addresses a very important need in a serious disease, 9 an unmet need that we would like to be able to enhance 10 the efficiency of the review and bring the action 11 earlier, so that the drug could be available, so this 12 new indicated use can be available earlier for patients 13 if it's appropriate to add this use to the label.</p> <p>14 The idea here is that instead of the 15 submission being entirely complete at the time that 16 it's submitted, that this would allow for the majority 17 of the information that we would get into submission to 18 be -- to be present at the time of the initial 19 component of this. But certain elements might be 20 submitted a month or two months later.</p> <p>21 And, in particular, the completed study 22 reports and the integrated summaries can come in a 23 little bit later, approximately two months later. But 24 the initial submission includes all of the datasets, 25 these protocols, and many, many other such elements</p>
<p style="text-align: right;">Page 27</p> <p>1 study or trial need to be in the post-marketing 2 requirement at the time of approval. It's important to 3 be able to provide this information in sufficient time 4 prior to the approval action, so that there can be 5 review and discussion and clarification of these PMRs. 6 And so, what we've set up here is a new process to set 7 up timelines to assure that the development of these 8 PMRs are optimized, and there's sufficient time for 9 appropriate clarification discussion.</p> <p>10 So, in addition, we recognize that over time 11 some PMRs may take a number of years to complete, the 12 situation may change, scientific and clinical 13 environment may have changed or evolved. And so, it is 14 important that these PMRs be reviewed, and they can 15 already be reviewed without this enhancement. But this 16 allows for another level of review of the PMRs to 17 determine whether they still are relevant and 18 appropriate, or whether some change in the PMR or need 19 for the PMR has changed. And of course, we will be 20 updating our MAPPs and SOPs and guidances with these 21 new timelines and processes.</p> <p>22 Next slide. Another program, which I think is 23 very exciting, and this comes out of a pilot program 24 that had been ongoing -- that has been ongoing in the 25 Office of Oncology Drugs, OOD, which is called -- which</p>	<p style="text-align: right;">Page 29</p> <p>1 that are essential for us to sort of kick off our 2 review.</p> <p>3 As you may know, we largely do take the 4 datasets and we review both the efficacy and safety. 5 We do our own analysis of all of these things. And so 6 getting the datasets and protocols and statistical 7 analysis plan really allows us to kick off our review 8 earlier, and be able to do the analysis that are 9 essential for us to be able to complete and determine 10 whether the label update or a new indication is 11 appropriate.</p> <p>12 The goal here would be for us to be able to 13 take action earlier, a month earlier, even two months 14 earlier, based upon our ability to kick off the review 15 earlier. So we think this is an innovative approach, 16 and we'll be looking forward to seeing this coming to 17 the fore.</p> <p>18 And, obviously, we will be providing 19 information in a public facing webpage, have a public 20 workshop to discuss the program and our learnings from 21 this, and the assessment of the effectiveness of this 22 program, whether it achieves the goals or trying to 23 move -- to move action dates earlier so that we can, 24 you know, get drugs available to patients with these 25 new indications earlier.</p>



Page 30

1 Next slide, please. The next program I'm  
 2 going to talk about is creation of two new meetings.  
 3 As there has been obviously great new innovation in the  
 4 areas of drug development, as sponsors look at new  
 5 platforms for creating drugs or new targets, sometimes  
 6 novel issues come up even before the program has gone  
 7 too far before -- well, before it's gone into humans.  
 8 And as early development is proceeding, issues may be -  
 9 - need to be addressed that could use FDA input to  
 10 facilitate development.

11 Typically, array these may be subject to what  
 12 we've sometimes referred to as pre-IND meetings. But  
 13 this program called INTERACT, sort of instantiates that  
 14 in a more formalized way. The program really comes  
 15 from a pilot program that's being -- as part of what --  
 16 that has been in CBER and this program allows us to be  
 17 expanded. And again, the intent here is to set up  
 18 meetings where a sponsor may have a very specific  
 19 question typically that emerges from innovative  
 20 programs, such as where there's a new platform, and  
 21 allows us to have a discussion with the sponsor, give  
 22 them earlier advice, and hopefully, therefore  
 23 facilitate their development, which may otherwise be  
 24 delayed.

25 Another meeting -- another new meeting is what

Page 31

1 we refer to as a Type D meeting, where we have what are  
 2 called Type C meetings. These are meetings that can  
 3 cover a wide range of different issues that occurred  
 4 during development -- everything from issues relating  
 5 to clinical trial or pharmacology information,  
 6 toxicology, chemistry, manufacturing information, a  
 7 wide range of different issues might come up.

8 And Type C meetings can often have a number of  
 9 different issues that are pulled together by the  
 10 sponsor to support a meeting between the sponsor and  
 11 FDA to provide so that we can provide input on this  
 12 range of issues.

13 Well, a Type D meeting is intended to be more  
 14 focused where there might only be one or two issues  
 15 that are narrower. And because it's a smaller number  
 16 of issues, the timelines can be accelerated, which then  
 17 of course, allows for more efficient development as FDA  
 18 advice can be sought and provided earlier than -- in  
 19 the Type C meeting format. So, we hope that this does  
 20 facilitate development by giving feedback earlier.

21 In addition, what is not uncommon is that  
 22 after there's a meeting, particularly where there are a  
 23 number of issues, there may be areas that the sponsor  
 24 wishes to get clarification, there may have been an  
 25 agreement, but sponsor may want to make sure they

Page 32

1 understood it completely. And that they -- that they  
 2 understood fully what the direction from the FDA was.  
 3 And so, we've added a process by which meetings --  
 4 which questions which are really just clarifications of  
 5 issues that came up at a prior meeting can be submitted  
 6 and input given back in a timely fashion back to  
 7 company.

8 We will have a public workshop about these  
 9 meetings and appropriate training and of course,  
 10 updated guidance, which will also include updated  
 11 guidance on best practices in the management and  
 12 communication to make sure that these important  
 13 interactions are facilitated and as efficient as  
 14 possible.

15 Next slide. I think as many are aware, we've  
 16 seen a certainly a marked increase in the number of  
 17 programs that are targeting rare diseases over the past  
 18 decade or even more. One of the challenges in rare  
 19 disease drug development is that for many rare  
 20 diseases, where there still is a great need -- great  
 21 unmet need for treatments, trials can be challenging.  
 22 In particular, for example, the need to develop  
 23 endpoints that reflect and can capture patient benefit  
 24 from drug therapy may not yet be available, or well  
 25 understood -- or the characteristics of these endpoints

Page 33

1 may not be very well understood.

2 So this is an exciting pilot program in which  
 3 a sponsor, early in their development of a drug for  
 4 rare disease, can come to us with a proposal for a  
 5 novel approach at that point and it allows us to work  
 6 closely with him on the development of that endpoint  
 7 over a series of meetings.

8 The idea here is both to facilitate the  
 9 development of an endpoint for a particular disease,  
 10 but also to encourage innovation in how endpoints are  
 11 crafted and created, and developed. Endpoints that we  
 12 hope -- approaches to endpoints that we hope will be  
 13 applicable not just to the particular rare disease for  
 14 which that endpoint was developed, but for others  
 15 similar rare diseases, capturing similar issues that  
 16 may facilitate development across other rare diseases  
 17 or even diseases that are not rare.

18 The intent here is to encourage this  
 19 interaction between sponsor and FDA staff to enhance  
 20 the development of these novel, innovative approaches  
 21 to endpoints that facilitate the development of rare  
 22 diseases as well as potentially in common diseases.

23 We will include multiple public workshops to  
 24 talk about these strategies for endpoint development  
 25 that we hope will then allow us to come up with

<p style="text-align: right;">Page 34</p> <p>1 principles and concepts and policy that may then be  2 captured in guidances that then enhance the development  3 of endpoints more generally.  4 Next slide, please. Another program to note  5 is for what are called use related risk analysis as  6 well as human factor validation studies. Before a  7 human factor validation study, which addresses the use  8 of combination products, drug device or biologic device  9 combination products. Of course, a human factor  10 validation study shows that the end user, whether a  11 patient or healthcare practitioner, should  12 appropriately use this combination device.  13 One determination as to whether a human factor  14 validation study is actually needed is what's called  15 the use-related risk analysis. It assesses the types  16 of risks that might occur and determines whether those  17 risks are sufficient to be -- that need to be addressed  18 by such a study or might not need to be addressed by  19 such a study.  20 We're seeing an increasing number of requests  21 for review of these URRAs, and now we built a program  22 with timelines and resources to be able to evaluate  23 these use-related risk analysis in their appropriately  24 timely fashion, which can then inform whether or not a  25 human validation -- human factor validation study is</p>	<p style="text-align: right;">Page 36</p> <p>1 that we would need to support a regulatory decision.  2 So from those challenges, we've developed this  3 real-world evidence program. And this pilot program  4 basically seeks to have greater interactions between  5 the sponsor and FDA. The idea here is that rather than  6 get a finally developed study protocol forwarded to us,  7 that we -- you would start sort of earlier, provide  8 input to the -- to sponsors earlier. The idea would be  9 that initially, we would have sort of a concept sheet  10 proposal.  11 If this looks very promising then it really  12 might ultimately be able to be developed into a study  13 that that could be sufficient for supporting a  14 regulatory decision. This would be then entered into  15 this pilot program, and the program would include the  16 opportunity for multiple interactions back and forth  17 between the company and the FDA, sort of developing the  18 stages -- through the stages of the development of the  19 -- of this real-world evidence protocol.  20 The idea would be that each of the key  21 components could be then discussed -- the source of  22 data, the analysis approaches to the data, the  23 development of control comparative groups, and the like  24 could be discussed and the FDA feedback can be  25 provided. So then ultimately the protocol that then</p>
<p style="text-align: right;">Page 35</p> <p>1 needed, and as well as design elements related to that  2 human factor validation study, so this should help in  3 the timeline and timely development of these  4 combination of products. A guidance that would be  5 relevant to this, would also be -- would also be  6 developed.  7 Next slide. I think another very exciting  8 program is related to real-world evidence. Of course,  9 this has been an area of great interest and importance  10 over the past year's emerging PDUFA VI, and there's  11 been a great deal of work in FDA, Industry and  12 academics and other stakeholders on the use of real-  13 world data and creating real-world evidence that can  14 support -- potentially support regulatory decisions.  15 This area is certainly challenging. It's a  16 novel approach to the use of real-world data. And  17 there are many issues related to the types of data,  18 sources of data, how the data is to be analyzed,  19 comparison groups that emerge as we try to look at  20 studies that utilize real-world data and create real-  21 world evidence and are intended to support regulatory  22 decision making. And so, these challenges have to be  23 met. It require a lot of discussion between sponsors  24 and FDA on the appropriateness of the study design,  25 whether it's sufficient to be able to develop the data</p>	<p style="text-align: right;">Page 37</p> <p>1 would be implemented has a greater chance of developing  2 data that is more as it could be potentially if --  3 depending upon how the data emerges, potentially could  4 support a regulatory decision, and therefore, be able  5 to support an expansion of label with new indication,  6 new population of use.  7 So, this we hope will also provide broader  8 lessons in how such robust studies could be -- study  9 protocols can be developed. We'll be reporting the  10 submissions on public facing annual report. And this  11 also going to be a public workshop and meeting which  12 will discuss the kinds of learnings from these cases,  13 that could then provide more general and broader input  14 as to how to craft the right kind of study that can  15 have sufficient robustness to support important  16 regulatory decisions.  17 And of course, the learnings from this, as we  18 develop new policies and approaches, can be then  19 crafted into guidances to reflect this experience from  20 the pilot program. So, I think this is an exciting way  21 of further utilizing real-world data, real-world  22 evidence, and helping in working with sponsors to  23 channel the interest in this towards what we hope will  24 be studies that can ultimately be utilized to support  25 regulatory decisions.</p>

<p style="text-align: right;">Page 38</p> <p>1 Next slide, I think, that's a summary of the  2 PDUFA VII program, so I'll turn it back to you, Graham.  3 MR. THOMPSON: Alrighty. So Cartier, and  4 Lucy, you have five minutes, it's all yours.  5 MS. ESHAM: Sure. And thank you, Peter. That  6 was a great summary. And, again, I'm just going to  7 underscore a couple of things.  8 I would say that, you know, one of the sort of  9 evergreen issues as we go into these PDUFA discussions  10 is really, how can we ensure that we are setting up  11 processes and a system that enable scientific dialogue  12 throughout the development and review cycles to best  13 ensure that we are able -- setting up a system that  14 enables us to do early issue identification, and early  15 issue resolution wherever possible. And I think the  16 outcome of this agreement is very exciting in that  17 aspect.  18 As Peter outlined, there is the new -- there's  19 an expansion of the INTERACT program that was very  20 successful at CBER that's not going to be available for  21 products undergoing review at CDER. It establishes  22 timelines for both, so that the expectations of how to  23 prepare and be prepared for those meetings, as well  24 establish and supported by appropriate resources.  25 The ability to have the new Type D meeting to</p>	<p style="text-align: right;">Page 40</p> <p>1 The other thing that that Peter mentioned, but  2 again, I'm just going to underscore for the audience  3 today is, that there will be public meetings and  4 updated guidance on meeting management and meeting  5 practices. And what I want to underscore there is this  6 is the ability for industry to also learn about are we  7 ensuring that we are best preparing ourselves for the  8 most productive meetings, and that's really important.  9 That will be a very important engagement and  10 understanding to be gained through the commitments in  11 this PDUFA letter.  12 Peter also mentioned the new processes to  13 ensure that for any post-market requirements that a  14 product may have, that the engagements happening during  15 the review cycle are done in a manner to best ensure  16 agreement on a solid study plan. So, a solid approach  17 to achieving those post-market requirements once --  18 prior to approval. And then the ability of science  19 evolves or thinking evolves to go back and a process to  20 have the study requirements reviewed by the Agency,  21 whenever appropriate.  22 And we're also very excited, and again, I  23 think it's always good when you see a program -- the  24 STAR pilot program, which is modeled after something we  25 saw very beneficial in the oncology space, the RTOR</p>
<p style="text-align: right;">Page 39</p> <p>1 have focused conversation. So, I think this is of  2 particular import when you have a particular  3 challenging issue, or a novel issue where you want the  4 ability to have a focused discussion, is a very  5 exciting new offering in this PDUFA agreement.  6 The ability to have a prioritization for  7 sponsors' requests where there is very little precedent  8 known or there's a really -- it's a very novel program,  9 the ability to at least have -- if you received a  10 written only response to have a prioritization of a  11 sponsors' request to convert that to a face-to-face.  12 Again, there is a very nice offering in this PDUFA  13 agreement. Again, all of these meetings are both for  14 CBER and CDER.  15 And Peter mentioned the follow-up meetings.  16 And again, this is an issue that's been discussed over  17 the years, and I think that this is a very nice process  18 -- a newly established process to really enable a  19 quicker -- a quicker timeline to do this simple and  20 clarifying questions to make sure you heard what you  21 heard, and to verify that before you -- perhaps you're  22 going to go off in a wrong direction. And again,  23 that's just going to create efficiencies in the  24 process, both for FDA and for biopharmaceutical  25 sponsors.</p>	<p style="text-align: right;">Page 41</p> <p>1 program. And to be very clear, this is not in  2 replacement of RTOR, it is in addition to. So, it is a  3 pilot program for efficacy supplements across FDA to  4 really -- but take what we saw worked very well in the  5 oncology space and apply it in a pilot program to  6 efficacy supplements to gain learnings about how that  7 sort of two parts submission may enable more efficient  8 and effective review.  9 So again, that's something that's very  10 exciting, and I think it's always good to have pilot  11 programs that are expanding on areas that we saw work  12 very well. So, we're very excited to see that get  13 started and look forward to the learnings that we  14 obtained from it.  15 With that I'm going to turn to my colleague  16 Lucy.  17 MS. VERESHCHANGA: Thank you, Cartier. And I  18 would like to emphasize Peter's comments on the  19 increased use of real-world evidence.  20 So, the PDUFA VII provisions will build on  21 successes that were started in PDUFA VI, also builds on  22 some of the 21st Century Cures milestones. And as  23 Peter mentioned, there been quite a few stakeholder  24 discussions and efforts over the past 5 plus years. So  25 we're really looking forward to successfully building</p>

<p style="text-align: right;">Page 42</p> <p>1 on all those efforts. So, this is why industry 2 supports a pilot program for real-world evidence. 3 And importantly, the pilot will include an 4 increased public transparency element. So, as Peter 5 mentioned, all the learnings coming out will have to be 6 publicly posted, there are multiple stakeholder 7 workshops attached, and opportunity for stakeholders to 8 provide input and really have meaningful discussions -- 9 how to increase regulatory acceptance of real-world 10 evidence. And that arguably can be used not just for 11 safety purposes, but also can support efficacy 12 indications. 13 So, I would also emphasize previous provisions 14 for rare diseases. And industry and FDA, definitely 15 want to continue to ensure robust support for rare 16 disease drug development. And specifically PDUFA VII 17 establishes Rare Disease Endpoint Advancement Program. 18 And it will help sponsors to understand better how to 19 engage with the regulators on developing endpoints, 20 specifically for rare diseases. I'll stop here. 21 MR. THOMPSON: Okay. Thank you everyone so 22 far. We're a little ahead of schedule, but I think 23 we're going to move into taking a break anyway. 24 And we're in the next slide, I know the slide 25 says 10:25, but I ask everyone to be back at 10:15 and</p>	<p style="text-align: right;">Page 44</p> <p>1 enhancements and these are in that section of the 2 commitment letter, if you'd taken a look at it. And 3 one is patient-focused drug development, another model- 4 informed drug development. And the third, complex 5 innovative trial designs. 6 And these are -- essentially these were the 7 three that were under active discussions with industry 8 in the past year. And these are the ones where we had 9 some evolution of the commitment and what's involved in 10 this program. 11 And so, if we can go to the next slide, 12 please. And I'm going to just give you a little 13 background, because these three are in fact 14 continuations and extensions of the work that was 15 continuing from work done under PDUFA VI, and in some 16 cases even before that. A little bit of background 17 before we get into the proposed enhancement. 18 And so, the first one, patient-focused drug 19 development. Here we're -- our goal is to advance the 20 patient's voice in drug development and decision- 21 making. And what we recognize is that patient input, 22 if it's collected in ways that are methodologically 23 sound, and produce valid and reliable sort of 24 assessments and endpoints that can be used, this can 25 provide evidence for regulatory decision-making.</p>
<p style="text-align: right;">Page 43</p> <p>1 we can send out a notification in the chat as well. I 2 will come back then. 3 And while everyone's on break, just another 4 plug for the public docket, if you want to submit 5 written comments. With that, we'll see everyone back 6 here at 10:15. 7 (Recess) 8 9 Regulatory Decision Tools Proposed Enhancements 10 11 MR. THOMPSON: The next session, which is 12 regulatory decision tools, to get ready. That's you, 13 Theresa. And we'll begin in just about half a minute. 14 All right. Thank you. And if you could 15 advance to the next slide. Okay. 16 So, we're going to move on to our overview of 17 post-enhancements on regulatory decision tools. Our 18 presenter will be Theresa Mullin, and our speaker as 19 usual will be Lucy and Cartier. And Theresa, you can 20 start whenever you're ready. 21 MS. MULLIN: Okay. Thank you, Graham. Hello, 22 everybody. Good morning. I'm Theresa Mullin. And 23 it's my pleasure to take you through this section of 24 the enhancements proposed for PDUFA VII. 25 And I'm going to be focusing on three</p>	<p style="text-align: right;">Page 45</p> <p>1 And similarly, patient preference information 2 can help inform regulatory decision-making if it's 3 collected in a way that's methodologically sound. And 4 what we find is that studies may have quality problems. 5 And so, they may not be as useful as we ideally would 6 like them to be. The information that's collected is 7 not as useful in decision-making. And so, that's not 8 the best use of the time, an investment of patient's 9 time and resources expended to collect this 10 information. 11 And so, in PDUFA VI we've been developing a 12 series of methodological guidance, focused on clinical 13 outcome assessments or COAs. And those are still under 14 development now. And we, you know, expect to have 15 those finished before the end of this current 16 authorization cycle. But the enhancements for the 17 coming period are really building on that. 18 And so, they include expanding training both 19 to prompt internally focus training on new divisions 20 and stakeholders within CDER and CBER with an emphasis 21 on those methods and tools. And also, a train -- 22 focused training and outreach to industry and other 23 users of this mythological guidances so that they have 24 a good -- they know they're there, their awareness, 25 understanding of them, and that they're making maximum</p>

<p style="text-align: right;">Page 46</p> <p>1 use in order to have high quality evidence being 2 submitted to FDA.</p> <p>3 In addition to that, we'll be issuing a 4 request for information to collect input from 5 stakeholders to understand what the methodological 6 challenges are, and what needs to be further discussed. 7 And that will form a basis of planning agendas from two 8 workshops that would be held during PDUFA VII, to 9 really explore those methodological issues.</p> <p>10 Another component of this commitment refers to 11 the virtual catalog of standard core PDUFA outcome 12 assessment measures that FDA has been developing using 13 the budget authority funds that we received through 14 Cures that were initially authorized under Cures and 15 have been appropriated by Congress under the Cures Act, 16 or following what was described in the Cures Act, but 17 in our annual appropriations.</p> <p>18 And these non-fee funds are -- would continue 19 to be used and would -- we would not be using these 20 (inaudible) funding for this. But there's a reference 21 to this work in the commitment letter with the idea 22 that this is an important component of patient-focused 23 drug development. And what we would be doing is 24 seeking additional stakeholder input about priority 25 disease areas and domains that would be of interest to</p>	<p style="text-align: right;">Page 48</p> <p>1 willing to accept up to eight proposals per year, one 2 to two per quarter is the, you know, the cadence at 3 which things would be expected. And these basically 4 would involve a pair of meetings that are focused on 5 the same drug development issues.</p> <p>6 And the second meeting in this case would 7 occur approximately 60 days after receiving the 8 briefing materials that, you know, following that first 9 meeting. And the discussion would be on those 10 (inaudible) program issues if there -- a sponsor wants 11 to have this kind of consultation with agency and the 12 eight programs have already been taken up for a given 13 year, they can still come into the normal and other 14 traditional meetings options that are available to 15 sponsors.</p> <p>16 In addition, there will be a request for 17 information the FDA would issue to understand what 18 areas of development or MIDD work would be of greatest 19 priority to outside stakeholders for future guidance 20 development.</p> <p>21 Next slide, please. And this is the third 22 one, the final one that I'll talk about today. And 23 it's on complex innovative trial designs. Now, we had 24 a pilot for this as well in PDUFA VI, and it was 25 similar in the sense of a paired meeting approach. And</p>
<p style="text-align: right;">Page 47</p> <p>1 be included in this virtual catalog.</p> <p>2 And the last thing that I'll mention with 3 patient-focused drug development is that there's a 4 piece in there for developing a future guidance on 5 patient preference. And this would be development in 6 2026 time frame, and that's another addition to enhance 7 the quality of the kinds of submissions we been 8 receiving for patient-focused drug development.</p> <p>9 So, next slide, please. Another enhancement 10 is focused on model-informed drug development, MIDD. 11 And MIDD can really improve the efficiency of trial 12 designs and reduce uncertainties and help actually 13 developers and the agency explore those uncertainties 14 to find out which matter and how to better design our 15 drug development programs.</p> <p>16 And it's -- we've had a pilot in PDUFA VI with 17 a paired meeting involved, consult with companies or 18 companies coming to consult with FDA about their plans 19 and how they are using these models. That pilot is 20 very successful, and so the goal here under PDUFA VII 21 is to continue and turn that pilot into a formal 22 program, continuing program. It's no longer a pilot. 23 But keep it within that same footprint that was 24 established under PDUFA VI.</p> <p>25 And so, what is involved is the agency being</p>	<p style="text-align: right;">Page 49</p> <p>1 this is really focused on a wide range of indications. 2 Really many different designs had come in through this 3 program.</p> <p>4 And they all involve this computational 5 intense analytic techniques and situations that had to 6 be used, a lot of time interaction is necessary to make 7 this really worthwhile between FDA and the sponsors. 8 And we find that in addition to the later-stage 9 development, they're increasingly -- these kinds of 10 designs are being used in earlier phases of drug 11 development.</p> <p>12 And so here, the enhancement that's been 13 committed to is that again will be transfer -- translate 14 or rather transitioning from a pilot to a full-grown 15 program here with the goal that this would continue to 16 advance and facilitate the use of adaptive designs and 17 it would be easier designs.</p> <p>18 And, again, it's a pilot program -- a paired 19 meeting program. And in this case the second meeting 20 would be approximately 90 days after receiving the 21 materials following that first meeting. There would be 22 one to two per quarter accepted by CDER and CBER 23 together, that's the total for FDA, up to eight per 24 year.</p> <p>25 And in addition to that, the other components</p>

<p style="text-align: right;">Page 50</p> <p>1 of enhancement here are that the whole goal here is to  2 have not just this individual sponsor who is submitting  3 this innovative design be gaining that experience and  4 knowledge but to have others as well. So, a piece of  5 this pilot program is that the trial designs developed  6 through paired meeting program may be presented by FDA  7 as case studies, including the drug that was studied  8 and may not have been approved yet by FDA. That's one  9 of the understandings from people entering this  10 program. It's not a pilot anymore. Sorry.</p> <p>11 And there -- when FDA discusses a company  12 joining this program, there is an understanding and  13 discussion of the information that FDA plans to share  14 in those case studies. And when feasible, FDA would  15 notify the sponsor in advance of sharing that  16 information publicly.</p> <p>17 Sponsors who don't participate in the paired  18 meeting program again have an opportunity to come in  19 through other meeting, traditional meeting channels.  20 And there will be a public workshop that the agency  21 plans to have to discuss various aspects of complex  22 designs, basic designs and other novel designs, and  23 that would be in the 2024 timeframe.</p> <p>24 And finally, there is a commitment to issue a  25 draft guidance on use of methodologic -- use of phasing</p>	<p style="text-align: right;">Page 52</p> <p>1 a significant amount of resources being provided under  2 the PDUFA VI agreement, I believe over 60 FTEs, I  3 believe 63 FTEs were provided under the PDUFA VI  4 agreement.</p> <p>5 So as we going to PDUFA VII, what we wanted to  6 do is to make sure that those resources provided under  7 PDUFA VI are maintained and continue that very  8 important work of focusing on patient-focused drug  9 development. And we wanted to expand some resources to  10 continue to advance our thinking. So, I think in terms  11 of the patient-focused drug development, we're very  12 excited about the commitment of relating to the ability  13 to have some workshops, the ability for community to  14 have public input, to continue to advance our thinking  15 and our shared understanding about how to submit and  16 evaluate patient perspective data to support benefit,  17 risk evaluations and to support labeling activities.</p> <p>18 We're also -- we are very supportive of the  19 continued development of the virtual catalog that -- on  20 standard core sets of clinical outcome assessments that  21 Theresa mentioned, and we look forward to continuing to  22 provide input to continue to strengthen that catalog.</p> <p>23 And lastly, I'll just underscore, we're also  24 very excited about the commitment to have draft  25 guidance on the use of patient preference studies. So,</p>
<p style="text-align: right;">Page 51</p> <p>1 methodology in critical trials for drugs and biologics.  2 And that is aimed for in the 2025 time period.</p> <p>3 And with that -- those are the new  4 enhancements for regulatory tools in PDUFA VII. And  5 so, with that I'll close.</p> <p>6 MR. THOMPSON: All right. Can we do the next  7 slide. We'll move on to Cartier and Lucy. Thank you.</p> <p>8 MS. ESHAM: Thank you, Theresa, for that  9 excellent summary. And I'll just again provide a few  10 color commentary. Think this really -- has really been  11 an evolution going back to PDUFA V, and it's a  12 continuation of that journey that started significantly  13 in PDUFA V where there was a commitment in the PDUFA V  14 agreement to have post a series of Voice of the Patient  15 meetings which were extraordinarily enlightening where  16 we as a community really learned not only the  17 importance but how to think about what matters to  18 patients and how to think about capturing patient  19 experience data.</p> <p>20 That led to the PDUFA VI agreement where the  21 goal there was to really think about what is needed,  22 what do we -- what resources do we need to provide the  23 FDA to sort of collectively advance a systematic  24 integration of patient experience data into drug  25 development and review processes. And that resulted in</p>	<p style="text-align: right;">Page 53</p> <p>1 again, this marks sort of a continued evaluation of our  2 shared understanding and shared thinking and  3 advancement of how we are collecting patient  4 perspective data, how that can be utilized for specific  5 regulatory decision-making, to ensure that the voice of  6 the patient is in fact becoming integrated into how we  7 approach development and review of drugs and biologics.</p> <p>8 With that, I'll turn to my colleague, Lucy.</p> <p>9 MS. VERESHCHAGINA: Thanks, Cartier. And to  10 echo Theresa and Cartier, complex innovative trial  11 designs and model-informed drug development is another  12 example how PDUFA VII builds on successes from the  13 previous cycles, specifically PDUFA VI, and will  14 continue to advance innovative drug development and  15 regulatory decision tools to the benefit of patients.</p> <p>16 And I would like to specifically emphasize  17 public process and public workshops series on novel,  18 complex, adaptive and Bayesian designs, that they will  19 issue guidance on Bayesian approaches. So the work  20 will continue and build on the efforts from PDUFA VI.</p> <p>21 PDUFA VII also continues model-informed drug  22 development, pair missing programs, as Theresa  23 mentioned, and importantly will be enhanced by issuance  24 of request of information to elicit stakeholder input  25 for identifying focus areas for future policy or</p>

<p style="text-align: right;">Page 54</p> <p>1 guidance development. So, we look forward to this  2 enhanced stakeholder engagement. And as Cartier said,  3 we're very excited about these continuing efforts.  4 MR. THOMPSON: Okay. Thank you very much.  5  6 Post-Market Safety Proposed Enhancements  7  8 MR. THOMPSON: We're going to move on now to  9 our fourth session on Post-Market Safety. Our FDA  10 presenter for this topic is going to be Terry Toigo and  11 same industry speaker as always. Terry, you're up  12 next, and you can begin whenever you're ready.  13 MS. TOIGO: Okay. Thanks, Graham. As Janet  14 Woodcock mentioned before the technical issue started  15 with the -- her presentation, drug safety is a critical  16 part of FDA's public health mission. As Andy mentioned  17 on -- in PDUFA IV, drug safety was added to the  18 commitment.  19 And since then we've continued to use the user  20 fees to enhance the drug safety system. Our goal  21 remains to improve public health by increasing patient  22 protection while continuing to enable access to needed  23 medical products for patients. So, I'm going to, in  24 the next four slides, I'll walk through our commitments  25 related to REMS and Sentinels, which are part of PDUFA</p>	<p style="text-align: right;">Page 56</p> <p>1 success. This will also help us ensure that sufficient  2 data collection is built into the design of REMS for  3 determining whether or not a REMS is meeting its goal.  4 We'll meet this commitment by creating new  5 guidances or updating existing guidances or policies  6 and procedures to determine whether modifications to  7 the REMS or revisions to the REMS, assessment plan are  8 needed, and whether that REMS is still necessary to  9 ensure whether the benefits of the drug outweigh its  10 risks.  11 We believe that the PDUFA VII REMS assessment,  12 REMS commitment package will enhance FDA's ability to  13 determine whether or not REMS are meeting their goal.  14 The next three slides, if you could move to  15 the next one, address commitments to optimize the  16 Sentinel Initiative. In the last 5 years, the Sentinel  17 Initiative, which includes both the Sentinel System and  18 BEST, or the Biologics Effectiveness and Safety System,  19 has become an integral component of FDA's routine  20 regulatory review program. With operational processes  21 and policies and ongoing scientific training programs  22 and clear evidence of regulatory impact. Sentinel  23 analyses have influenced dozens of regulatory  24 determinations, including labeling changes and  25 presentations to advisory committees.</p>
<p style="text-align: right;">Page 55</p> <p>1 VII.  2 Next slide, please. So, as part of the  3 reauthorization of PDUFA V in 2012, FDA committed to  4 standardize and assess the effectiveness of REMS and to  5 better integrate them into our healthcare system.  6 These activities included two guidances that were  7 published in January of 2019. The guidance did help  8 advance the science of REMS program assessment and  9 helped sponsors develop the REMS assessment plan.  10 But a remaining area of concern is to complete  11 timely assessments, and for us to be able to determine  12 whether REMS is doing a good job of meeting its goals  13 and ensuring that the benefits of a particular product  14 outweigh its risks and whether FDA should take action  15 when -- when a REMS is not performing as expected.  16 So, although there were not any specific REMS  17 commitments in PDUFA VI, FDA did continue its REMS  18 standardization effort. PDUFA VII commitments  19 established, as you can see on this slide, established  20 FDA review performance goals for -- after reviewing  21 REMS methodological approaches and study protocol for  22 REMS assessment.  23 Also included is an FDA commitment to develop  24 and incorporate REMS assessment planning into the  25 design of REMS to help identify key metrics for</p>	<p style="text-align: right;">Page 57</p> <p>1 This work has in many cases enabled FDA to  2 resolve safety concerns in-house and then thus  3 prevented FDA from sending additional information  4 requests to companies or in some cases requiring post-  5 marking studies. FDA is implementing several  6 enhancements, including new data linkages and data  7 sources like Medicare data in these Sentinel centers,  8 both of which help improve Sentinel's capability.  9 The growing complexity and then the  10 sophistication of the Sentinel Initiative has  11 introduced a different set of challenges and heightened  12 our resource considerations. And, as you can see from  13 the bullets on the slide, the commitment will provide  14 continued support to help FDA sustain a strong post-  15 market population-based surveillance capacity, will  16 meet these commitments by maintaining the quality and  17 the quantity of data available through the Sentinel  18 Initiative, and processes and tools for determining how  19 and when the data are utilized. Engaging in staff  20 training, communicating with sponsors and the public  21 through dissemination of scientific advances at public  22 meetings and public training.  23 Next slide, all right. Additional resources,  24 as described in this slide and the next one, will  25 enable FDA to focus on improvements to Sentinel areas</p>

<p style="text-align: right;">Page 58</p> <p>1 efficiency and BEST on product safety by initiating  2 scientific development projects in Sentinel and BEST  3 around areas of insufficiencies that are of mutual  4 importance to -- with industry and that's product  5 safety and pregnancy and negative controls, which I'll  6 discuss in the next slide.</p> <p>7 But, monitoring of safety of it's -- of the  8 safety of its regulated products is a major part of  9 FDA's mission to protect public health. Because  10 pregnant women have historically been excluded from  11 drug development trials, there's often limited or no  12 human data to inform the safety of use of the drugs in  13 pregnancy and labeling at the time drugs are approved.</p> <p>14 The goal of the pregnancy safety post-  15 marketing and PMRs and PMC studies is to inform  16 labeling on the safety of use and pregnancy and to  17 detect or evaluate safety signals in a timely manner.</p> <p>18 So, the first of our new commitments to  19 optimize the Sentinel Initiative includes supports for  20 the development of a consistent approach for assessing  21 the outcomes of pregnancies in women exposed to drugs  22 and biologic products. We plan to develop a framework  23 for how data from different types of post-approval  24 safety studies, pregnancy safety studies have been used  25 by FDA, and to identify gaps in knowledge that need --</p>	<p style="text-align: right;">Page 60</p> <p>1 can be used in robustness evaluation to address the  2 consistency of real-world evidence with respect to  3 study design analysis or variable measurements. And as  4 listed on this slide, the commitment also involves a  5 public workshop and two methods development projects.  6 And the deliverable for this commitment is a final  7 report that is due at the end of PDUFA VII.</p> <p>8 And -- so, in the area of post-market safety,  9 I think as these commitments demonstrate, FDA will  10 continue to use user fees to enhance the drug safety  11 system through modernization and improvement of REMS  12 assessment and optimization of the Sentinel Initiative.</p> <p>13 And by doing so, we will continue to improve  14 public health by increasing patient protection while  15 continuing to enable access to needed medical products.  16 So with that, that ends the discussion on the post-  17 market safety commitments. And I will turn it back to  18 Graham. Thank you.</p> <p>19 MR. THOMPSON: I'll take that and turn it over  20 to Cartier and Lucy for the industry perspective. And  21 thank you very much Terry.</p> <p>22 MS. ESHAM: Yes, thank you, Terry. And, again  23 I will concur with the absolute import of the ability  24 of the FDA to maintain a quality safety system. And  25 this is reflected in the historic and continued</p>
<p style="text-align: right;">Page 59</p> <p>1 that will need to be filled by demonstration projects.  2 We'll then hold a public workshop on post-  3 approval safety studies in pregnant women, to  4 facilitate the determination of optimal post-market  5 study design, which could include Sentinel resources  6 from the Sentinel Initiative. And then using the  7 feedback from the initial framework and the workshop,  8 we'll conduct five demonstration projects to address  9 gaps in knowledge about performance characteristics of  10 different study designs in the context of the proposed  11 framework developed.</p> <p>12 And then finally, we'll update the proposed  13 framework with the results of the demonstration  14 projects to develop a guidance or a MAPP to implement a  15 standardize process for determining the necessity and  16 the type of pregnancy PMRs or other post-market studies  17 or activities.</p> <p>18 Next slide. The second new commitment to  19 further optimize the Sentinel Initiative involves  20 development of new methods to support causal inference  21 for product safety questions, that will also help our -  22 - advance our understanding of how real-world data may  23 be used for studying product effectiveness questions.</p> <p>24 FDA is building BEST in Sentinel methodology  25 to improved our understanding of how negative controls</p>	<p style="text-align: right;">Page 61</p> <p>1 significant commitments and resources provided under  2 the PDUFA agreement.</p> <p>3 I will also, you know, I think, I will  4 underscore the commitment to have the publication of  5 information to improve communication with sponsors and  6 the public regarding general methodologies for Sentinel  7 enquiries we think will be of high value. And  8 additionally, really thinking about not just  9 maintaining the current role of the Sentinel initiative  10 but evaluating the possibilities of use of data such as  11 real-world evidence that could be utilized for other  12 purposes such as regulatory changes for post-market  13 requirements or commitments, labeling changes, et  14 cetera, really continues to advance the value of the  15 Sentinel Initiative.</p> <p>16 With that, I'll turn it over to my colleague,  17 Lucy.</p> <p>18 MS. VERESHCHAGINA: Thanks, Cartier. I would  19 emphasize FDA's and industry commitment to patient  20 safety. And also as Cartier mentioned, we try to take  21 a holistic approach to how we view PDUFA VII provisions  22 and make sure that to the extent possible will leverage  23 the ongoing effort, continue building on that and put  24 enhancements in place, specifically as Cartier  25 mentioned on increased use of real-world evidence and</p>



<p style="text-align: right;">Page 62</p> <p>1 how we can advance Sentinel analytical capabilities to  2 support the use of Sentinel, to address product safety  3 and also to address how real-world evidence can be used  4 for demonstrating drug effectiveness.</p> <p>5 I would also emphasize that PDUFA VII includes  6 important initiatives related to safety of pregnant  7 populations. And a specific example there is public  8 workshop on post-market safety studies in pregnant  9 women to facilitate determination of appropriate post-  10 market study designs. And it would include industry  11 experiences on how Sentinel and other real-world data  12 resource can be used for these purposes. And would  13 like to also echo the importance of the new Sentinel  14 demonstration project for specifically addressing the  15 pregnancy outcomes in women and really the support that  16 PDUFA VII will provide for implementation of a  17 standardized process for determining necessity and type  18 of pregnancy post-marketing studies.</p> <p>19 So, I'll stop here.</p> <p>20 MR. THOMPSON: Okay. Thank you, everyone.  21</p> <p>22 MR. THOMPSON: We're going to move into our  23 next session which is on Chemistry, Manufacturing and  24 Controls. Our FDA presenter for this topic will Carol  25 Rehkopf. And you can begin whenever you are ready.</p>	<p style="text-align: right;">Page 64</p> <p>1 So, Four-Part Harmony is something that we  2 committed to, and it includes acknowledging what was  3 provided in an application and where, identifying the  4 issues and efficiencies that we've -- that we have  5 identified in clearly explaining that information. And  6 also information that's need to achieve resolution of  7 any issues or deficiencies that were identified. All  8 of this is in an effort to help us get to a regulatory  9 decision.</p> <p>10 So, FDA is committed to updating procedures  11 and providing training on the four central components  12 of Four-Part Harmony. These include describing what  13 was in the application, a description of those issues  14 and deficiencies, what's needed to -- for FDA to  15 understand the issue better or to address the  16 deficiency and an explanation of why it's needed.</p> <p>17 To assure good FDA communication, training  18 will be updated on the CMC assessment process as well.  19 And this is related to the mid-cycle and late-cycle  20 review meetings that we have. The goal really is to  21 ensure that the mid-cycle and late-cycle meeting  22 expectations are met. This also includes the status of  23 the NDA or BLA CMC assessment, and making sure that's  24 communicated well, in addition to any issues that have  25 been identified that would preclude approval.</p>
<p style="text-align: right;">Page 63</p> <p>1  2 Chemistry, Manufacturing, and Controls Proposed  3 Enhancements  4</p> <p>5 MS. REHKOPF: Very good. Thank you so much.  6 As mentioned, my name is Carol Rehkopf. I was one of  7 the negotiators during this PDUFA cycle. And the same  8 subgroup was one that I supported. And it's a real  9 pleasure to be with you today. Next slide, please.</p> <p>10 So, as Andy mentioned at the start of this  11 meeting, this section is really a new commitment. The  12 CMC section comes through manufacturing and controls.  13 This new topic is an opportunity really for us to  14 enhance our communications in this space and to also  15 advance the use of innovative manufacturing  16 technologies. And what I'm going to do today is really  17 summarize the various commitments. And I encourage you  18 to read the commitment letter itself to understand the  19 details more fully.</p> <p>20 So, in this effort to enhance communications,  21 including providing structured CMC information requests  22 and communication at appropriate time points within the  23 review cycle of the product lifecycle -- I'm sorry, of  24 the product life cycle. We refer to the structure  25 communication as Four-Part Harmony.</p>	<p style="text-align: right;">Page 65</p> <p>1 We have committed to a third-party assessment  2 on sponsoring FDA communication practices through  3 product quality information request. And so that's  4 something that we planned to perform. We really want  5 to focus on the area of assessments and the application  6 of Four-Part Harmony and how well we're doing in the  7 space. We want to identify trends across information  8 requests as well.</p> <p>9 Both FDA and industry believe that enhanced  10 communication between review teams and industry on  11 inspection-related activities are important.  12 Therefore, for applications, not including supplements,  13 where FDA feels that the manufacturing process must be  14 observed, the FDAs agreed to the goal of notifying a  15 company about those pre-license or pre-approval  16 inspections at least 60 days in advance or no later  17 than the mid-cycle meeting when facilities need to be  18 inspected in those cases. So, again, this is when  19 manufacturing is in process. This will help to ensure  20 that FDA can observe operations during an inspection  21 and will help facilities plan accordingly.</p> <p>22 Next side, please. Thank you. So, during the  23 COVID-19 public health emergency, travel essentially  24 stopped. And therefore we had to think of other ways  25 to assess manufacturing facilities when it was</p>

<p style="text-align: right;">Page 66</p> <p>1 feasible. Because of this, FDA expanded its use of  2 alternative tools for assessing facilities named in  3 applications, including exercising its authority to  4 request records and other information in advance of or  5 in lieu of an inspection.  6 So, where appropriate, the agency increased  7 the use of that available information, including  8 inspection reports shared by trusted foreign regulatory  9 partners we have around the world, through mutual  10 recognition agreements and other confidentiality  11 agreements. These are areas where FDA continues to  12 learn and understand what is possible. Given this  13 experience, FDA has agreed to issue a guidance document  14 on the current thinking and best practices related to  15 the use of those alternative tools to assess  16 manufacturing facilities that are named in pending  17 applications moving beyond the pandemic.  18 Again, those examples include things like  19 alternative tools as in inspection reports from those  20 trusted regulatory partners across the globe and also  21 things like record requests or requests for other  22 information from applicants or facilities and the use  23 of new technologies as a possibility as well.  24 Next slide, please. Development programs for  25 CDER- and CBER-regulated drugs and biologics intended</p>	<p style="text-align: right;">Page 68</p> <p>1 regulated products.  2 So, what we intend to do is starting or -- is  3 to start this in fiscal year 2023. And the commitment  4 includes issuance of new procedure on approaches to  5 address CMC challenges for CDER-regulated products with  6 accelerated clinical development timelines and will  7 include things such as early engagement with sponsors  8 in different science and risk-based approaches.  9 The MAPP will incorporate modern  10 pharmaceutical principles and modern regulatory tools  11 such as those detailed in ICH Q12. Specifically, for  12 sponsors participating in the CMC development and  13 readiness pilot, FDA will provide specific CMC advice  14 during product development, by providing two additional  15 CMC-focus Type B meetings and an additional limited  16 number of CMC-focused discussions based on readiness  17 and define CMC milestones.  18 This increased communication between FDA  19 review staff and the applicant is intended to ensure  20 that there is a mutual understanding of what activities  21 must be completed and what information should be  22 provided at the appropriate time points.  23 These time points include things that are  24 required in a NDA and BLA submission prior to the end  25 of a review cycle or post-approval for example. All of</p>
<p style="text-align: right;">Page 67</p> <p>1 to, you know, help the serious diseases that were  2 contemplating and to meet unmet medical needs, we often  3 have to think about accelerated clinical development  4 timelines. So, products with accelerated clinical  5 development activities face challenges oftentimes when  6 it comes to CMC development.  7 We really are looking to have the CMC  8 development activities align with that accelerated  9 clinical development and those clinical timelines.  10 Overcoming these CMC challenges for aligning  11 these activities requires additional interaction with  12 FDA oftentimes, so that during the product development  13 itself the use of science and risk-based approaches can  14 be employed so that the clinical benefits of earlier  15 patient access to these products can be realized.  16 So, in the spirit of advancing the use of  17 innovative manufacturing technologies, a new pilot  18 program called the CMC Development and Readiness Pilot  19 or CDRP will be used in an attempt to expedite the CMC  20 development of IND products are expected to have this  21 clinical benefit for earlier patient access.  22 Sometimes accelerated clinical development  23 occurs faster than the CMC development. We know this,  24 right? So, the goal of the pilot is to achieve  25 increased CMC readiness for those CBER- and CDER-</p>	<p style="text-align: right;">Page 69</p> <p>1 this is really meant to ensure that the CMC readiness  2 of the product is in place.  3 Next slide, please. A public workshop is  4 planned where we intend to talk about CMC aspects of  5 expedited development, and will include case studies,  6 lessons learned, barriers to the adoption of  7 manufacturing technologies, regulatory strategies for  8 the adoption of advanced manufacturing, including  9 submission strategies for implementation of certain  10 innovative technologies across multiple commercial  11 products and multiple manufacturing sites.  12 Stakeholder input about the pilot will also be  13 solicited. And the topics of the workshop will include  14 the best practices and lessons learned from the pilot,  15 things from the CDER Emerging Technology Team and the  16 CBER Advanced Technology Team programs from both the  17 industry and regulatory perspectives.  18 I mentioned case studies from previous  19 innovative technology submissions will be presented.  20 And barriers, what are the technical and regulatory  21 barriers to the adoption of innovative manufacturing  22 technologies.  23 Regulatory strategies for the adoptions of  24 advancements of these technologies will be included.  25 And it will include things like submission strategies</p>

<p style="text-align: right;">Page 70</p> <p>1 for the implementation of certain innovative                  2 technologies across, like I said, the multiple                  3 commercial products or multiple manufacturing sites,                  4 and that science of risk-based approach.                  5 A draft strategy documents will be issued in                  6 2024 that will outline the specific action that the                  7 agency will take after this workshop. The actions                  8 described will be based on the lessons learned and from                  9 the agency experience with submissions involving the                  10 advanced manufacturing technologies that we're talking                  11 about. It will also include feedback from the workshop                  12 itself. And it will be available for public input.                  13 The strategy document may include updating or                  14 creating new procedures MAPPs, SOPs, guidances, and                  15 scientific or other relevant programs related to the                  16 topics discussed in the workshop. The strategy                  17 document will also include proposed timelines for                  18 specific actions outlined in the document. And FDA, as                  19 I said, will consider public input and finalize the                  20 strategy document within certain period of time.                  21 So, to close, what I'd like to say is that we                  22 hope that these commitments in this new section will                  23 result in enhanced communications and the advancement                  24 of and the use of innovative and manufacturing                  25 technologies.</p>	<p style="text-align: right;">Page 72</p> <p>1 a pilot program may, to some, seem limiting, it is very                  2 much modeled after what we view as a very successful                  3 approach to the innovative clinical trial design, a                  4 pilot program that Theresa mentioned as part of her                  5 presentation. And that is -- while it is a pilot, the                  6 pilot will produce those extra engagements on -- to                  7 focus discussions on readiness and define CMC                  8 milestones.                  9 But what will be of important to everyone is                  10 it does provide that sort of ability to share those                  11 learnings through case studies, through workshops that                  12 will result in a strategy document that will be                  13 published prior to the end of the next PDUFA cycle that                  14 will really, hopefully better advance us towards that                  15 ultimate goal of having, ensuring that these                  16 conversations are happening at the right time, and that                  17 those meetings are effective and productive.                  18 So, far apart, again there was a lot of work                  19 that went into those. I think that I'm just                  20 underscoring a couple of things that we think are going                  21 to be of significant benefit. Lucy?                  22 MS. VERESHCHAGINA: Thanks, Cartier. And I                  23 would like to echo industry's excitement on the,                  24 explicitly including manufacturing provisions and PDUFA                  25 VII performance goals (inaudible) and would like</p>
<p style="text-align: right;">Page 71</p> <p>1 With that, I'll turn it over to Graham. Thank                  2 you.                  3 MR. THOMPSON: And, again, I'll turn it over                  4 to Lucy and Cartier. Thank you so much everyone.                  5 MS. ESHAM: Thank you. Thank you, Carol, and                  6 hopefully it is apparent. There was a significant and                  7 appropriate amount of focus on this very important                  8 topic that was relatively new to the PDUFA                  9 negotiations.                  10 And the reason for this was, from the -- by a                  11 pharmaceutical perspective, there was a growing sense                  12 of import and almost urgency about wanting to ensure                  13 that we were aligning on an effective process for CMC                  14 engagement, both to ensure that meetings were happening                  15 at the necessary times both in development and review,                  16 and that the meetings held were productive and                  17 effective for all sides, for both the regulator and the                  18 industry.                  19 And so, there again I think -- I think there's                  20 a very positive -- many positive outcomes. And I'll                  21 underscore a few. The work that will be done to sort                  22 of promote the training, the third-party assessment to                  23 really promote a more structured CMC information                  24 request process we think is going to be of high value.                  25 The pilot program that Carol mentioned, well,</p>	<p style="text-align: right;">Page 73</p> <p>1 emphasize that industry and FDA consider and discuss                  2 the emerging lessons we learned from the COVID-19                  3 pandemic response. And this is why PDUFA VII will                  4 include a draft guidance on the use of alternative                  5 tools to assess manufacturing facilities named in                  6 pending applications and how to utilized new or                  7 existing technology platforms as appropriate.                  8 I also would like to emphasize what Carol                  9 said, that in advance of issuing this draft guidance,                  10 FDA will hold a public workshop. So, it's again                  11 opportunity for all stakeholders to provide input, how                  12 to advance utilization and implementation of innovative                  13 manufacturing technologies. And then, as Carol                  14 mentioned, FDA will issue a draft strategy document                  15 that will outline the specific actions that the agency                  16 will take. So, again, we're excited about these new                  17 provisions in PDUFA VII.                  18 MR. THOMPSON: Okay. Thanks so much everyone.                  19                  20 MR. THOMPSON: We're now going to be moving                  21 into session six here, which is our Digital Health and                  22 Informatics review. And our FDA presenter for this                  23 topic is Mary Ann Slack. And Mary Ann, you can begin                  24 whenever you are ready.                  25</p>

<p style="text-align: right;">Page 74</p> <p>1 Digital Health and Informatics Proposed Enhancements</p> <p>2</p> <p>3 MS. SLACK: Thank you. Sound check. Graham,</p> <p>4 you can hear me well?</p> <p>5 MR. THOMPSON: Can hear you loud and clear.</p> <p>6 MS. SLACK: Okay. Wonderful. Well, let me</p> <p>7 apologize if my voice gets scratchy. The allergies</p> <p>8 have got me by the throat today. If you could go on to</p> <p>9 the next slide, we'll get right in to it. Next slide,</p> <p>10 please. Thank you.</p> <p>11 Okay. So we'll start with commitment to</p> <p>12 expand capacity in digital health technologies. And I</p> <p>13 know that everybody here is familiar with digital</p> <p>14 health technologies and their impact on healthcare.</p> <p>15 They hold a lot of promise in healthcare, and</p> <p>16 also in drug development, drug biologic medicinal</p> <p>17 product development. The use of these DHTs can support</p> <p>18 and enable a conduct of decentralized clinical trials,</p> <p>19 either fully and hybrid, and parts of traditional</p> <p>20 clinical trials. They allow collection of data in the</p> <p>21 trial participants' day-to-day environment, it can</p> <p>22 support safety monitoring without requiring frequent</p> <p>23 visits to a traditional investigational site, et</p> <p>24 cetera.</p> <p>25 But CDER and CBER actually have limited</p>	<p style="text-align: right;">Page 76</p> <p>1 So, moving forward through with PDUFA VII,</p> <p>2 we'll be creating a DHT framework document to guide the</p> <p>3 use of the DHT-derived data in regulatory decision-</p> <p>4 making, and we'll be putting in place a committee, a</p> <p>5 cross-organizational committee to support that</p> <p>6 implementation, particularly collaborating with the</p> <p>7 recently launched digital health center of excellence</p> <p>8 an this framework is established and implemented. If</p> <p>9 we could -- excuse me.</p> <p>10 So, some of the benefits of this commitment</p> <p>11 obviously increase our ability and regulatory</p> <p>12 acceptance, because we actually have that review</p> <p>13 expertise and capabilities. We can provide more</p> <p>14 clarity through guidances on expectations for sponsors</p> <p>15 developing these novel DHTs. It has the potential to</p> <p>16 enhance the inclusion of patient populations in</p> <p>17 clinical trials, enhancing review consistency,</p> <p>18 supporting communication, consistent communication and</p> <p>19 so forth, a myriad of other things.</p> <p>20 And now I'll move on to the next slide. I'm</p> <p>21 conscious of time. Next slide, please. Oh, I'm so</p> <p>22 sorry. You have it up there.</p> <p>23 So, this contains a lot of information on this</p> <p>24 slide. And you'll see there are connected but</p> <p>25 different commitments on here or agreements on here.</p>
<p style="text-align: right;">Page 75</p> <p>1 experience. And we don't have enough expertise in</p> <p>2 evaluating DHT-generated data yet. We are getting DHT-</p> <p>3 based submissions and they've been steadily increased</p> <p>4 and then they're not going to go away. But the</p> <p>5 successful implementation of these DHTs in clinical</p> <p>6 trials depends on both sponsors and FDA being able to</p> <p>7 carefully assess the performance for their intended use</p> <p>8 and developing our capacity and expertise in that area,</p> <p>9 enhancing knowledge and capabilities in the areas of</p> <p>10 clinical outcome assessment, data standards, data</p> <p>11 management, et cetera. We need to build that capacity.</p> <p>12 So, if you look at this commitment, you can</p> <p>13 see that it's recognizing both the potential and the</p> <p>14 challenges that the use of DHTs bring. And it helps</p> <p>15 FDA to meet those challenges and facilitate the</p> <p>16 effective use and review of DHT-generated data in new</p> <p>17 medicinal products development.</p> <p>18 For instance, it increases FDA's capacity and</p> <p>19 expertise to advise the pharmaceutical industry in</p> <p>20 development and implementation of DHTs and how to</p> <p>21 evaluate those outputs. In addition to expanding</p> <p>22 capacity in this area, FDA is committed to holding a</p> <p>23 series of public meetings and workshops, conducting</p> <p>24 issued-focused demonstration projects, and issuing new</p> <p>25 or updated guidances as the need dictates.</p>	<p style="text-align: right;">Page 77</p> <p>1 The upside is that although FDA has long been accepting</p> <p>2 regulatory submissions electronically, we still have a</p> <p>3 lot of process and system inefficiencies, including the</p> <p>4 ability to automatically accept, validate and</p> <p>5 processing very large datasets, to be able to use</p> <p>6 modern technologies, cloud, for instance, cloud</p> <p>7 technology to extract and manage important information</p> <p>8 and execute resource-intensive algorithms on this. And</p> <p>9 we have made progress and we're still continuing to</p> <p>10 make progress, but there's a lot of opportunity out</p> <p>11 there.</p> <p>12 So for instance, you have all seen, I'm sure.</p> <p>13 And if you haven't, please go out and take a look at</p> <p>14 FDA's Technology Modernization Action Plan, and the</p> <p>15 Data Modernization Action Plan, because they speak</p> <p>16 about key initiatives, key priorities that we're moving</p> <p>17 forward with and that this commitment helps to support.</p> <p>18 One is, cloud-forward, making it easy and agile to</p> <p>19 embrace the cloud, to use package services, and an</p> <p>20 agile and secure network architecture. Data center</p> <p>21 consolidation, for instance, for more streamlined</p> <p>22 operation. A modernized data environment.</p> <p>23 The DMAP itself proposes a framework to drive</p> <p>24 the data strategy for deploying new systems that will</p> <p>25 allow FDA to manage and analyze data more effectively,</p>

<p style="text-align: right;">Page 78</p> <p>1 more efficiently.</p> <p>2 The cloud environment. Some of the challenges</p> <p>3 that we have right now with the cloud posture, cloud-</p> <p>4 forward posture, we still have challenges, we have</p> <p>5 difficulty to receive and process complex applications,</p> <p>6 especially those applications that are having, using</p> <p>7 very large datasets, because it's difficult for us to</p> <p>8 receive them directly electronically. It's tough</p> <p>9 sometimes to readily extract triage and streamline</p> <p>10 submitted data because of the way it comes in. There</p> <p>11 is opportunity for improved, more streamlined</p> <p>12 communications between FDA and sponsors.</p> <p>13 Our current environment doesn't support</p> <p>14 sharing content or efficient content submissions to</p> <p>15 multiple regulators. For instance, if you think about</p> <p>16 Project Orbis with the Oncology Centre of Excellence,</p> <p>17 we have limited support for sponsored regulator</p> <p>18 collaborations in exchange, for instance, information</p> <p>19 requests.</p> <p>20 So, looking at this, looking at this</p> <p>21 commitment, this agreement, you can see that there are</p> <p>22 multiple things that are listed here that address that.</p> <p>23 One is the resources to monitor and modernize the</p> <p>24 electronic submissions gateway and shift it to a cloud-</p> <p>25 based operation, to introduce the idea of these</p>	<p style="text-align: right;">Page 80</p> <p>1 gene therapies is increasing, and it's going to</p> <p>2 continue to increase and it's going to increase</p> <p>3 rapidly. And their IT environment right now is</p> <p>4 fragmented, it's not current, it's not modernized. And</p> <p>5 while it can take advantage, and absolutely are and</p> <p>6 will be taking advantage of all of these FDA</p> <p>7 modernization, there are biologics specific things that</p> <p>8 must -- that lift needs to be there. There are</p> <p>9 biologic-specific things that must be taken into</p> <p>10 account.</p> <p>11 The process, the trains need to keep running</p> <p>12 while this modernization takes place. And this</p> <p>13 commitment recognizes that and provides additional</p> <p>14 resources to support that data and technology</p> <p>15 modernization to lift it from -- give it the lift to</p> <p>16 get beyond the current stage of spending all of their</p> <p>17 time trying to maintain an old architecture to being</p> <p>18 able to use and...</p> <p>19 It also references and recognizes that there</p> <p>20 is a need for resources to develop additional expertise</p> <p>21 and capacity for CBER and CDER and contracting</p> <p>22 resources to support and manage the increase in the</p> <p>23 volume and the diversity of bio informations data and</p> <p>24 computation biology information that is coming in, and</p> <p>25 regulatory submissions. This commitment acknowledges</p>
<p style="text-align: right;">Page 79</p> <p>1 demonstration projects that would explore not just</p> <p>2 taking the standard operations and moving it to a</p> <p>3 cloud-based environment, but to promote innovation,</p> <p>4 what could be done, how could we modernize our</p> <p>5 regulatory review submissions activities, what could be</p> <p>6 done in terms of secure collaboration spaces.</p> <p>7 We also are looking at doing all of it to</p> <p>8 further the TMAP and the DMAP. And we're looking to do</p> <p>9 all of this through this first commitment, which is to</p> <p>10 further enhance transparent environment of our</p> <p>11 activities and our modernization plans, leveraging</p> <p>12 these regular meetings between FDA and industry, IT</p> <p>13 leadership, and providing and monitoring update plans</p> <p>14 and updates against those plans and discussing</p> <p>15 reflecting on where the plan might need to shift</p> <p>16 because something is changing over the, you know,</p> <p>17 externally, over the course of time. And to be doing</p> <p>18 the same on other PDUFA-relevant initiatives.</p> <p>19 Now, likewise, CBER is in a unique position.</p> <p>20 They need modernization of their critical IT. And this</p> <p>21 is not to imply that CBER stands alone and they'll have</p> <p>22 a parallel environment because that's not the case.</p> <p>23 But where they find themselves right now, as you heard</p> <p>24 earlier from Chris, in a situation where the volume and</p> <p>25 the complexity of biologic submissions, like cell and</p>	<p style="text-align: right;">Page 81</p> <p>1 that and supports that so that FDA can continue to do</p> <p>2 and to improve on the -- and I see that I'm coming in a</p> <p>3 little choppy. I don't know if it's my voice or if</p> <p>4 it's -- again, I apologize for that. I'm not sure what</p> <p>5 to do about it.</p> <p>6 MR. THOMPSON: You sound better now actually.</p> <p>7 MS. SLACK: Oh, you're coming in choppy too.</p> <p>8 It's probably my audio, I apologize.</p> <p>9 The benefits of all of this obviously are to</p> <p>10 enhance and improve our ability to operate for CBER, to</p> <p>11 enhance the support of complex biologics for FDA writ</p> <p>12 large and for the PDUFA program, its improved knowledge</p> <p>13 management, harmonizing with existing activities,</p> <p>14 improved data access and management and analytics. And</p> <p>15 I'll just stop right there and hand it back to Graham</p> <p>16 and Lucy and Cartier.</p> <p>17 MR. THOMPSON: Thank you so much. Lucy and</p> <p>18 Cartier, you're on.</p> <p>19 MS. ESHAM: So, thank you Mary Ann. And again</p> <p>20 -- oh, sorry I believe you're going first, Lucy. My</p> <p>21 bad. Go ahead, Lucy.</p> <p>22 MS. VERESHCHAGINA: No, that's fine. So as</p> <p>23 Mary Ann said, the technology and data modernization</p> <p>24 effort has been a priority for FDA over the past few</p> <p>25 years, and industry strongly supports these efforts.</p>

<p style="text-align: right;">Page 82</p> <p>1 And specifically Digital Health Technologies and its 2 increased use in regulatory decision-making being a 3 topic that generated a lot of attention and discussion 4 over the past couple of years. 5 So, industry, we as industry, we're very 6 excited about this efforts in PDUFA VII and about the 7 opportunities for FDA to work with all the stakeholders 8 on this issues, particularly on the public workshops, 9 on the use of Digital Health Technologies for 10 regulatory decision-making. 11 And I would like to stress that patient input 12 will be critical here to make sure that we're able to 13 successfully integrate the tools into drug development 14 and regulatory review processes. 15 Second, I would like to stress the importance 16 of regulatory consistency and coordination across FDA. 17 And PDUFA VII includes some provisions to make sure 18 that FDA is able to promote that consistency with 19 regards to DHT-based policy procedures, and analytical 20 tool development. 21 Also, I think that's another example where 22 industry and FDA will be able to leverage some of the 23 emerging COVID-19 lessons learned where appropriate, 24 and we'll see multiple examples, how Digital Health 25 Technology has been used during the pandemic by</p>	<p style="text-align: right;">Page 84</p> <p>1 And so, the data and technology, I'm just going to 2 underscore a few things, the data and technology 3 monetization strategy commitments that are in the 4 letter were done in a very thoughtful manner. And that 5 is to best ensure that the significant resources that 6 are required are able to be used in the most effective 7 way possible. 8 So as part of the commitments to achieve and 9 that go along with this publication, and implementation 10 of this modernization strategy, there are a number of 11 engagement and assessment processes that will ensure 12 that there's sort of an iterative approach as these 13 capacities continue to get built and implemented. 14 It includes some very specific commitments 15 such as completing transition of the ESG to the cloud. 16 It also allows for assessment of challenges to the 17 adoption of cloud-based technologies, but looking for 18 and identifying solutions to those challenges by 19 demonstration projects. 20 So again, I think when you read this in 21 detail, I hope that it is clearly reflected that this 22 was done in a very thoughtful manner. I'll also 23 underscore the import and agreement that that resources 24 were required to ensure that CBER had the data and IT 25 capacity that it needed. So again, the data and</p>
<p style="text-align: right;">Page 83</p> <p>1 necessity, right, specifically for remote data 2 collections, increased use of wearable technologies. 3 And we as industry think that these tools have a lot of 4 potential to build leverage beyond COVID, including, as 5 Mary Ann mentioned, for decentralized clinical trials. 6 I think those trials have a lot of potentials, 7 including for increasing diversity in patient 8 populations, participating in clinical trials. 9 And we believe that the digital health 10 technology tools have the potential to enhance 11 participation from communities that historically were 12 not able to benefit from clinical trials. Of course 13 FDA and industry needs to analyze those lessons we 14 learned and then translate this information on DHTs 15 used during pandemic into more durable learnings when 16 appropriate beyond the pandemic. I'll stop here, 17 Cartier. 18 MS. ESHAM: Thank you, Lucy. And again, thank 19 you, Mary Ann for a great presentation. And just to 20 underscore, there was a significant amount of work that 21 went into coming up with the sections of the commitment 22 letter, and they are extraordinarily important as we 23 think about how to best ensure the FDA has the capacity 24 and resources it needs to meet the growing demands of 25 regulatory review of complex and very large data sets.</p>	<p style="text-align: right;">Page 85</p> <p>1 technology modernization strategy, we are viewing that 2 as an enterprise-wide a CDER, CBER wide activity. But 3 CBER did require and needed some specific resources to 4 ensure that they are best able to meet the demands of 5 the data and IT needs to review biologics. 6 And lastly, we also provided some resources to 7 ensure -- to build, to create stronger capacity for 8 bioinformatics and computational biology needs. And 9 so, this will help support reviews and submissions 10 containing a variety of biologic data such as next- 11 generation sequencing. So again, we think this will 12 ensure that both the industry and the regulator are 13 aligned with the needs of modern drug development and 14 review processes. With that, I'll turn it back to 15 Graham. Thank you. 16 MR. THOMPSON: Okay. Thank you so much, 17 everyone. All right. We're going to move into our 18 last session before lunch, which is on finance. And 19 our presenter for this topic will be Josh Barton, and 20 you may start whenever you're ready. 21 22 Finance and Hiring Proposed Enhancements 23 24 MR. BARTON: All right. Graham, can you hear 25 me?</p>

<p style="text-align: right;">Page 86</p> <p>1 MR. THOMPSON: Yep, we can hear you loud and 2 clear.</p> <p>3 MR. BARTON: All right. Great. Thanks.</p> <p>4 Hi, good morning, everybody. Thanks to all 5 the attendees who were able to join us today. My name 6 is Josh Barton. I'm the Director of the Resource 7 Capacity Planning staff in CDER, and I led the 8 Financial Group for FDA.</p> <p>9 I'm going to speak first to the financial 10 topics in the agreement and then I will also speak to 11 the hiring topics. While the hiring topic was not 12 primarily under the remit of the financial group in the 13 PDUFA VII process, both areas are really foundational 14 to ensuring the continued success of the PDUFA program 15 and providing the resources and expertise needed to 16 implement the new PDUFA VII enhancements described by 17 my colleagues earlier today.</p> <p>18 If we go on the next slide, in PDUFA VII the 19 financial topics were focused on building the -- 20 financial building on the financial enhancements that 21 were implemented in PDUFA VI, to advance the 22 sustainability of the PDUFA program resources and to 23 enhance the operational agility of the PDUFA program. 24 Topics included resource capacity planning, financial 25 transparency, and some updating to the fee setting</p>	<p style="text-align: right;">Page 88</p> <p>1 decision-making processes. The specific commitments in 2 this area for capacity planning include publishing an 3 implementation plan in the first year of PDUFA VII, 4 which will outline our approach to the continual 5 improvement of the capacity planning adjustment, how it 6 will continue to mature the overall capacity planning, 7 resource capacity planning capability, and how it'll 8 integrate the resource capacity planning analytics in 9 the agency's resource and operational decision making 10 processes.</p> <p>11 This is similar to PDUFA VI commitments where 12 we published a implementation plan in the first year of 13 the PDUFA VI program. You can also find a lot of 14 background information on the agency's website on this 15 topic, including that original implementation plan.</p> <p>16 In addition, we'll provide annual updates on 17 progress to this implementation plan in years 2 through 18 5 of the agreement, and we'll also document how the 19 capacity planning adjustment funds are being utilized 20 in each year's annual financial report. There will 21 also be an independent third-party evaluation of the 22 resource capacity planning capability which will be 23 commissioned and published to the FDA's website in 24 2025.</p> <p>25 Next slide. The financial transparency</p>
<p style="text-align: right;">Page 87</p> <p>1 process.</p> <p>2 So, first speaking to resource capacity 3 planning. So resource capacity planning is a 4 capability designed to use data and analysis to help 5 inform resource needs for the PDUFA program. The 6 concept for this capability really grew out of the 7 PDUFA VI negotiations, which included commitment to 8 establish the resource capacity planning capability, to 9 modernize our time reporting approach and to establish 10 a new methodology to address review workload needs, 11 which is called the capacity planning adjustment.</p> <p>12 In PDUFA VI, we implemented these commitments, 13 including the time reporting about the foundational 14 RCP, Resource Capacity Planning capability, and 15 establish the new methodology for the capacity planning 16 adjustment. The PDUFA VII commitments are largely 17 focused on continuing to mature the Resource Capacity 18 Planning capability.</p> <p>19 As we collect more data on resource needs and 20 refined methodologies for forecasting review workload, 21 the resource capacity planning capability will continue 22 to mature.</p> <p>23 In addition, across PDUFA VII, we will also be 24 working to further integrate resource capacity planning 25 analytics and the agency's resource and operational</p>	<p style="text-align: right;">Page 89</p> <p>1 enhancements, these are primarily continuing 2 commitments that were established in PDUFA VI to 3 provide more transparency around our financial status 4 of the PDUFA program. So, this continues the 5 publishing of a 5-year financial plan each year as well 6 as a public meeting to discuss the plan and other 7 financial topics each year.</p> <p>8 There are some additional commitments to 9 public -- to address certain topics within that 5-year 10 financial plan. And these two here, they really speak 11 to the strategic hiring and retention adjustment, which 12 will actually address on the on the next slide. But in 13 terms of reporting requirements in the 5-year plan, 14 we'll report on personnel compensation and benefits 15 costs that exceed the funds provided by the PC&amp;B, 16 Personnel Costs and Benefits, portion of the inflation- 17 adjustment.</p> <p>18 As noted, this is related to the strategic 19 hiring retention adjustment. And we'll also speak to 20 the agency's plan for managing costs related to 21 personnel beyond PDUFA VII. Next slide, please.</p> <p>22 So, in terms of updates to the fee setting 23 process, the annual fee setting process which is 24 described in the Federal Register notice published at 25 the beginning of August each fiscal year. There are a</p>

<p style="text-align: right;">Page 90</p> <p>1 couple of -- a couple of updates or modifications to  2 the process. The -- in terms of the capacity planning  3 adjustment, which is that mechanism establishing PDUFA  4 VI to account for changes in review workload needs.  5       There are some modifications to clarify the  6 scope of the inputs used in the methodology. There's  7 also the establishment of a new strategic hiring and  8 retention adjustment to provide funding to cover costs  9 for retaining and hiring highly qualified scientific  10 and technical staff for the PDUFA program. And there  11 are also some updates to the operating reserve  12 adjustment process so that to help manage financial  13 risks of the program, by establishing a minimum, a  14 minimum amount of available operating reserves to be  15 maintained each year.  16       So, this minimum amount would start at an  17 amount equivalent to 8 weeks of operation in the first  18 year of the program in FY '23. And that would step up  19 to 10 weeks of operations by fiscal year 2025. Next  20 slide, please.  21       So those are the highlights of the financial  22 topics. And as mentioned, I'll also address the  23 hiring. Hiring is an area that is, you know, critical  24 to the continued success of the PDUFA program and the  25 ability to implement the enhancements discussed earlier</p>	<p style="text-align: right;">Page 92</p> <p>1 discussions of hiring and financials, just like in  2 previous cycles, because we really want to make sure  3 that all the great PDUFA VII initiatives that we  4 include in the goals, whether it's actually  5 implementable, and that FDA has supportive resources  6 and technical expertise in place to work on all these  7 provisions.  8       We also wanted to make sure that there is  9 great public transparency and accountability around  10 hiring and financials. And we want to make sure that  11 all the PDUFA VI financial reforms that were put in  12 place, continue to mature throughout PDUFA VII.  13       One of the examples that I would like to  14 highlight is enhanced reporting. Specifically,  15 issuance of the 5-year financial plan, and annual  16 updates that as Josh mentioned will be posted. And the  17 related annual public meeting.  18       Again, the opportunity for all stakeholders to  19 review the report and provide the input and feedback to  20 the agency and ensures there is transparency in place  21 on programmatic financial measures. And again, allows  22 for that public discussion of maturation of FDAs  23 resource planning capabilities. So, I'll stop here and  24 pass it to Cartier.  25       MS. ESHAM: Thanks, Lucy. Thanks, Josh.</p>
<p style="text-align: right;">Page 91</p> <p>1 today, as hiring is really critical to ensuring we have  2 the ability to hire and retain the necessary scientific  3 and technical expertise to deliver on the program. So  4 next slide.  5       In recognition of the criticality of the  6 hiring and retention, under PDUFA VII, FDA will  7 continue to report on hiring goals on the FDA website.  8 And there'll also be a targeted third-party assessment  9 of hiring and retention capabilities. This will be  10 conducted by an independent contractor with expertise  11 in HR operations and will be overseen by the directors  12 of CDER and CBER.  13       This assessment will build on findings of  14 previous evaluations conducted under PDUFA VI and will  15 focus on improvements and remaining challenges. The  16 assessment will be published in 2025. And will be  17 followed by a public meeting to discuss its findings  18 and the agency's plan to address any recommendations  19 coming out of that report.  20       So that's the finance and the hiring. And  21 with that, I can turn this back to Graham.  22       MR. THOMPSON: All right. Thank you so much,  23 Josh. Cartier and Lucy, you're up.  24       MS. VERESHCHAGINA: Thank you, Josh. I can  25 start. So in the standard update had whereabouts (ph)</p>	<p style="text-align: right;">Page 93</p> <p>1 Again, you know, this is really the core of the entire  2 PDUFA commitment mission, right. And if we're not able  3 to provide the FDA with the resources it needs, and if  4 the FDA is not able to onboard the resources it needs,  5 then we're really not doing our jobs. And so these  6 provisions are of critical importance both in ensuring  7 that capability and ensuring that there is  8 transparency, about how they're able to meet, how  9 they're able to meet these commitments.  10       So, the one thing I'll underscore as an  11 example of that is, one thing that was provided in the  12 commitment is the ability for the FDA to utilize an  13 independent contractor to do -- that has specific  14 expertise in assessing human resource operations so  15 that they can conduct a targeted assessment of the  16 hiring and retention of staff.  17       It is the hope that these kinds of assessments  18 provide important insights so that the agency is able  19 to continue to learn and potentially improve upon the  20 ability to recruit and retain the world class expert  21 personnel that it has today and what we need to -- what  22 we want to ensure that it has tomorrow. There will be  23 a public meeting so that those insights will be  24 available to the public. And we'll be able to hear  25 about what the FDA is doing to address any</p>



<p style="text-align: right;">Page 94</p> <p>1 recommendations that are part of that assessment.  2 So again, that's just an example of ensuring  3 that there is transparency, the ability to assess and  4 continue to learn, and hopefully continue to improve  5 the FDA's ability to again onboard world class  6 personnel that is of vital importance to ensuring  7 they're able to meet their critical mission of  8 protecting and promoting public health. So, with that,  9 I will turn back to Graham and thank you very much.  10 MR. THOMPSON: Okay. Thank you so much,  11 everyone. Our plan right now is to enter into lunch.  12 We are well ahead of schedule. I don't think we need  13 an hour and 15 minutes for lunch, but how about 15  14 minutes longer. So, we'll say a 45-minute break right  15 now for lunch, returning here at 12:15 p.m. And we  16 could send out a notification in the chat too, just to  17 let people know. And maybe we can even take the slides  18 down and edit that during this break, yeah. But 12:15  19 p.m. we'll see everybody back here. And thank you so  20 much.  21 (Recess)  22 MR. THOMPSON: And we'll be beginning in just  23 a minute.  24 MR. ABRAHAMS: Please, can someone confirm my  25 audio is okay?</p>	<p style="text-align: right;">Page 96</p> <p>1 agreed to participate.  2 Our four speakers today will be Michael  3 Abrahams, Cynthia Bens, Annie Kennedy and Ed Neilan.  4 So, I'm going to give a little extra time. I'll say  5 everyone has 10 minutes. And Michael, you are on deck  6 first, if we could advance and load his slides. So  7 Michael Abrahams is from Public Citizens Health  8 Research Group, and you may begin whenever you're  9 ready.  10  11 Public Stakeholder Perspectives  12  13 MR. ABRAHAMS: Good afternoon. I'm Michael  14 Abrahams, senior health researcher at Public Citizen  15 and I have no financial conflicts.  16 Next slide, please. We have many suggestions  17 to improve the draft PDUFA commitment letter.  18 Beginning with performance measures used to set goals  19 for that program. The currently proposed measures we  20 believe our simplistic timeline code is focused on  21 pleasing the regulated industries desire for reviews.  22 For example, at the top of the slide, I give one of  23 those types of measures.  24 It is the percentage of new applications that  25 are acted upon within a certain amount of time, in this</p>
<p style="text-align: right;">Page 95</p> <p>1 MR. THOMPSON: I can hear you.  2 MR. ABRAHAMS: Thanks. Yes, I can. My video  3 as well?  4 MR. THOMPSON: And for those who aren't  5 speaking yet, if you don't mind being on mute. Thank  6 you. I think we can go ahead and get started. Welcome  7 back. Everyone have a nice lunch. We are going to  8 move into our afternoon. And as we do so, I'd like to  9 remind folks that if you missed the other part, the  10 purpose of the meeting here is to gather input from the  11 public on the proposed recommendations for the  12 authorization of the Prescription Drug User Fee Act or  13 PDUFA program.  14 If you'd like to contribute further input on  15 this process, we've opened a public docket for those  16 who wish to submit written comments. And for those who  17 missed part of the early meeting, we will post the  18 slides, a recording of the meeting and the transcript  19 to our meeting website in the near future after the  20 meeting.  21 Okay. So, we're going to move into our next  22 session, which is to hear some perspectives from some  23 public stakeholders. So we invited public stakeholders  24 who are consistently active and engaged throughout our  25 public stakeholder engagement process. And these four</p>	<p style="text-align: right;">Page 97</p> <p>1 case, 10 months. Instead of those sorts of measures,  2 or in addition to those sorts of measures for  3 performance, we think the FDA should develop and  4 proffer in this commitment letter short and long term  5 public health impact goals and measures. Things that  6 give us information about how the FDA's decisions  7 impact, you know, human health. And I offer on this  8 slide at the bottom of the slide five examples of such  9 of these measures. Let me just briefly highlight the  10 first three.  11 We'd like to see these measures say something  12 each year about how many applications are rejected in a  13 way that allows the Agency to demonstrate to Congress  14 and the public how good they did at playing defense for  15 the American public for bad prescription drugs, and  16 biologics. The second item on this slide at the  17 bottom, we think that there should be tallies regarding  18 warnings and withdrawals that result from approvals.  19 That gives us a sense of where the FDA may have made  20 some mistakes or missteps, when they approved  21 medications.  22 And then finally the third item on this slide,  23 a suggestion that the FDA regular report how often it  24 uses gold standard evidence, randomized control trials,  25 well-designed phase III trials as opposed to less</p>

<p style="text-align: right;">Page 98</p> <p>1 robust types of evidence which have become all too 2 common in the regulatory process.</p> <p>3       Next slide, please. Related to FDA reviewer 4 and advisory committee activities, we recommend that 5 the Agency develop performance measures based on 6 surveys of FDA reviewers and advisory committee 7 members, and I've made this suggestion before. And 8 these would be looking at the experience that these 9 reviewers have reviewing NDA/BLA applications. Past 10 surveys have been too infrequent and have had 11 concerning results.</p> <p>12       Just one example, in 2003 an HHS Office of 13 Inspector General report found that among surveyed CDER 14 reviewers, only 64 percent were confident in FDA 15 decisions regarding the safety of a drug. Now, we 16 think and feel strongly that candid FDA staff and 17 advisory committee member perspectives on the adequacy 18 of the Agency's review and decision-making processes 19 are certainly germane to the performance of the 20 program. And that should be measured and presented to 21 the public and to Congress on a regular basis.</p> <p>22       The kinds of measures that we're suggesting 23 are at the bottom of this slide, and I'm just going to 24 highlight the second one. It would be useful for the 25 public to see the percent of reviewers at the end of</p>	<p style="text-align: right;">Page 100</p> <p>1 application, and the data in it is ultimately the 2 responsibility of the sponsor, not the FDA. The FDA is 3 a watchdog for the American people.</p> <p>4       Next slide, please. There are several places 5 in the commitment letter were, "expediting drug 6 development," is the clear goal, including under 7 Section K of the letter, and I'm reading a quote from 8 that section, it's on the slide here. "Enhancing -- 9 ensuring the sustained success of the breakthrough 10 therapy program is one of the goals. Use of new 11 surrogate endpoints as a primary basis for product 12 approval, and exploring real-world evidence for 13 decision-making."</p> <p>14       Okay. Such goals, we believe should be 15 revised by adding statements, such as the fine. There 16 should be limits to surrogate endpoint use to those 17 that have been scientifically validated and deemed by 18 the majority of the medical community to be predictive 19 of clinically meaningful outcomes. It should be 20 explicitly stated. It should further -- that is the 21 letter should further caution that things like real- 22 world evidence and other shortcuts to approval must not 23 supplant well-designed randomized trials.</p> <p>24       The need for these cautions and standards is 25 supported by research which shows that as of 2018, 81</p>
<p style="text-align: right;">Page 99</p> <p>1 the year who felt they were free from direct or 2 indirect pressures from the regulated industry when 3 they were reviewing applications.</p> <p>4       Next slide, please. More generally, 5 commitment letter language should be recast, revised, 6 right, to emphasize the FDA's regulatory role, and 7 responsibilities -- its regulatory role and 8 responsibility. Presently, for example, it has 9 prominent language in the commitment letter like this, 10 and I'm quoting from the middle of this slide. And 11 this is a quote from the commitment letter. "The goal 12 of the program is to promote the efficiency and 13 effectiveness of first cycle review process and 14 minimize the number of review cycles necessary for 15 approval, et cetera."</p> <p>16       And we believe such language should be 17 modified by adding that a primary program goal in 18 addition to what's been stated, a primary program goal 19 is to protect public health by minimizing the 20 probability that unsafe or ineffective drugs or 21 biologics into the market. It should be stated more 22 over, the commitment letter should state that although 23 the Agency offers technical assistance to sponsors in 24 the preparation of their applications, important 25 function that it serves, ensuring the quality of the</p>	<p style="text-align: right;">Page 101</p> <p>1 percent of NDA approvals, evolved, accelerated fast 2 track priority review pathways, not traditional 3 pathways. And the faster approvals under PDUFA, other 4 research has shown have correlated -- these faster 5 approvals have correlated with the marketing of 6 products that were less safe than those marketed before 7 PDUFA was instituted.</p> <p>8       Next slide, please. The draft commitment 9 letter states the following. This is a quote right at 10 the top of the slide, "FDA's philosophy is that timely 11 interactive communication with sponsors during drug 12 development is a core Agency activity to help achieve 13 the Agency's mission, et cetera."</p> <p>14       Okay. The FDA's review and approval of the 15 BLA for Aducanumab for the treatment of Alzheimer's 16 disease revealed, and we think it's the tip of the 17 iceberg, that such interactive communications 18 established under PDUFA have resulted in 19 inappropriately close collaborations between Agency and 20 sponsors that have compromised the integrity of NDA/BLA 21 reviews.</p> <p>22       To address this problem, the commitment letter 23 should be modified to include provisions that do the 24 following listed at the bottom of the slides, very 25 specific recommendations. Characterize the FDA's</p>

<p style="text-align: right;">Page 102</p> <p>1 primary role as being the gatekeeper, the watchdog and 2 the judge of industry products. Not a partner, 3 certainly not a financial partner. 4 This is to -- for the industry is an 5 opportunity for FDA to reassert and to codify its 6 objectivity and independence, so important we believe 7 to the regulatory process. This letter should also 8 establish procedures that separates staff involved in 9 the pre-application submission interactions with 10 sponsors from the staff that formally reviews and 11 scores it. 12 And finally, the letter should require the FDA 13 to establish staff training on how to minimize the 14 risks of regulatory capture of agency sponsors. 15 And my last slide, please, slide number 7. 16 Finally, here are several more actions the Agency 17 should pursue as part of the PDUFA reauthorization 18 process. I don't have time to go through all of them. 19 I've gone through several of them in our stakeholder 20 discussion meeting. I asked that staff take a careful 21 look at them once again, but let me just highlight two 22 for this audience currently, the second point on this 23 slide. 24 The PDUFA reauthorization process should be 25 used to -- or the commitment letter should be used to</p>	<p style="text-align: right;">Page 104</p> <p>1 the FDA for the opportunity to share some insights on 2 the importance of the Prescription Drug User Fee 3 program, and also to reflect on the PDUFA VII goals 4 letter. As Graham mentioned, I'm Cynthia Bens, and I 5 serve as senior vice president of public policy at the 6 Personalized Medicine Coalition or PMC. 7 For those who aren't familiar with this, PMC 8 is a nonprofit education and advocacy organization that 9 has more than 220 members from top sectors of health 10 care, who are working together to advance personalized 11 medicine in ways that benefit patients with cancer or 12 diseases, some common chronic diseases and infectious 13 diseases. 14 As you heard throughout the morning, the PDUFA 15 program is really critical. And it's a source of 16 funding that provides to ensure the timeliness of drug 17 reviews, also to encourage innovation and drug 18 development and promote initiatives at the FDA that 19 leverages the best science. We believe that having a 20 well-resourced, focused and flexible FDA is essential 21 to achieving our mission at our organization of 22 bringing forward the best treatments for each patient, 23 and ensuring they're delivered based on a person's 24 biology, medical history, circumstances and values. 25 PMC's analyses have shown that personalized</p>
<p style="text-align: right;">Page 103</p> <p>1 revise the reauthorization negotiation process to make 2 the meetings between industry and the FDA fully open to 3 the public. There seems to me and to many of us who 4 have been at the table on the stakeholder side, there's 5 no need for secret meetings separately between industry 6 and the FDA to hash out this letter. 7 And skipping down into item number 5 on this 8 slide, we think the commitment letter should create 9 opportunities for the FDA to commission third-party 10 objective studies that quantify the avoided or realized 11 harm resulting from NDA/BLA approval decisions. This 12 seems to us to be a critical public health reporting 13 responsibility of the FDA. And it takes us full circle 14 back to the beginning of my presentation where I've 15 recommended some additional performance measures in 16 that regard. 17 We encourage the FDA to use this presentation 18 to substantially revise their commitment letter. My 19 last slide has my contact information to facilitate 20 that. Thank you very much. 21 MR. THOMPSON: Okay. Thank you very much, 22 Michael. Next up, we have Cynthia Bens from the 23 Personalized Medicine Coalition. If we can advance the 24 slide. Cynthia, you're all set and if you're ready. 25 MS. BENS: Great. Good afternoon. Thanks to</p>	<p style="text-align: right;">Page 105</p> <p>1 medicines account for more than 20 percent of FDA's new 2 drug approvals each year. That number steadily 3 increased from 5 percent when we started looking at 4 approval trends 16 years ago. Initiatives advanced by 5 the FDA in recent years have fostered many notable 6 regulatory firsts, including the approval of the first 7 cell and gene therapies and a one therapies and tissue 8 agnostic therapies. 9 We believe that enhancements included in the 10 PDUFA VII goals letter will advance the future of 11 personalized medicine, and will continue to yield 12 benefits for a wide range of patients, including those 13 with unmet medical needs. It's really difficult to 14 summarize all the ways why PDUFA VII is going to make a 15 meaningful change for the field of personalized 16 medicine in less than 10 minutes. So, I'm going to 17 focus on three main areas that we're pleased to see in 18 the PDUFA VII goals letter. 19 These include staffing to support cell and 20 gene therapy review, additional considerations for 21 advancing the regulatory use of real-world evidence and 22 real world data, and the use of digital health tools 23 for regulatory decision-making and support of 24 personalized medicine. 25 In comments provided at the beginning of the</p>

<p style="text-align: right;">Page 106</p> <p>1 PDUFA VII process, we highlighted that FDA needed  2 additional resources to fulfill the Agency's mission to  3 protect and promote public health, while meeting the  4 challenges posed by the increasingly complex regulatory  5 landscape. This need is particularly pronounced in the  6 area of cell and gene-based therapy review. Cell and  7 gene therapies have the potential to yield  8 unprecedented improvements in clinical outcomes for  9 some disease areas. And they continue to be an  10 important area for personalized medicine.  11 Just up until this point, 22 cell and gene  12 therapies have already been approved by the FDA. And  13 FDA anticipates that by 2025 it will be reviewing  14 between 10 and 20 cell and gene therapies applications  15 each year. We've been particularly concerned with the  16 size of the workload facing FDA as a result of the need  17 to evaluate the increasing number of new cell and gene  18 therapy products.  19 PDUFA VII will allow the addition of  20 significant numbers of FTEs across the FDA divisions by  21 2027. And it's reassuring to us that PDUFA VII  22 resources will be devoted to addressing staffing gaps  23 and building capabilities necessary to support the  24 clinical assessment and evaluation of manufacturing  25 processes for cell and gene therapies.</p>	<p style="text-align: right;">Page 108</p> <p>1 contributions in advancing all of our understanding of  2 which patients will benefit the most from treatments.  3 And this trend wasn't slowed down by the COVID-19  4 pandemic.  5 Out of necessity, nontraditional approaches to  6 data-gathering and clinical studies were required to  7 facilitate patient participation. Analysis also needed  8 to be conducted on real-world data sources to more  9 quickly understand treatment patterns for hospitalized  10 COVID patients.  11 With the exception of the pilot, which begins  12 early in the PDUFA VII cycle, the remaining commitments  13 fall near the end, and we'd encourage FDA to accelerate  14 their timeline for RWE and RWD commitments as it's  15 feasible. It's promising that participation in the  16 pilots contingent upon a willingness to publicly  17 disclose elements of an RWE pilot submission.  18 Depending on the level of disclosure, this type of  19 transparency will allow stakeholders to more  20 efficiently leverage real-world datasets.  21 But just given the limitations on the size of  22 the pilot, and uncertainty about how much information  23 ultimately will be disclosed, we'd also encourage FDA  24 to provide additional venues for researchers, health  25 data organizations, and other non-industry stakeholders</p>
<p style="text-align: right;">Page 107</p> <p>1 PMC appreciates that in addition to expanding  2 FDA's workforce that attention has been paid in PDUFA  3 VII to furthering the development of appropriate  4 regulatory frameworks for assessing the safety and  5 effectiveness of these life-changing therapies. We at  6 PMC also believe that data collected about an  7 individual's lifestyle, their biology and treatment  8 outcomes can be harnessed to complement traditional  9 clinical trials and can help transform the future of  10 personalized medicine.  11 In prior comments, PMC supported additional  12 staffing, resources and guidance development under  13 PDUFA VII to allow the Agency to make further  14 transformations and we use an acceptance of RWEE beyond  15 early phase trials and for purposes beyond  16 demonstrating product safety. We are encouraged that  17 PDUFA VII includes several RWE commitments, such as the  18 proposed pilot program facilitating earlier advice on  19 the quality and acceptability of RWE and supportive new  20 labeling claims, a public workshop on RWE and updates  21 to RWE guidance.  22 We want the Agency to move forward in a  23 science-focused manner. But we also recognize that FDA  24 is thinking on the use of RWE and RWD has been evolving  25 for some time. RWE and RWD can make significant</p>	<p style="text-align: right;">Page 109</p> <p>1 to interact with the Agency on RWE and RWD issues.  2 Finally, PMC called on the FDA at the start of  3 PDUFA VII to take steps that would accelerate the  4 acceptance of digital health technologies and protocols  5 for decentralized trials. Advances in sensing  6 technologies and self-management platforms have become  7 important tools for personalized medicine.  8 And in fact, a growing number of ongoing  9 clinical trials feature the use of wearables  10 environmental sensors to include more diverse  11 populations, patients in difficult geographic regions  12 and patients who cannot travel due to the ongoing  13 pandemic.  14 We applaud the inclusion of several PDUFA VII  15 commitments in establishing a framework for promoting  16 regulatory consistency across the FDA on DHTs,  17 increasing FDA's capacity in this area, and for hosting  18 a workshop on the use of DHTs for regulatory decision-  19 making leaving to DHT guidances. We believe that DHTs  20 can enhance trial efficiency, parallel to the delivery  21 of real-world care, and may even provide personalized  22 insights at the point of care.  23 I'll close by saying that we know that much of  24 what we highlight is potential areas for improvements  25 at FDA with respect to RWE, RWD and DHTs won't be</p>

Page 110

1 possible without continued modernization of FDA's IT  
 2 infrastructure.

3 So, PMC supports the inclusion of PDUFA VII  
 4 resources to increase the Agency's capacity to accept  
 5 and review large datasets as existing needs dictate and  
 6 also as new opportunities emerge.

7 So, thanks again to all of you for your time  
 8 and for FDA for letting me participate. My PMC  
 9 colleagues and I look forward to working with Congress  
 10 as the PDUFA reauthorization process moves to the  
 11 legislative phase. Thank you.

12 MR. THOMPSON: Thank you so much, Cynthia.  
 13 Next up, we have Annie Kennedy, and, you know, your  
 14 slides are loaded. All right. You can start whenever  
 15 you're ready.

16 MS. KENNEDY: Super, thank you. Thank you for  
 17 inviting me to present today on behalf of the EveryLife  
 18 Foundation for Rare Diseases and our broader rare  
 19 disease community. I'm Annie Kennedy and I serve as  
 20 the chief of policy and advocacy for the EveryLife  
 21 Foundation for Rare Diseases.

22 We are a rare disease policy organization that  
 23 believes that no disease is too rare to deserve a  
 24 treatment and rare disease therapies should be safe and  
 25 effective. To that end, we convene a robust coalition

Page 111

1 comprised of patient advocacy organizations,  
 2 biopharmaceutical partners, coalition groups and other  
 3 relevant stakeholders with shared interests in policy  
 4 focused on rare therapy development and regulatory  
 5 infrastructure. These remarks are a reflection of the  
 6 engagements of this coalition over the past few years.

7 I'd like to start today with a tremendous  
 8 thank you. Thank you to the leadership and the  
 9 personnel here at the FDA and those within our  
 10 therapeutic development ecosystem. I think while the  
 11 term unprecedented has probably been overused over the  
 12 last 18 months, I'm not sure what other term we could  
 13 use that would be appropriate for this forum here today  
 14 to capture the climate of the forced evolution in which  
 15 we've all worked and lived.

16 And we'd be remiss to not acknowledge the  
 17 leadership and tireless work conducted by this Agency  
 18 to protect our nation and our loved ones throughout the  
 19 many phases of the pandemic. We are also grateful that  
 20 while your capacity has been stretched to attend to the  
 21 global pandemic, you also understood that the urgency  
 22 of rare disease was not waning, but wasn't in fact,  
 23 instead further exacerbated by the pandemic, and  
 24 urgency that's being felt by the more than 30 million  
 25 Americans living with rare diseases, a disproportionate

Page 112

1 percentage of whom estimated to be more than 50 percent  
 2 of whom are children.

3 And as most here are well aware 95 percent of  
 4 more than 7,000 rare diseases have no FDA-approved  
 5 therapy. Yet the technologies and methodologies  
 6 deployed during the pandemic by stakeholders here today  
 7 that resulted from COVID-19 underscore the  
 8 opportunities for innovations that have been long  
 9 championed by our rare disease community stakeholders,  
 10 and further reflected the core themes within the PDUFA  
 11 agreements of scientific rigor, transparency, and  
 12 stakeholder engagement.

13 So, from pivoting and deploying new  
 14 innovations to protect our public's health throughout  
 15 our COVID-19 pandemic, we thank you. But we also thank  
 16 you for not taking our foot off the accelerator. Thank  
 17 you for understanding that rare disease is also a  
 18 public health crisis deserving of continued urgent  
 19 attention. And that continued commitment to  
 20 understanding is clearly evident in the PDUFA VII  
 21 enhancements we're discussing here today.

22 So, I'd like to start with a bit of a broader  
 23 focus and take a moment to reflect on the last 10  
 24 years. We as communities and collaborative  
 25 stakeholders have experienced a tremendous evolution of

Page 113

1 patient engagement and related areas since their  
 2 infancy in PDUFA V to their continued development via  
 3 21st Century Cures and PDUFA VI and now their continued  
 4 maturation today.

5 And this time, the landscape has shifted for  
 6 our rare disease community. We've seen a deepened  
 7 engagement and understanding of the patient perspective  
 8 via numerous approaches such as the patient-focused  
 9 drug development meetings, both FDA-led and externally  
 10 led, of the more than 70 PFDD meetings convened to  
 11 date, at least half have focused on rare diseases.

12 We've had opportunities for meaningful  
 13 participation in formal service on advisory committees,  
 14 the formation and patient engagement advisory committee  
 15 at CDRH reporting on the use of patient engagement  
 16 information and reviews of approved products. We've  
 17 benefited from the implementation of the patient  
 18 experience data table in November of 2017 and further  
 19 expanded in 2019, which enabled a new level of  
 20 transparency and engagement between review division and  
 21 relevant stakeholders around the integration of patient  
 22 experience data within regulatory review.

23 And CDER issued -- the CDER issued a series of  
 24 guidance documents for conducting patient-focused drug  
 25 development have been critical tools in providing

<p style="text-align: right;">Page 114</p> <p>1 stakeholders with practices for collecting 2 comprehensive representative input methods to identify 3 what's important to patients, selecting developing and 4 modifying fit for purpose clinical outcome assessment, 5 and incorporating clinical outcome assessments into 6 endpoints for regulatory decision-making. 7       And the numerous other guidances that are 8 informing patient engagement and patient-focused drug 9 development activities for drugs, cell and gene-based 10 therapies, diagnostics and medical devices have been 11 critical and have transformed our landscape. But most 12 importantly are the lives changed and saved through 13 products approved to treat rare conditions, especially 14 those that have benefited from the inclusion of more 15 robust patient insights and patient experience data is 16 a part of the reviewing process. 17       And it's important to note that these 18 approvals have not come because FDA has lower the 19 evidentiary bar for rare disease products. Rather, 20 they came because FDA and Congress have recognized the 21 need for a nuanced approach to review of such products, 22 given the unique nature of rare diseases, including 23 patient populations, trial sizes and other critical 24 data points and by instituting a structured approach to 25 listen to the voice of the patient in a meaningful way.</p>	<p style="text-align: right;">Page 116</p> <p>1       We are very pleased to see the priorities 2 we've articulated throughout this process reflected in 3 these commitments. We would also encourage that as we 4 work towards further refinement of these commitments, 5 we think about how we can incentivize and allow for 6 collaboration between sponsors, the Agency and patient 7 organizations on these critical concepts within the 8 pre-competitive space, and not just when connected to a 9 specific IND. 10       To a degree possible, we'd like to see FDA 11 commit even more to advance rare disease policy, 12 including by going above and beyond the commitments set 13 in the letter, such as by exceeding stated deadlines. 14 As an example, during PDUFA V, the FDA convened more 15 PFDD meetings than what was put forward in the 16 agreement, helping to significantly advance our field. 17 The same type of commitment to do more is needed to 18 today. 19       So, in conclusion, the EveryLife Foundation 20 and our rare disease community are encouraged by the 21 provisions within the PDUFA VII commitment letter. We 22 are so grateful to all the community members who've 23 worked so hard to ensure that the needs, priorities, 24 opportunities and urgency of our community is so 25 strongly reflected in these considerations.</p>
<p style="text-align: right;">Page 115</p> <p>1 The FDA has demonstrated its commitment to science and 2 to ensuring appropriate processes are in place to 3 quantify the perspective of the patient and the 4 caregiver. 5       The EveryLife Foundation is very pleased to 6 see the FDA's commitment to advancing the field of 7 patient engagement clearly evident in the PDUFA VII 8 commitment letter released last month. 9       The rare disease endpoint advancement pilot, 10 the STAR pilot, advancing patient-focused drug 11 development within CBER and refining and advancing 12 policies to support use of real-world evidence and 13 innovative trial designs are all just examples of the 14 commitments agreed to by FDA and industry that over the 15 performance period will further support patient 16 engagement in patients with rare conditions. 17       Given the promise and anticipation in 18 innovative development and rare disease, we are 19 particularly gratified to see the expanded emphasis on 20 enhancing critical innovation areas through resources, 21 public workshops, pilots and guidances to address 22 emerging issues such as real-world evidence, Bayesian 23 modeling and enhanced engagement formats such as the 24 proposed proposals for Interact (ph), MIDD and the new 25 type D meeting models.</p>	<p style="text-align: right;">Page 117</p> <p>1       And our collective community organization 2 partners are eager to continue to lean in and work with 3 the agencies, sponsors, patient communities and 4 Congress to ensure that communities' patient experience 5 continues to inform considerations and decision-making 6 all throughout the product development lifecycle. 7       Thank you for your tireless work on behalf of 8 our rare disease community, and for your commitment to 9 ensuring that the promise of today's pipelines will 10 change the health outcomes for this generation of 11 patients. Thank you. 12       MR. THOMPSON: Thank you very much, Annie. 13 Finally, we have Ed Neilan from the National 14 Organization for Rare Diseases (ph). If we can advance 15 the slide. All right. Ed, if you're there ready, you 16 can begin whenever you like. 17       MR. NEILAN: I was just trying to turn on the 18 video. I don't know if you -- 19       MR. THOMPSON: Well, we can hear you. 20       MR. NEILAN: -- (Cross talk). 21       MR. THOMPSON: We can hear you and you click 22 the video button in the bottom left. 23       MR. NEILAN: I've clicked it a couple times. 24 It says the host has stopped it. All right. Well, oh, 25 there you go. There's a button for it. Thank you very</p>

<p style="text-align: right;">Page 118</p> <p>1 much. Yeah, thanks.</p> <p>2 Hello, I'm Dr. Edwin Neilan. I'm a</p> <p>3 pediatrician and a medical geneticist and the chief</p> <p>4 medical and scientific officer at NORD, the National</p> <p>5 Organization for Rare Disorders. Prior to joining NORD</p> <p>6 4 months ago, I served on the faculties of Boston</p> <p>7 Children's Hospital and Harvard Medical School for 13</p> <p>8 years and worked at Sanofi Genzyme for 4-1/2 years.</p> <p>9 Collectively, I've worked on a dozen rare</p> <p>10 disease clinical trials which have led to six FDA new</p> <p>11 drug approvals. My professional focus is the care and</p> <p>12 treatment of patients with rare diseases. So, I'm</p> <p>13 delighted to represent NORD now, and to share here our</p> <p>14 views on proposed recommendations for PDUFA VII.</p> <p>15 Next slide, please. Founded in 1983, NORD</p> <p>16 represents over 320 different rare disease patient</p> <p>17 organizations, and the over 30 million Americans who</p> <p>18 are struggling with rare diseases. We are committed to</p> <p>19 identifying, treating and curing rare diseases through</p> <p>20 programs of education, advocacy, research and patient</p> <p>21 services. This in support of and on behalf of our</p> <p>22 member organizations in the broader rare disease</p> <p>23 community that I speak to you today.</p> <p>24 NORD was pleased to accept FDA's invitation to</p> <p>25 present at the prior July 23 meeting when Rachel Sher,</p>	<p style="text-align: right;">Page 120</p> <p>1 Institute and NORD, the RDCA data analytics platform or</p> <p>2 RDCA DAP is an FDA-funded project that will create a</p> <p>3 widely available data resource through which</p> <p>4 researchers, Android developers can access and analyze</p> <p>5 the identified patient level data on rare diseases and</p> <p>6 how they progress leading to new insights about those</p> <p>7 diseases.</p> <p>8 Thus the work of the RDCA DAP can help foster</p> <p>9 the success of the PDUFA VII proposed RDEA pilot</p> <p>10 program by providing potential drug development</p> <p>11 sponsors even prior to the start of their own clinical</p> <p>12 studies with access to otherwise very hard to find</p> <p>13 patient level rare disease data, and associated</p> <p>14 statistical analysis tools that will allow sponsors to</p> <p>15 develop better proposals for the design and endpoints</p> <p>16 of their rare disease clinical trials for discussion</p> <p>17 with FDA during the pilot RDEA consultation process.</p> <p>18 Next slide please. Another high priority in</p> <p>19 PDUFA VII is ensuring that CBER's results match the</p> <p>20 demands being placed on it. As we heard earlier cell</p> <p>21 and gene therapies hold great promise for the more than</p> <p>22 7,000 rare genetic diseases. In recent years, there</p> <p>23 has been a dramatic increase in the number of gene</p> <p>24 therapy INDs.</p> <p>25 Since 2018, CBER has been receiving more than</p>
<p style="text-align: right;">Page 119</p> <p>1 NORD's vice president for policy, described our</p> <p>2 priorities for PDUFA VII. Since then NORD has</p> <p>3 participated in the stakeholder meetings and</p> <p>4 appreciates FDA's efforts to keep the stakeholder</p> <p>5 community apprised of the negotiations. I'm pleased to</p> <p>6 say that NORD's priorities are well reflected in the</p> <p>7 draft commitment letter. We are grateful to FDA and</p> <p>8 industry partners for your commitment to the needs of</p> <p>9 rare disease patients.</p> <p>10 Let me describe a few of these priorities in</p> <p>11 more detail. Next slide, please. NORD was thrilled to</p> <p>12 see the inclusion of the proposed Rare Disease Endpoint</p> <p>13 Accelerator or RDEA Pilot Program in the goals letter.</p> <p>14 Establishing appropriate efficacy endpoints in rare</p> <p>15 diseases is often challenging because of a lack of</p> <p>16 regulatory precedent, small trial populations and</p> <p>17 limited understanding of disease natural history.</p> <p>18 The RDEA pilot will provide sponsors with an</p> <p>19 invaluable opportunity to work closely with FDA at an</p> <p>20 early stage to overcome these challenges. Of note, the</p> <p>21 work that NORD has been doing as part of the ongoing</p> <p>22 Rare Disease Cures Accelerator, or RDCA, is in line</p> <p>23 with the goals of the pilot RDEA program and could help</p> <p>24 facilitate its ultimate success.</p> <p>25 Led collaboratively by the Critical Path</p>	<p style="text-align: right;">Page 121</p> <p>1 200 INDs for cell and gene therapies each year. This</p> <p>2 is good news for rare disease patients. But to realize</p> <p>3 the promise of gene therapies, it is critical that FDA</p> <p>4 keeps up both in regulatory science and in its reviews</p> <p>5 of associated applications. On top of that marked</p> <p>6 increase in gene therapy INDs, CBER has now also</p> <p>7 experienced a massive further increase in INDs, many</p> <p>8 related to COVID-19.</p> <p>9 At the end of 2019, CBER had over 900 active</p> <p>10 INDs. Then during 2020, CBER received 6,954 INDs.</p> <p>11 Under the proposed PDUFA VII agreement, CBER would</p> <p>12 receive 123 new FTEs. This further increase in</p> <p>13 staffing is essential. It will allow CBER to spend</p> <p>14 additional time on meetings with sponsors and on the</p> <p>15 review of submissions. But it will also permit FDA</p> <p>16 staff to engage in other equally important work like</p> <p>17 policy and guidance development.</p> <p>18 In addition, as noted earlier, CBER's IT needs</p> <p>19 are also a concern. So NORD is encouraged that</p> <p>20 modernization of CBER's IT systems is also a goal in</p> <p>21 this PDUFA cycle.</p> <p>22 Next slide, please. NORD is grateful to see</p> <p>23 that another one of our rare disease priorities is</p> <p>24 strongly reflected in the PDUFA VII goals letter that</p> <p>25 is better incorporating the patient voice into the drug</p>

<p style="text-align: right;">Page 122</p> <p>1 development and regulatory review processes. NORD                  2 knows the value of FDA's patient engagement efforts                  3 having worked with FDA on multiple listening sessions                  4 and patient-focused drug development meetings.                  5 Critical to the goals of patient-focused drug                  6 development is improving the availability of                  7 appropriate clinical outcome assessments or COAs. The                  8 goals letter describes FDA's continued commitment to                  9 developing a virtual catalogue of standard core sets of                  10 COAs, which NORD very much supports. This work is in                  11 line with both the project that NORD is engaged with,                  12 with C-Path to launch a broad new Rare Disease Clinical                  13 Outcomes Assessment Consortium, as well as other --                  14 excuse me, as well as another FDA-funded project that                  15 NORD is engaged in with Northwestern University's                  16 clinical outcome assessment team or NUCOAT, which will                  17 develop and validate COAs with applicability across a                  18 range of both chronic and rare conditions by assessing                  19 physical function using both patient-reported and                  20 performance measurement outcomes.                  21 Next slide, please. Finally, NORD also                  22 supports PDUFA VII's goal of ensuring that valuable                  23 drug development lessons and innovations learned during                  24 the COVID-19 pandemic are maintained. Given the                  25 scarcity of rare disease specialists, patients with</p>	<p style="text-align: right;">Page 124</p> <p>1 Keep in mind, we won't be responding live to                  2 comments, but they will be transcribed and be part of a                  3 public record, and a broken record on this. But please                  4 do submit any comments you have to the public docket,                  5 we do appreciate having them and -- yeah. So, to                  6 facilitate a transparent process, we do encourage                  7 speakers here to note any financial interests that you                  8 have that are related to your comment. If you do not                  9 have such interests, you may state that for a record.                  10 If you prefer not to provide this information, you can                  11 still provide your comments regardless.                  12 So, we collected online requests for comment                  13 as part of the meeting registration process, and we                  14 have eight people signed up. Each speaker will have 5                  15 minutes to speak. And as I stated previously, I'll                  16 verbally announce if there's -- if you're approaching                  17 your time, and then shortly again if you go over time.                  18 So, the speakers -- if we can go to the next                  19 slide, the speakers will be in this order starting on                  20 the top left going down. So, we will begin with Robert                  21 Falb, if you are here.                  22                  23 Public Comments                  24                  25 MR. FALB: Hi, good afternoon. My name is</p>
<p style="text-align: right;">Page 123</p> <p>1 rare diseases are often forced to take time off from                  2 work and to travel great distances to see their                  3 providers and participate in clinical trials.                  4 During the COVID-19 pandemic, the use of                  5 remote monitoring digital health tools and other                  6 technologies that produce real-world data has enabled                  7 increased utilization of fully or partially                  8 decentralized clinical trials. These advances should                  9 become permanent fixtures in drug development, and NORD                  10 applauds FDA for taking steps to do just that. The                  11 commitments set forth in the goals letter around                  12 advancing RWE program and the digital health technology                  13 framework will be essential to achieving these goals.                  14 Next slide, please. So thank you very much                  15 for this opportunity to share NORD's views on PDUFA VII                  16 proposals. NORD stands ready to continue our                  17 engagement on behalf of the rare disease community in                  18 the process of reauthorization as PDUFA VII moves to                  19 Congress. Thank you very much.                  20 MR. THOMPSON: All right. Thank you very                  21 much, Ed. I believe that concludes the presentation                  22 portions of today's meeting. So, we're going to move                  23 into our final session, which is the open public                  24 comment. This is another important mechanism to engage                  25 public in the conversation.</p>	<p style="text-align: right;">Page 125</p> <p>1 Robert Falb, and I'm the director of U.S. policy and                  2 advocacy for the Alliance for Regenerative Medicine or                  3 ARM and I have no financial conflicts. We appreciate                  4 the opportunity to provide comments during this public                  5 meeting. By way of background, ARM is the leading                  6 international advocacy organization dedicated to                  7 realizing the promise of regenerative medicines and                  8 advanced therapies.                  9 We are the voice of the sector representing                  10 more than 400 members worldwide. ARM appreciates the                  11 support that FDA has provided in advancing the                  12 development of cell and gene therapies and commends the                  13 Agency and the industry negotiators for their efforts                  14 that produced the PDUFA VII commitment letter. This is                  15 vitally important work and we know it is not easy.                  16 It is a very exciting and critical time for                  17 the regenerative medicine sector. Scientific                  18 understanding of how to harness the potential of these                  19 therapies that are meant to cure some of our most                  20 devastating diseases continues to advance at a                  21 remarkable pace. With -- when PDUFA VI was                  22 reauthorized in 2017, ARM calculated that there were                  23 580 advanced therapy developers conducting more than                  24 480 clinical trials globally. Today ARM estimates that                  25 in the United States alone, there are over 1,100</p>



<p style="text-align: right;">Page 126</p> <p>1 ongoing clinical trials. And globally there are 2 additional 15,021 trials.</p> <p>3 PDUFA VII recognizes the growth in this sector 4 and takes many important steps to address the 5 challenges that will confront the Agency in the coming 6 years. It includes many different tools to share 7 information and help improve communication between the 8 Agency and sponsors. We are supportive of these 9 initiatives as they are core to an efficient and 10 effective regulatory review process.</p> <p>11 However, a continuing concern to ARM and then 12 when we -- and one that we have discussed previously 13 with CBER is the increasing alliance on written 14 responses to requests from cell and gene therapy 15 developers to discuss important and oftentimes 16 sensitive issues. Our member developers are utilizing 17 cutting-edge methods and approaches that raise new 18 complex community questions. We urge the Agency to 19 grant more face-to-face or teleconference meeting 20 requests, as they can actually be more efficient and 21 informative for both the Agency and sponsor.</p> <p>22 Timely and interactive CBER sponsor 23 communications are vital if the full promise of these 24 therapies is to be realized. A PDUFA VII top priority 25 for ARM is to ensure that CBER has the resources to</p>	<p style="text-align: right;">Page 128</p> <p>1 those therapies targeting rare diseases. We encourage 2 FDA to report out on the lessons learned from these 3 pilots and what actions will be incorporated into 4 regular practice and when.</p> <p>5 ARM appreciates the Interact meeting 6 formalization and the creation of the type D meeting, 7 but stress that it is important how they are 8 operationalized that will determine how valuable and 9 effective they truly are. Regarding Interact, we would 10 recommend that FDA track the number of requests made 11 and how many are granted. We encourage CBER to 12 actively engage in the Agency's implementation of these 13 new meeting goals so that the benefits to advance 14 therapy product developers are fully realized.</p> <p>15 Patient engagement is an important aspect of 16 ensuring that cell and gene therapies deliver on their 17 promise. It is important to incorporate the patient 18 voices, drug development and regulatory decision- 19 making. PDUFA VII includes specific patient -- 20 specific patient initiatives to ensure that this 21 perspective is heard.</p> <p>22 In conclusion, regenerative medicine sector is 23 the next frontier in the fight against some of our most 24 devastating diseases and disorders. These therapies 25 have just begun to demonstrate their power to improve</p>
<p style="text-align: right;">Page 127</p> <p>1 recruit, train and retain reviewers. We are very 2 pleased with a commitment to substantially strengthen 3 CBER staff capacity and capability. It is significant 4 that of the 351 targeted hires for fiscal year 2023 5 through '27 for CBER and CDER, 228, or approximately 65 6 percent will be dedicated to CBER.</p> <p>7 Another priority concern for ARM is the 8 bottleneck caused by the CMC review of cell and gene 9 therapy product applications, which the Agency has 10 acknowledged accounts for approximately 80 percent of 11 review resources. We are very pleased to say that the 12 commitment letter includes several strategies to 13 address this issue and are very supportive of the CMC 14 development and readiness pilot program.</p> <p>15 We urge CBER to move ahead expeditiously on 16 all the CMC initiatives and implement the pilot as 17 quickly as possible to help address the bottleneck. 18 Furthermore, we encourage strong leadership and 19 direction from CBER in establishing this pilot so that 20 the unique challenges of CBER-regulated products are 21 addressed.</p> <p>22 We are also interested in the Real World 23 Evidence pilot, Rare Disease Advancement Endpoint pilot 24 and the STAR Pilot which all hold promise and could 25 help in the advancement of drug development, especially</p>	<p style="text-align: right;">Page 129</p> <p>1 patient lives. And there's still much work to be done. 2 PDUFA VII will help to advance the field so 3 these treatments can meet their potential and be more 4 accessible to patients. Thank you.</p> <p>5 MR. THOMPSON: Thank you very much, Robert. 6 Next up, we have Brad Jordan. Are you here?</p> <p>7 MR. JORDAN: I'm here.</p> <p>8 MR. THOMPSON: All right. Floor is yours.</p> <p>9 MR. JORDAN: Okay. Good afternoon. My name 10 is Brad Jordan, and I'm the senior director of 11 Regulatory Policy at Flatiron Health and independent 12 affiliate of the Roche Group. I'm a Roche and a Amgen 13 shareholder.</p> <p>14 On behalf of Flatiron, I would like to thank 15 you for the opportunity to comment today on the success 16 of the PDUFA VII negotiations and to provide our 17 recommendations for potential enhancements that will 18 support the future use of real world data in the final 19 agreement.</p> <p>20 Flatiron Health is a health tech company 21 dedicated to helping cancer centers thrive and deliver 22 better care for patients today and tomorrow. We 23 translate patient experiences into real world evidence 24 to improve treatment, inform policy and advance 25 research.</p>

<p style="text-align: right;">Page 130</p> <p>1 Real world data and real world evidence can  2 complement evidence from clinical trials to evaluate  3 the safety and effectiveness of drugs and devices. It  4 can help fill critical evidence gaps by capturing the  5 experiences of patients who are not typically included  6 in clinical trials, such as people with rare conditions  7 or whose cancers possess rare genetic mutations.  8 There has been substantial growth in the use  9 of RWE for regulatory purposes, and Flatiron has been  10 proud to play a role in this growth and in pushing the  11 frontiers of RWD sourcing, collection and analysis. We  12 expect the use of RWE to continue to expand as new  13 sources of data become available, and methods to  14 collect, analyze and derive insights from these data  15 continue to evolve.  16 As outlined in the PDUFA VII commitment  17 letter, the advancing RWE program pilot for drug  18 sponsors will establish programs that can improve the  19 quality and acceptability of future RWE by sharing  20 learnings from RWE submissions, and providing targeted  21 regulatory guidance. Flatiron appreciates FDA efforts  22 to advance the use of RWE, and we encourage the Agency  23 to consider accelerating these efforts to establish  24 these new programs.  25 In doing so, these programs can more rapidly</p>	<p style="text-align: right;">Page 132</p> <p>1 other DHT-based measurements.  2 Also in the future, well-designed  3 observational studies may be used to support post-  4 approval requirements, for example, with drugs approved  5 through the accelerated approval pathway. RWE  6 organizations like Flatiron are crucial to advancing  7 the use of RWD in ways that can contribute to the PDUFA  8 VII goals and eventually realize the full potential of  9 RWE as we play an active role in the collection and use  10 of health care data.  11 Routine engagement with these organizations  12 will enhance FDA's insights, submission, quality  13 management and analysis in the near term, as well as  14 help the Agency respond to changes in technology over  15 time. Through broad stakeholder engagement and the  16 Agency's transparency, organizations like Flatiron and  17 sponsors that utilize RWD can better focus their  18 development efforts to help ensure the success of FDA's  19 modernization efforts and use of RWE to improve patient  20 outcomes.  21 At Flatiron, we are constantly optimizing the  22 collection, curation and use of RWE intended for  23 regulatory decision-making. It is therefore extremely  24 important to have a mechanism for data organizations  25 like Flatiron to engage directly with FDA outside the</p>
<p style="text-align: right;">Page 131</p> <p>1 lead to new understandings, new use cases for RWE, and  2 more rapid incorporation of RWE into regulatory  3 decisions. Additionally, we strongly support FDA's  4 efforts to establish a digital health technology  5 framework as now and in the future a variety of data  6 sources and technology platforms may be combined to  7 generate evidence to support drug approvals, endpoint  8 development, and innovative trial designs.  9 A comprehensive approach to technology  10 modernization is needed and should include input from  11 stakeholders from across the health and technology  12 sectors. As FDA considers public comments on PDUFA  13 VII, Flatiron respectfully requests that the Agency  14 establish a pathway to consult with data organizations,  15 such as ours, who are generators of RWE to gain a  16 greater understanding of methodological and  17 technological considerations, as the role of RWE is  18 further advanced for use in regulatory decision-making.  19 We welcome how the use of RWD is woven into  20 many of the goals outlined in the FDA PDUFA VII  21 commitment letter. In addition to the broader goal of  22 advancing the use of RWE in regulatory decision-making  23 through the pilot, FDA's goal to optimize the Sentinel  24 Sentinel Initiative and develop the DHT framework will  25 make use of RWD acquired through EHR systems or from</p>	<p style="text-align: right;">Page 133</p> <p>1 scope of the drug sponsors development program.  2 In these cases, participation of a data  3 provider in meetings with the Agency may be at the  4 discretion of the drug sponsor. And therefore the  5 ability to extract learnings and input from FDA on  6 optimizing the use of RWD may progress at a slower  7 pace. We therefore respectfully request that FDA  8 consider a framework by which these direct engagements  9 with data organizations can occur.  10 Thank you again for the opportunity to  11 contribute our input and we look forward to additional  12 opportunities for feedback in the PDUFA VII  13 authorization process.  14 MR. THOMPSON: Thank you very much, Brad.  15 Next up we have Paul Melmeyer. Are you here? Paul,  16 are you -- if you can hear...  17 MR. MELMEYER: Yes, apologies. Can you hear  18 me?  19 MR. THOMPSON: You're good. We hear you, all  20 set.  21 MR. MELMEYER: Very good. Thank you very  22 much. Good morning, and good afternoon, everyone. I  23 am Paul Melmeyer with the Muscular Dystrophy  24 Association and we serve the over 300,000 Americans  25 with rare neuromuscular diseases, most of whom do not</p>

<p style="text-align: right;">Page 134</p> <p>1 have an FDA-approved treatment indicated for their  2 disease and even fewer of whom have a treatment that  3 substantially alters the course of their disease. I  4 have no disclosures.</p> <p>5 We are here to offer a strong support for the  6 PDUFA VII agreements and will support the enactment of  7 the agreement in Congress next year and the  8 implementation thereafter. There are several  9 provisions included within the agreement that we  10 believe will accelerate the development and approval of  11 more and better therapies for the neuromuscular disease  12 community. To start work today is meeting started. We  13 are very pleased to see the influx of resources  14 dedicated to CBER's gene and cell-based therapeutic  15 reviews.</p> <p>16 MDA's number one priority for this PDUFA cycle  17 outlined in our August 2020 comments submitted to FDA  18 and industry negotiators was a surge in resources for  19 reviewing gene therapies. Our community knows the  20 impact of these transformative therapies, the impact  21 that these therapies can have as ZOLGENSMA, one of the  22 very first gene therapies approved by FDA, has been  23 substantially improving the lives of children with  24 spinal muscular atrophy.</p> <p>25 Furthermore, with gene therapies for Duchenne</p>	<p style="text-align: right;">Page 136</p> <p>1 rare disease clinical trials. We called for further  2 innovation on rare disease clinical trials. And we are  3 very pleased to see the proposed creation of the rare  4 disease endpoint advancement pilot program. Our  5 community is no stranger to the use of antiquated  6 endpoints with little connection to what is actually  7 meaningful to the patient, as evidenced by the  8 continued use of the six-minute walk test, the ALS,  9 FRS, a handful of neuropathy scales, and more that are  10 all rather outdated and do not reflect what patients  11 actually view as meaningful.</p> <p>12 We hope endpoints in neuromuscular disease  13 trials will be included within this pilot. And we hope  14 that the lessons from the pilot will not be limited to  15 just a handful of development programs that are  16 currently negotiated to be allowed under the pilot.</p> <p>17 Fourth, with the advancements made in patient-  18 focused drug development, over the previous two  19 agreements, we called for taking these efforts one step  20 further, by further facilitating the use of patient  21 preference information and patient experience data and  22 regulatory submissions. We're very pleased to see the  23 inclusion of guidances and public meetings aimed at  24 this very goal, as well as all the data collected in  25 PFDD meetings and PFDD instructed studies, as with all</p>
<p style="text-align: right;">Page 135</p> <p>1 muscular dystrophy, Limb-girdle muscular dystrophy,  2 Pompe disease, ALS and more in the pipeline, any  3 unnecessary delay in developing, reviewing, and  4 hopefully approving these therapies must be avoided.</p> <p>5 We hope these additional resources will accomplish this  6 goal.</p> <p>7 Second, we called for the consistent use of  8 regulatory flexibility across the FDA when reviewing  9 rare neuromuscular disease therapies. We called for  10 the expansion of Oncology Center of Excellence programs  11 to outside of oncology, including taking the O out of  12 RTOR, and we're very pleased to see the proposed  13 creation of the split real-time application review  14 program.</p> <p>15 And similarly, we see no reason why we  16 couldn't similarly expand project facilitate outside of  17 OCE as well. We hope further efforts to ensure  18 consistent regulatory reviews across divisions are  19 undertaken, either as part of this agreement by  20 modernizing FDA's internal data systems or otherwise.</p> <p>21 As recent -- as a recent report highlighted, the  22 varying approaches to assessing and determining  23 substantial evidence of effectiveness used across the  24 Agency.</p> <p>25 Third, we called for further innovation on</p>	<p style="text-align: right;">Page 137</p> <p>1 the data collected in these studies. As such data can  2 be most impactful when actually considered as part of a  3 regulatory submission, perhaps even as confirmatory  4 evidence.</p> <p>5 Fifth and finally for today, we are very  6 supportive of the innovations proposed for expedited  7 review pathways, including the breakthrough therapy  8 pathway and the accelerated approval pathway. We are  9 pleased to contribute to a proposal put forward by  10 Friends of Cancer Research and other colleagues that  11 called for certain reforms in our expedited approval  12 pathways, including moving beyond breakthrough and  13 better integrating expedited development programs with  14 the needs of CMC in innovative treatments. We're very  15 pleased to see such considerations included in this  16 agreement.</p> <p>17 There's plenty more to say certainly,  18 including on complex innovative trial designs, real-  19 world evidence, decentralized clinical trials and more.</p> <p>20 But to stick to our time allotment, we'll include those  21 thoughts in our written comments.</p> <p>22 Thank you again for the time today.</p> <p>23 MR. THOMPSON: Thank you very much, Paul.</p> <p>24 Next up, we have Jerry Roth. (Cross talk).</p> <p>25 MR. ROTH: Hi.</p>

<p style="text-align: right;">Page 138</p> <p>1 MR. THOMPSON: Hi. We can hear you.</p> <p>2 MR. ROTH: All right. Let's see if we can get</p> <p>3 clicked in. Okay. Hi, I'm Jerry Roth. I'm</p> <p>4 representing Hill Dermaceuticals as one of the owners.</p> <p>5 We're a small manufacturing development company of</p> <p>6 topical products for adults and children. And I will</p> <p>7 be very brief.</p> <p>8 I've been involved with the PDUFA fees, user</p> <p>9 fees since the inception in the early '90s. And there</p> <p>10 was -- this is one of the few -- I believe one of the</p> <p>11 few government programs that does not have any</p> <p>12 provisions of, you know, for small companies and I</p> <p>13 would like to say that not every company that develops</p> <p>14 is a multi-billion dollar company.</p> <p>15 And I want to be very clear here. I'm not</p> <p>16 here -- I do believe the user fees, but I do believe</p> <p>17 the companies should not one-size-fits-all. And I also</p> <p>18 would like to be very clear that I believe the</p> <p>19 submission fee for NDA applications should -- I'm not</p> <p>20 talking of that and believe it should be any caps. I</p> <p>21 believe the Agency uses the same amount of resources to</p> <p>22 review one of our NDA applications as they do a big</p> <p>23 format application.</p> <p>24 But what I like to refer to is the --</p> <p>25 specifically is the facility fees and the product fees.</p>	<p style="text-align: right;">Page 140</p> <p>1 the Agency continue to consider this of possibly</p> <p>2 putting caps on small businesses for the amount of</p> <p>3 fees. And if when you compete internationally, it's</p> <p>4 very difficult to try to compete internationally and</p> <p>5 then pay the fees, you know, the continuing to rise in</p> <p>6 the United States or put on by the agency.</p> <p>7 That being said, appreciate your time. Thank</p> <p>8 you and enjoy the meeting.</p> <p>9 MR. THOMPSON: Thank you very much, Jerry.</p> <p>10 Next up we have Dru West. Are you here?</p> <p>11 MS. WEST: Yes, I'm here. Turning to --</p> <p>12 MR. THOMPSON: You may begin.</p> <p>13 MS. WEST: I activated the video and the</p> <p>14 camera, I hope.</p> <p>15 MR. THOMPSON: You -- yeah, we can see you and</p> <p>16 you sound fine.</p> <p>17 MS. WEST: Okay, good. First of all, I want</p> <p>18 to thank you for the opportunity to speak today</p> <p>19 regarding the prescription drug user fees. My name is</p> <p>20 Dru West and I am the president of the USA Patient</p> <p>21 Network. We do not accept donations or support from</p> <p>22 any pharmaceutical or device manufacturers and we are</p> <p>23 completely independent patient voice.</p> <p>24 As a nonprofit, we are composed of advocates</p> <p>25 who represent a multitude of other advocacy groups, who</p>
<p style="text-align: right;">Page 139</p> <p>1 At the present time, whether you have a -- if you're a</p> <p>2 \$15 million company with a 20,000 square foot facility,</p> <p>3 you pay the same price, the fee to the Agency as, I</p> <p>4 won't mention any names, but big pharma company or</p> <p>5 multibillion-dollar company who may make 25 to 50</p> <p>6 products.</p> <p>7 And when I started here, I remember the first</p> <p>8 product fee was \$5,000. The last time they separated</p> <p>9 these fees was well over 100 per product. And I would</p> <p>10 like for the Agency to consider and I'd like one point</p> <p>11 is they need to consider now or possibly slowing down</p> <p>12 the growth of the fees or the increase of the fees and</p> <p>13 have centralized this out for companies of different</p> <p>14 sizes.</p> <p>15 I may -- I'm not the only one. I may be</p> <p>16 speaking for several companies, many companies don't</p> <p>17 speak up, but the percentage of fees regarding to the</p> <p>18 gross revenues is highly disproportional to the size of</p> <p>19 the company. And it's hard to, you know, to believe</p> <p>20 that the amount of resources on a smaller facility</p> <p>21 would be the same as on a multi-million -- multi-</p> <p>22 thousand square foot facility.</p> <p>23 And lastly, that we'd like -- I believe this</p> <p>24 will be the first seed. I'm going to be here next year</p> <p>25 just to not complain, but to suggest that this -- that</p>	<p style="text-align: right;">Page 141</p> <p>1 in turn represent thousands of patients, caregivers,</p> <p>2 and family members who have been helped and sometimes</p> <p>3 harmed by prescription medications and treatments.</p> <p>4 Our members are patients and caregivers who</p> <p>5 are acutely aware of the urgency and need for effective</p> <p>6 and safe medications and treatments. The USA Patient</p> <p>7 Network values the important and challenging work that</p> <p>8 the FDA does to serve and protect our public health.</p> <p>9 And we are also grateful that there are individuals and</p> <p>10 companies in industry who want to develop drugs and</p> <p>11 biologics that will help people have healthier lives.</p> <p>12 So, we deeply appreciate and understand that</p> <p>13 it takes both industry and the FDA to work together to</p> <p>14 bring safe and effective drugs to the public. Patients</p> <p>15 take medications because they're told that the</p> <p>16 medication or treatment offers hope, hope to cure or</p> <p>17 reduce the health impact of a medical condition.</p> <p>18 That hope sits squarely in the face of</p> <p>19 patients and doctors and trust to the FDA to make sure</p> <p>20 that drugs are safe, effective and also hopefully</p> <p>21 affordable. The FDA is the guardian at the gate for</p> <p>22 safe and effective medicines and treatments.</p> <p>23 Users fees have helped the FDA perform the</p> <p>24 goal of bringing medications and biologic treatments to</p> <p>25 the public in a timely manner. But paying a user fee</p>

<p style="text-align: right;">Page 142</p> <p>1 should not entitle any applicant to a prolonged 2 approval timeline or product on the market when a 3 product no longer demonstrates clinical benefits. 4 We would like to see the FDA use its full 5 authority as it continues to monitor and assess the 6 safety and effectiveness of all products. In addition 7 to industry asking FDA to complete timely reviews and 8 approvals, we ask that the FDA set clear instructions 9 and deadlines with industry for studies to be completed 10 on a timely basis, and when necessary to remove 11 medications that are not proven to be effective and 12 safe. 13 We are encouraged the FDA wants to strengthen 14 assessment of effectiveness and safety through as many 15 meetings as possible and not just through MedWatch 16 system or the Sentinel Initiative. We support ongoing 17 consistent assessment of current safety monitoring 18 tools for improvements. We ask that safety information 19 be easy to access in understandable language be 20 available to the public. 21 We are particularly concerned about the 22 medications approved through accelerated approval 23 pathway where a surrogate marker has been identified 24 for approval of the drug. If the goal of accelerated 25 approval is faster access to treatments that offer</p>	<p style="text-align: right;">Page 144</p> <p>1 reauthorization negotiations. 2 Because we believe that having firsthand 3 knowledge is vital for safe production of drugs, we ask 4 that in-person manufacturing facility inspections be 5 the standard to monitor product manufacturing, and that 6 they be resumed as soon as possible. We also ask the 7 pre-market safety concerns be resolved before drug 8 approval rather than relying on the use of volunteer 9 REMS strategies afterwards. 10 Again, I want to thank you for the opportunity 11 to share the USA Patient Network's concerns at this 12 meeting. And I look forward to the process that 13 continues. Thank you. 14 MR. THOMPSON: Thanks very much, Dru. Next 15 up, we have Kim Witczak, if I'm pronouncing that 16 correctly. 17 MS. WITCZAK: Yes, you did. Good afternoon. 18 Can you see me and hear me? 19 MR. THOMPSON: Yeah, audio and video are both 20 good. 21 MS. WITCZAK: Great. Good afternoon. My name 22 is Kim Witczak, and I'm speaking on behalf of Woody 23 Matters, a drug safety organization started in 2003 24 after the death of my husband due to an undisclosed 25 side effect with antidepressants. Woody Matters</p>
<p style="text-align: right;">Page 143</p> <p>1 meaningful advantage to patients with serious 2 conditions, then it is equally important that 3 confirmatory trials be completed in a timely manner to 4 confirm there actually is a meaningful advantage. 5 We ask that the FDA use the full power of its 6 authority to insist that post-market commitments be 7 completed in a timely manner, or to withdraw a drug 8 from the market if a sponsor does not complete report 9 confirmatory studies with due diligence, or if a study 10 fails to confirm a drug's clinical benefit. 11 To maintain the trust and hope in the FDA, we 12 ask in addition to -- in addition to performance scores 13 based on speed of approval, that the FDA self-monitor 14 and evaluate its own drug approval decisions and 15 actions as to the real safety and efficacy, and to 16 share this information with the public on a regular 17 basis. 18 Not only does the FDA need to know how its 19 decisions affect the public health, but the public 20 needs to know that their faith and trust in the FDA is 21 rightly earned. We are pleased to hear that the FDA's 22 increased support for patient engagement in the PDUFA 23 VII letter and we hope -- and we ask that consumer and 24 public health advocates be allowed to attend or at 25 least observe the FDA meetings with industry during</p>	<p style="text-align: right;">Page 145</p> <p>1 represents the voice of thousands of families who live 2 everyday with the consequences of the current drug 3 safety system. 4 We make sure the real-world patient 5 perspective is represented in health care 6 conversations, such as the one we're having today. I 7 am also on the board of directors for USA Patient 8 Network, an independent patient voice advocating for 9 safe, effective and accessible medical treatments. And 10 I have no financial conflicts of interest. 11 Over the past year-and-a-half, the pandemic 12 has highlighted the need for having a strong regulatory 13 agency that can respond quickly. It has also shined a 14 light on other things such as issues with conflicts of 15 interest, political interference, and the importance of 16 a strong safety mechanism when it comes to our medical 17 products. 18 This is my third PDUFA authorization cycle 19 that I've participated in. In reviewing the draft 20 materials for today's meeting, I would like to make the 21 following comments. The priority -- oops, sorry here. 22 The priority once again seems to focus on expedited and 23 speedy approvals. With the public being the ultimate 24 end consumer of the FDA-approved products, performance 25 goals should be based on safety and efficacy, not just</p>

<p style="text-align: right;">Page 146</p> <p>1 speed. It shouldn't be an either/or proposition.  2 I get it, the industry expectation of FDA is  3 to approve their products quickly so they can get on  4 the market faster. But sometimes this is at the  5 expense of safety. And obviously COVID has highlighted  6 the pressure and public's desire for speed as well.  7 As a consumer representative on the FDA's  8 Psychopharmacologic Drugs Advisory Committee, almost  9 every drug that has come before our committee has had  10 some sort of fast-tracking pathway like breakthrough  11 therapy, accelerated approval, priority review for an  12 unmet need, and have used the REMS program as a catch-  13 all for safety.  14 In my opinion, we need to stop relying so much  15 on the voluntary REMS strategy to flag safety issues  16 instead of focusing on pre-market resolution of safety  17 concerns. Everyone knows that the voluntary REMS are  18 very rarely effective. We also need better, quicker  19 response and communication of adverse events and harms.  20 I still support a previous idea of separating  21 staff responsible for pre-market approval and from  22 post-market safety. We need a proactive surveillance  23 from a variety of sources unlike what we're witnessing,  24 playing out in real time with the COVID vaccines.  25 There needs to be an attitude of safety first, and a</p>	<p style="text-align: right;">Page 148</p> <p>1 million and years to build. It all comes down to  2 motivation. And as I always say when it comes to  3 safety, it's only as good as the motivation and  4 intention behind it.  5 I strongly support the FDA staff and retention  6 efforts because we need the FDA to do this important  7 work. They need to have the space for free thinking  8 and ability to debate over everchanging science.  9 Unfortunately, right now with the vaccines, it has also  10 seemed to become a political environment. Politics  11 should not be driving these decisions.  12 Next, I would like to -- I also appreciate the  13 FDA's ability to pivot during the pandemic. But now we  14 need to get back to in-person inspections, as well as I  15 would love to see Adcom meetings with remote options  16 continuing.  17 And finally, there has to be a culture of  18 openness and transparency within the FDA. There should  19 be no closed-door meetings when it comes to PDUFA. The  20 public should be included in these initial and  21 negotiation meetings. I'd also like to see a concerted  22 effort involved in getting different types of patient  23 and consumer voices. It's important to get the real-  24 world middle of America patient who has no agenda or  25 financial interests. Their voices are often drowned</p>
<p style="text-align: right;">Page 147</p> <p>1 desire to actively investigate reports of harms versus  2 quickly dismissing or disregarding them as not related  3 to product.  4 We also -- number next, we need to leverage  5 resources to fund outside non-conflicted experts,  6 consultants and make investments in upgraded technology  7 that is designed to detect -- to detect a big or detect  8 and aid in proactive surveillance.  9 We need to redesign the FAERS MedWatch system.  10 This is an important post-market safety tool with a big  11 data solution that can be easily customized to capture  12 many fields of information. It needs to allow someone  13 to view and search all reports by a key word in the  14 report, then an algorithm can be built that can connect  15 a string of words together.  16 The other thing that's desperately needed in  17 this system is a public facing as -- so that the data  18 tools available to anyone, it needs to be intuitive and  19 user-friendly. We need to be able to see who reported  20 on the event. Was it patient-reported, physician,  21 hospital, manufacturer-reported? It also should  22 include the patient narratives in the reports.  23 Right now we're only able to see codes and not  24 really the story of what happened. The technology and  25 solutions are out there and it doesn't need to take 60</p>	<p style="text-align: right;">Page 149</p> <p>1 out by patient and consumer groups supported by  2 industry interests.  3 Lastly, we need annual performance reviews of  4 FDA's ongoing work. Specifically, it'd be great to  5 know the number, percentages of drugs approved that  6 were subject after approval with warnings or  7 withdrawals, or number of drugs that are using the gold  8 standard of having at least two phase III placebo-  9 controlled trials or an update on the drugs with REMS  10 at the time of approval.  11 I know as a consumer rep, I would love to hear  12 and learn more about the status of the drugs that we  13 have previously approved on my committee. At the end  14 of the day, we all need a strong FDA, one that is based  15 in science and not politics, and ultimately sees the  16 public as its customer and not just a partner servicing  17 the industry. We need -- we all need a good watchdog.  18 So, I appreciate your time and being open-  19 minded when considering my comments and others that  20 you're going to be hearing during the process. Thank  21 you.  22 MR. THOMPSON: Thank you very much, Kim. Next  23 up, we have Diana Zuckerman. Diana, are you here?  24 MS. ZUCKERMAN: Can you hear?  25 MR. THOMPSON: Okay. We can hear you. You're</p>

<p style="text-align: right;">Page 150</p> <p>1 all set.</p> <p>2 MS. ZUCKERMAN: Okay. I'm trying to be</p> <p>3 visible as well. I'm not sure this is going to happen.</p> <p>4 MR. THOMPSON: Oh, yeah, it looks like it's</p> <p>5 working. Oh, we just had you and then we lost you.</p> <p>6 There you go.</p> <p>7 MS. ZUCKERMAN: Try and (inaudible). Okay?</p> <p>8 Can you see me?</p> <p>9 MR. THOMPSON: Yeah.</p> <p>10 MS. ZUCKERMAN: I can't see myself. I'm</p> <p>11 hoping it works.</p> <p>12 MR. THOMPSON: We can see you. You're all</p> <p>13 good.</p> <p>14 MS. ZUCKERMAN: Okay. Great. Hi, I'm Dr.</p> <p>15 Diana Zuckerman, president of the National Center for</p> <p>16 Health Research, which is a patient-centered public</p> <p>17 health think tank. I'm -- I appreciate the opportunity</p> <p>18 to speak today. And I'm going to focus on some of the</p> <p>19 same issues, but also some different issues that we've</p> <p>20 heard about.</p> <p>21 In addition to speed, PDUFA performance</p> <p>22 measures need to evaluate whether patients are</p> <p>23 protected from ineffective or unsafe products being</p> <p>24 approved. As Commissioner Peggy Hamburg said,</p> <p>25 "Innovation needs to be in products for better, not</p>	<p style="text-align: right;">Page 152</p> <p>1 well-designed studies. And in most cases, these are</p> <p>2 going to be phase III randomized controlled trials. As</p> <p>3 an epidemiologist, I love big data. But it's very hard</p> <p>4 to use big data for products that haven't been on the</p> <p>5 market yet. So, for that reason, randomized controlled</p> <p>6 clinical trials are still going to be really important</p> <p>7 in the pre-market space, as well as the post-market</p> <p>8 space.</p> <p>9 The percentage of approved products that are</p> <p>10 subject to mandated post-marketing studies, and the</p> <p>11 percentage where those obligations were fulfilled is</p> <p>12 really important to know. We need to know were they</p> <p>13 started and ended on time, were they conducted as</p> <p>14 promised and as required, and did they or did they not</p> <p>15 confirm the safety and efficacy of those products.</p> <p>16 And your -- FDA recently had a meeting on some</p> <p>17 cancer drugs that had indications that for several</p> <p>18 years have been known not to have been confirmed, and</p> <p>19 yet those indications stayed in place for several</p> <p>20 years. It's that kind of activity that user fees</p> <p>21 should be -- should help speed things up.</p> <p>22 A newly published study indicates that too</p> <p>23 often a rejected application is subsequently</p> <p>24 resubmitted and approved when FDA ignores their own</p> <p>25 criticisms of the original application, even when those</p>
<p style="text-align: right;">Page 151</p> <p>1 just new." The performance goals have fallen short</p> <p>2 because the emphasis has been really only on speed and</p> <p>3 ease of approval, not on the quality of the outcome of</p> <p>4 FDA reviews, or of the products themselves.</p> <p>5 PDUFA has resulted in more and faster</p> <p>6 approvals and it's been a great success in that way.</p> <p>7 But not all those approvals have helped patients, and</p> <p>8 some have seriously harmed them. Premarket performance</p> <p>9 should also include evaluations of the percentage of</p> <p>10 applications that were rejected or withdrawn because</p> <p>11 there was a lack of evidence proving safety or</p> <p>12 efficacy, and should also evaluate the specific reasons</p> <p>13 why.</p> <p>14 It's that kind of transparency that will</p> <p>15 really help patients feel like they know what's going</p> <p>16 on at the Agency. When post-market surveillance works,</p> <p>17 it sometimes should result in FDA warnings, recalls or</p> <p>18 withdrawals and FDA should again provide the</p> <p>19 percentage. In this case, how many of these actions</p> <p>20 were taken for the 5 years after approval and the</p> <p>21 reasons for those actions. Again, that's the kind of</p> <p>22 performance that helps us understand how well things</p> <p>23 are working.</p> <p>24 Performance should also include the percentage</p> <p>25 of products that are approved based on at least two</p>	<p style="text-align: right;">Page 153</p> <p>1 criticisms remain valid. The controversial approval of</p> <p>2 Aduhelm is just the most salient example of that.</p> <p>3 And I would just like to say a few words about</p> <p>4 the commitment letter. The commitment letter changes</p> <p>5 policies and policies should be publicly debated by</p> <p>6 Congress and should include input from patients,</p> <p>7 consumer and public health advocates as part of any</p> <p>8 decision-making and any negotiations. Policies should</p> <p>9 not be negotiated behind closed doors at meetings that</p> <p>10 exclude these important perspectives.</p> <p>11 And now I just have five specific suggestions.</p> <p>12 Patient preferences and involvement, and we were very</p> <p>13 happy to hear efforts underway to improve those. But</p> <p>14 they should always include harmed patients, not just</p> <p>15 patients who have been recruited by industry, and who</p> <p>16 very often are the patients who are really desperate</p> <p>17 for treatment. We all understand that desperation.</p> <p>18 But all patient perspectives are important, including</p> <p>19 patients who've been harmed.</p> <p>20 Voluntary REMS strategies, as you know, are</p> <p>21 rarely proven to work. REMS needs a complete overhaul</p> <p>22 or REMS should be avoided. Instead, most safety</p> <p>23 concerns should be resolved before the products are</p> <p>24 approved. And just mention FDA's own analysis of</p> <p>25 opioid REMS has shown how ineffective that was, and</p>


Page 154

1 we've all paid the price for that as a country.  
 2 Number three, the commitment letter should  
 3 implement the National Academies public health  
 4 framework for regulatory oversight of opioids. Number  
 5 four, in-person manufacturing inspections do remain the  
 6 most effective way to determine problems. And for that  
 7 reason, although remote inspections were absolutely  
 8 needed during the pandemic, they should be the  
 9 exception moving forward. They should not take over  
 10 for those in-person inspections.  
 11 And number five, user fees should fund  
 12 independent objective studies to assess and quantify  
 13 the harms that resulted or were avoided due to the  
 14 approval decisions that FDA made. I just want to add  
 15 one more thing. I was very glad to hear today about  
 16 trying to enhance the Sentinel project. I've been a  
 17 strong supporter of those kinds of big data. But, so  
 18 much money has been spent on them, so many years have  
 19 gone by, and it's distressing to hear that there's  
 20 still efforts underway trying to figure out how to get  
 21 that -- those data sets to actually be objective,  
 22 useful pieces of information.  
 23 And my last remark is just to say, again, I  
 24 quote Peggy Hamburg that she saw the FDA as a public  
 25 health agency, I think all of us who admire and respect


Page 155

1 the FDA continue to see it as a public health agency.  
 2 And we want to make sure that the user fees aren't  
 3 interfering with that public health mission.  
 4 And unfortunately, when decisions are made  
 5 behind closed doors, it's very hard to feel confident  
 6 about the public health mission. Thanks very much.  
 7 MR. THOMPSON: Thanks very much, Diana. I'm  
 8 definitely going to get this name poorly, but Nishan  
 9 Yau (ph), are you here? Yeah, we hadn't had  
 10 confirmation that they were going to be able to attend  
 11 today, so. I think with that, we will move to the end  
 12 of the public comment period, and move to the end of  
 13 the overall meeting.  
 14 So, thank you to all the public commenters in  
 15 both the last two sessions. This concludes our public  
 16 meeting on the proposed PDUFA reauthorization. We very  
 17 much value all the input that's been generated from  
 18 today's discussion. We look forward to receiving  
 19 further comments on the public docket.  
 20 Again, as a reminder, the recording for this  
 21 meeting and the slides and a full transcript will be  
 22 posted to the PDUFA VII webpage. And with that, thank  
 23 you all very much for attending and have a great rest  
 24 of the day.  
 25

Page 156

1 CERTIFICATE OF NOTARY PUBLIC  
 2 I, EMMANUEL PEZOA, the officer before whom the  
 3 foregoing proceedings were taken, do hereby certify  
 4 that any witness(es) in the foregoing proceedings,  
 5 prior to testifying, were duly sworn; that the  
 6 proceedings were recorded by me and thereafter reduced  
 7 to typewriting by a qualified transcriptionist; that  
 8 said digital audio recording of said proceedings are a  
 9 true and accurate record to the best of my knowledge,  
 10 skills, and ability; that I am neither counsel for,  
 11 related to, nor employed by any of the parties to the  
 12 action in which this was taken; and, further, that I am  
 13 not a relative, partner, officer, director, or attorney  
 14 employed by any of the parties to the action, financially or  
 15 otherwise interested in the outcome of the action.  
 16  
  
 17 EMMANUEL PEZOA  
 18  
 19  
 20  
 21  
 22  
 23  
 24  
 25

Page 157

1 CERTIFICATE OF TRANSCRIBER  
 2 I, MURALIDHAREN K.V., do hereby certify that  
 3 this transcript was prepared from the digital audio  
 4 recording of the foregoing proceeding, that said  
 5 transcript is a true and accurate record of the  
 6 proceedings to the best of my knowledge, skills, and  
 7 ability; that I am neither counsel for, related to, nor  
 8 employed by any of the parties to the action in which  
 9 this was taken; and, further, that I am not a relative  
 10 or employee of any counsel or attorney employed by the  
 11 parties hereto, nor interested in the outcome of the  
 12 action.  
 13  
  
 14 MURALIDHAREN K.V.  
 15  
 16  
 17  
 18  
 19  
 20  
 21  
 22  
 23  
 24  
 25



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

## CERTIFICATE OF TRANSCRIBER

I, MURALIDHAREN K.V., do hereby certify that this transcript was prepared from the digital audio recording of the foregoing proceeding, that said transcript is a true and accurate record of the proceedings 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.



MURALIDHAREN K.V.

<b>1</b>	<b>2020</b> 121:10 134:17	<b>54</b> 3:17 <b>580</b> 125:23	<b>able</b> 5:9 22:22 23:10 27:3 28:9 29:8,9,12 34:22 35:25 36:12 37:4 38:13 55:11 75:6 77:5 80:18 82:12 82:18,22 83:12 84:6 85:4 86:5 93:2,4,8,9,18,24 94:7 147:19,23 155:10
<b>1</b> 20:4,10 <b>1,100</b> 125:25 <b>10</b> 3:8 90:19 96:5 97:1 105:16 106:14 112:23 <b>100</b> 9:17 139:9 <b>103</b> 4:9 <b>10:15</b> 42:25 43:6 <b>10:25</b> 42:25 <b>110</b> 4:12 <b>117</b> 4:15 <b>123</b> 121:12 <b>124</b> 4:17 <b>13</b> 118:7 <b>15</b> 94:13,13 139:2 <b>15,021</b> 126:2 <b>15th</b> 8:18,19 <b>16</b> 105:4 <b>160</b> 12:15 <b>17539</b> 157:14 <b>18</b> 111:12 <b>19</b> 65:23 73:2 82:23 108:3 112:7 112:15 121:8 122:24 123:4 <b>1983</b> 118:15 <b>1992</b> 6:9 <b>1st</b> 19:25	<b>2021</b> 1:13 <b>2022</b> 8:19,23 20:4 20:10 <b>2023</b> 68:3 127:4 <b>2024</b> 50:23 70:6 <b>2025</b> 51:2 88:24 90:19 91:16 106:13 <b>2026</b> 47:6 <b>2027</b> 106:21 <b>21st</b> 41:22 113:3 <b>22</b> 106:11 <b>220</b> 104:9 <b>228</b> 127:5 <b>23</b> 90:18 118:25 <b>25</b> 3:10 25:21 139:5 <b>27</b> 127:5 <b>28</b> 1:13	<b>6</b> <b>6,954</b> 121:10 <b>60</b> 48:7 52:2 65:16 147:25 <b>63</b> 3:20 52:3 <b>64</b> 98:14 <b>65</b> 127:5	<b>abrahams</b> 2:12 94:24 95:2 96:3,7 96:13,14 <b>abrams</b> 4:5 <b>absolute</b> 60:23 <b>absolutely</b> 80:5 154:7 <b>academics</b> 17:7 35:12 <b>academies</b> 154:3 <b>accelerate</b> 108:13 109:3 134:10 <b>accelerated</b> 18:1 31:16 67:3,4,8,22 68:6 101:1 132:5 137:8 142:22,24 146:11 <b>accelerating</b> 130:23 <b>accelerator</b> 112:16 119:13,22 <b>accept</b> 48:1 77:4 110:4 118:24 140:21 <b>acceptability</b> 107:19 130:19 <b>acceptance</b> 42:9 76:12 107:14 109:4 <b>accepted</b> 49:22 <b>accepting</b> 77:1 <b>access</b> 18:12 54:22 60:15 67:15,21
<b>2</b>	<b>3</b> <b>30</b> 8:19,23 111:24 118:17 <b>300,000</b> 133:24 <b>320</b> 118:16 <b>351</b> 127:4	<b>7</b> 102:15 <b>7,000</b> 112:4 120:22 <b>70</b> 113:10 <b>74</b> 3:23	
<b>2</b> 88:17 <b>20</b> 105:1 106:14 <b>20,000</b> 139:2 <b>200</b> 121:1 <b>2003</b> 98:12 144:23 <b>2012</b> 55:3 <b>2017</b> 113:18 125:22 <b>2018</b> 100:25 120:25 <b>2019</b> 55:7 113:19 121:9	<b>4</b> 118:6 <b>4-1/2</b> 118:8 <b>400</b> 125:10 <b>43</b> 3:12,14 <b>45</b> 94:14 <b>480</b> 125:24 <b>4808420</b> 1:23	<b>8</b> 90:17 <b>80</b> 127:10 <b>81</b> 100:25 <b>8433</b> 156:16 <b>85</b> 3:25	
	<b>5</b> 3:3 41:24 56:16 88:18 89:5,9,13 92:15 103:7 105:3 124:14 151:20 <b>5,000</b> 139:8 <b>50</b> 112:1 139:5	<b>8</b> <b>8</b> 90:17 <b>80</b> 127:10 <b>81</b> 100:25 <b>8433</b> 156:16 <b>85</b> 3:25	
	<b>9</b> <b>90</b> 49:20 <b>900</b> 121:9 <b>90s</b> 138:9 <b>94</b> 4:2 <b>95</b> 112:3 <b>96</b> 4:4,6 <b>9:00</b> 1:14	<b>9</b> <b>90</b> 49:20 <b>900</b> 121:9 <b>90s</b> 138:9 <b>94</b> 4:2 <b>95</b> 112:3 <b>96</b> 4:4,6 <b>9:00</b> 1:14	
	<b>6</b> <b>6,954</b> 121:10 <b>60</b> 48:7 52:2 65:16 147:25 <b>63</b> 3:20 52:3 <b>64</b> 98:14 <b>65</b> 127:5	<b>a</b> <b>a.m.</b> 1:14 <b>ability</b> 11:23 20:15 22:11 23:5 29:14 38:25 39:4 39:6,9 40:6,18 52:12,13 56:12 60:23 72:10 76:11 77:4 81:10 90:25 91:2 93:12,20 94:3,5 133:5 148:8,13 156:10 157:7	

81:14 120:4,12 142:19,25 <b>accessible</b> 129:4 145:9 <b>accomplish</b> 135:5 <b>account</b> 80:10 90:4 105:1 <b>accountability</b> 92:9 <b>accounts</b> 127:10 <b>accrue</b> 20:20,21 <b>accurate</b> 156:9 157:5 <b>achieve</b> 12:6,7 64:6 67:24 84:8 101:12 <b>achieves</b> 29:22 <b>achieving</b> 40:17 104:21 123:13 <b>acknowledge</b> 111:16 <b>acknowledged</b> 127:10 <b>acknowledges</b> 80:25 <b>acknowledging</b> 64:2 <b>acquired</b> 131:25 <b>acronym</b> 28:5 <b>act</b> 1:9 46:15,16 95:12 <b>acted</b> 96:25 <b>action</b> 27:4 28:10 29:13,23 55:14 70:6 77:14,15 156:12,15 157:8 157:12 <b>actions</b> 15:1 70:7 70:18 73:15 102:16 128:3 143:15 151:19,21 <b>activated</b> 140:13 <b>active</b> 44:7 95:24 121:9 132:9	<b>actively</b> 128:12 147:1 <b>activities</b> 13:10 18:19 52:17 55:6 59:17 65:11 67:5 67:8,11 68:20 79:5,11 81:13 98:4 114:9 <b>activity</b> 11:11,17 20:8 85:2 101:12 152:20 <b>acutely</b> 141:5 <b>adaptive</b> 49:16 53:18 <b>adcom</b> 148:15 <b>add</b> 6:11 28:13 154:14 <b>added</b> 6:17 32:3 54:17 <b>adding</b> 99:17 100:15 <b>addition</b> 27:10 31:21 41:2 46:3 47:6 48:16 49:8 49:25 64:24 75:21 87:23 88:16 97:2 99:18 106:19 107:1 121:18 131:21 142:6 143:12,12 150:21 <b>additional</b> 6:14 11:15,16 12:2,15 13:8,10,12,15 14:11 15:4,5 17:25 19:9 24:15 26:19,20 46:24 57:3,23 67:11 68:14,15 80:13,20 89:8 103:15 105:20 106:2 107:11 108:24 121:14 126:2 133:11 135:5	<b>additionally</b> 22:24 61:8 131:3 <b>address</b> 12:5 22:12 56:15 59:8 60:1 62:2,3 64:15 68:5 78:22 87:10 89:9,12 90:22 91:18 93:25 101:22 115:21 126:4 127:13,17 <b>addressed</b> 30:9 34:17,18 127:21 <b>addresses</b> 28:8 34:7 <b>addressing</b> 62:14 106:22 <b>adequacy</b> 98:17 <b>adjustment</b> 87:11 87:16 88:5,19 89:11,17,19 90:3 90:8,12 <b>administration</b> 1:4 <b>admire</b> 154:25 <b>adoption</b> 69:6,8 69:21 84:17 <b>adoptions</b> 69:23 <b>aducanumab</b> 101:15 <b>aduhelm</b> 153:2 <b>adults</b> 138:6 <b>advance</b> 23:5,25 24:21 25:9 43:15 44:19 49:16 50:15 51:23 52:10,14 53:14 55:8 59:22 61:14 62:1 63:15 65:16 66:4 72:14 73:9,12 86:21 96:6 103:23 104:10 105:10 116:11,16 117:14 125:20 128:13 129:2,24 130:22	<b>advanced</b> 12:21 17:21 23:6 69:8 69:16 70:10 105:4 125:8,23 131:18 <b>advancement</b> 18:13 42:17 53:3 70:23 115:9 127:23,25 136:4 <b>advancements</b> 69:24 136:17 <b>advances</b> 57:21 109:5 123:8 <b>advancing</b> 67:16 105:21 108:1 115:6,10,11 123:12 125:11 130:17 131:22 132:6 <b>advantage</b> 80:5,6 143:1,4 <b>adverse</b> 146:19 <b>advice</b> 30:22 31:18 68:13 107:18 <b>advise</b> 75:19 <b>advisory</b> 56:25 98:4,6,17 113:13 113:14 146:8 <b>advocacy</b> 4:12 104:8 110:20 111:1 118:20 125:2,6 140:25 <b>advocates</b> 140:24 143:24 153:7 <b>advocating</b> 145:8 <b>affect</b> 143:19 <b>affiliate</b> 129:12 <b>affordable</b> 141:21 <b>afternoon</b> 95:8 96:13 103:25 124:25 129:9 133:22 144:17,21 <b>agencies</b> 117:3
--	---	--	---

<p><b>agency</b> 15:13 40:20 47:13,25 48:11 50:20 66:6 70:7,9 73:15 92:20 93:18 97:13 98:5 99:23 101:12 101:19 102:14,16 107:13,22 109:1 111:17 116:6 125:13 126:5,8,18 126:21 127:9 130:22 131:13 132:14 133:3 135:24 138:21 139:3,10 140:1,6 145:13 151:16 154:25 155:1</p> <p><b>agency's</b> 87:25 88:9,14 89:20 91:18 98:18 101:13 106:2 110:4 128:12 132:16</p> <p><b>agenda</b> 148:24</p> <p><b>agendas</b> 46:7</p> <p><b>agile</b> 77:18,20</p> <p><b>agility</b> 86:23</p> <p><b>agnostic</b> 105:8</p> <p><b>ago</b> 17:24 105:4 118:6</p> <p><b>agreed</b> 16:6,12 65:14 66:13 96:1 115:14</p> <p><b>agreement</b> 21:25 22:8 31:25 38:16 39:5,13 40:16 51:14,20 52:2,4 61:2 78:21 84:23 86:10 88:18 116:16 121:11 129:19 134:7,9 135:19 137:16</p> <p><b>agreements</b> 66:10 66:11 76:25</p>	<p>112:11 134:6 136:19</p> <p><b>ahead</b> 6:6 10:12 42:22 81:21 94:12 95:6 127:15</p> <p><b>aid</b> 147:8</p> <p><b>aimed</b> 51:2 136:23</p> <p><b>algorithm</b> 147:14</p> <p><b>algorithms</b> 77:8</p> <p><b>align</b> 67:8</p> <p><b>aligned</b> 85:13</p> <p><b>aligning</b> 67:10 71:13</p> <p><b>alignment</b> 22:1</p> <p><b>allergenic</b> 19:8,12 19:15,22 20:3,5,8 20:8,12,16,18,22 20:25 21:8</p> <p><b>allergenics</b> 19:5 21:9</p> <p><b>allergies</b> 19:16,18 20:24 74:7</p> <p><b>allergy</b> 19:17</p> <p><b>alliance</b> 125:2 126:13</p> <p><b>allotment</b> 137:20</p> <p><b>allow</b> 6:14 13:5 21:3 28:16 33:25 74:20 77:25 106:19 107:13 108:19 116:5 120:14 121:13 147:12</p> <p><b>allowed</b> 136:16 143:24</p> <p><b>allows</b> 27:16 29:7 30:16,21 31:17 33:5 84:16 92:21 97:13</p> <p><b>alrighty</b> 38:3</p> <p><b>als</b> 135:2 136:8</p> <p><b>alternative</b> 66:2 66:15,19 73:4</p>	<p><b>alters</b> 134:3</p> <p><b>alzheimer's</b> 101:15</p> <p><b>america</b> 148:24</p> <p><b>american</b> 97:15 100:3</p> <p><b>americans</b> 111:25 118:17 133:24</p> <p><b>amgen</b> 129:12</p> <p><b>amount</b> 52:1 71:7 83:20 90:14,16,17 96:25 138:21 139:20 140:2</p> <p><b>amounts</b> 13:25</p> <p><b>analyses</b> 56:23 104:25</p> <p><b>analysis</b> 3:6 29:5,7 29:8 34:5,15,23 36:22 60:3 87:4 108:7 120:14 130:11 132:13 153:24</p> <p><b>analytic</b> 49:5</p> <p><b>analytical</b> 62:1 82:19</p> <p><b>analytics</b> 81:14 87:25 88:8 120:1</p> <p><b>analyze</b> 77:25 83:13 120:4 130:14</p> <p><b>analyzed</b> 35:18</p> <p><b>andrew</b> 2:2 3:4 5:11</p> <p><b>android</b> 120:4</p> <p><b>andy</b> 54:16 63:10</p> <p><b>ann</b> 2:10 10:9 73:23,23 81:19,23 83:5,19</p> <p><b>annie</b> 2:14 4:10 96:3 110:13,19 117:12</p> <p><b>announce</b> 124:16</p> <p><b>announcement</b> 7:18</p>	<p><b>annual</b> 37:10 46:17 88:16,20 89:23 92:15,17 149:3</p> <p><b>anticipated</b> 8:20</p> <p><b>anticipates</b> 106:13</p> <p><b>anticipation</b> 115:17</p> <p><b>antidepressants</b> 144:25</p> <p><b>antiquated</b> 136:5</p> <p><b>anymore</b> 50:10</p> <p><b>anyway</b> 42:23</p> <p><b>apart</b> 72:18</p> <p><b>apologies</b> 5:2,10 133:17</p> <p><b>apologize</b> 74:7 81:4,8</p> <p><b>apparent</b> 71:6</p> <p><b>applaud</b> 109:14</p> <p><b>applauds</b> 123:10</p> <p><b>applicability</b> 122:17</p> <p><b>applicable</b> 33:13</p> <p><b>applicant</b> 20:6,9 68:19 142:1</p> <p><b>applicants</b> 14:19 66:22</p> <p><b>application</b> 28:5 64:3,13 65:5 100:1 102:9 135:13 138:23 152:23,25</p> <p><b>applications</b> 6:16 18:4 20:13 24:11 26:7 28:3 65:12 66:3,17 73:6 78:5 78:6 96:24 97:12 98:9 99:3,24 106:14 121:5 127:9 138:19,22 151:10</p> <p><b>apply</b> 20:25 41:5</p>
---	--	--	--

<p><b>appreciate</b> 124:5 125:3 140:7 141:12 148:12 149:18 150:17</p> <p><b>appreciates</b> 107:1 119:4 125:10 128:5 130:21</p> <p><b>apprised</b> 119:5</p> <p><b>approach</b> 12:5 17:11 21:7 25:2 29:15 33:5 35:16 40:16 48:25 53:7 58:20 61:21 70:4 72:3 84:12 87:9 88:4 114:21,24 131:9</p> <p><b>approaches</b> 9:25 15:14,15,18 16:25 17:1,8,14 18:6 25:10,13 33:12,20 36:22 37:18 53:19 55:21 67:13 68:4 68:8 108:5 113:8 126:17 135:22</p> <p><b>approaching</b> 23:2 124:16</p> <p><b>appropriate</b> 14:7 23:15 27:9,18 28:13 29:11 32:9 38:24 40:21 62:9 63:22 66:6 68:22 71:7 73:7 82:23 83:16 107:3 111:13 115:2 119:14 122:7</p> <p><b>appropriated</b> 46:15</p> <p><b>appropriately</b> 22:9 34:12,23</p> <p><b>appropriateness</b> 35:24</p> <p><b>appropriations</b> 46:17</p>	<p><b>approval</b> 11:16 17:15 18:2 21:4 26:21,24 27:2,4 40:18 58:23 59:3 64:25 65:15 68:25 99:15 100:12,22 101:14 103:11 105:4,6 132:4,5 134:10 137:8,11 142:2,22,24,25 143:13,14 144:8 146:11,21 149:6 149:10 151:3,20 153:1 154:14</p> <p><b>approvals</b> 19:17 97:18 101:1,3,5 105:2 114:18 118:11 131:7 142:8 145:23 151:6,7</p> <p><b>approve</b> 146:3</p> <p><b>approved</b> 11:15 26:18 50:8 58:13 97:20 106:12 112:4 113:16 114:13 132:4 134:1,22 142:22 145:24 149:5,13 150:24 151:25 152:9,24 153:24</p> <p><b>approving</b> 135:4</p> <p><b>approximately</b> 12:15 28:23 48:7 49:20 127:5,10</p> <p><b>architecture</b> 77:20 80:17</p> <p><b>area</b> 6:20 10:3 15:18,21 16:25 17:13,17,19 18:8 19:6 35:9,15 55:10 60:8 65:5 75:8,22 88:2 90:23 106:6,10 109:17</p>	<p><b>areas</b> 9:10,21 16:17 18:3,12,14 18:17 23:23 25:7 26:6,9,10 30:4 31:23 41:11 46:25 48:18 53:25 57:25 58:3 66:11 75:9 86:13 105:17 106:9 109:24 113:1 115:20</p> <p><b>arena</b> 11:11</p> <p><b>arguably</b> 42:10</p> <p><b>arm</b> 125:3,5,10,22 125:24 126:11,25 127:7 128:5</p> <p><b>array</b> 30:11</p> <p><b>articulated</b> 116:2</p> <p><b>aside</b> 11:18</p> <p><b>asked</b> 24:5,7 102:20</p> <p><b>asking</b> 24:5 142:7</p> <p><b>aspect</b> 38:17 128:15</p> <p><b>aspects</b> 50:21 69:4</p> <p><b>assess</b> 23:12 55:4 65:25 66:15 73:5 75:7 94:3 142:5 154:12</p> <p><b>assesses</b> 34:15</p> <p><b>assessing</b> 58:20 66:2 93:14 107:4 122:18 135:22</p> <p><b>assessment</b> 14:8 14:11,21 26:23 29:21 46:12 55:8 55:9,22,24 56:7 56:11 60:12 64:18 64:23 65:1 71:22 75:10 84:11,16 91:8,13,16 93:15 94:1 106:24 114:4 122:13,16 142:14 142:17</p>	<p><b>assessments</b> 16:1 44:24 45:13 52:20 55:11 65:5 93:17 114:5 122:7</p> <p><b>assistance</b> 99:23</p> <p><b>associated</b> 120:13 121:5</p> <p><b>association</b> 133:24</p> <p><b>assure</b> 27:7 64:17</p> <p><b>atrophy</b> 134:24</p> <p><b>attached</b> 42:7</p> <p><b>attempt</b> 14:25 67:19</p> <p><b>attend</b> 111:20 143:24 155:10</p> <p><b>attendees</b> 86:5</p> <p><b>attending</b> 155:23</p> <p><b>attention</b> 21:12 82:3 107:2 112:19</p> <p><b>attitude</b> 146:25</p> <p><b>attorney</b> 156:13 157:10</p> <p><b>audience</b> 21:23 40:2 102:22</p> <p><b>audio</b> 5:4,7,15 21:18 81:8 94:25 144:19 156:8 157:3</p> <p><b>august</b> 89:25 134:17</p> <p><b>authority</b> 46:13 66:3 142:5 143:6</p> <p><b>authorization</b> 45:16 95:12 133:13 145:18</p> <p><b>authorized</b> 46:14</p> <p><b>automatically</b> 77:4</p> <p><b>availability</b> 122:6</p> <p><b>available</b> 10:16 16:3 28:11,12 29:24 32:24 38:20 48:14 57:17 66:7 70:12 90:14 93:24</p>
--	---	---	--

120:3 130:13 142:20 147:18 <b>avoided</b> 103:10 135:4 153:22 154:13 <b>aware</b> 11:9 17:19 32:15 112:3 141:5 <b>awareness</b> 45:24	<b>basis</b> 21:6 46:7 98:21 100:11 142:10 143:17 <b>bayesian</b> 53:18,19 115:22 <b>becoming</b> 53:6 <b>beginning</b> 89:25 94:22 96:18 103:14 105:25 <b>begins</b> 108:11 <b>begun</b> 128:25 <b>behalf</b> 110:17 117:7 118:21 123:17 129:14 144:22 <b>believe</b> 24:20 52:2 52:3 56:11 65:9 81:20 83:9 96:20 99:16 100:14 102:6 104:19 105:9 107:6 109:19 123:21 134:10 138:10,16 138:16,18,20,21 139:19,23 144:2 <b>believes</b> 110:23 <b>beneficial</b> 19:21 40:25 <b>benefit</b> 7:7 23:12 32:23 52:16 53:15 67:21 72:21 83:12 104:11 108:2 143:10 <b>benefited</b> 113:17 114:14 <b>benefits</b> 16:19 55:13 56:9 67:14 76:10 81:9 89:14 89:16 105:12 128:13 142:3 <b>bens</b> 2:13 4:7 96:3 103:22,25 104:4 <b>best</b> 14:10 22:25 32:11 38:12 40:7	40:15 45:8 56:18 58:1,2 59:24 66:14 69:14 83:23 84:5 85:4 104:19 104:22 156:9 157:6 <b>better</b> 16:15 23:5 42:18 47:14 55:5 64:15 72:14 81:6 120:15 121:25 129:22 132:17 134:11 137:13 146:18 150:25 <b>beyond</b> 66:17 80:16 83:4,16 89:21 107:14,15 116:12 137:12 <b>big</b> 138:22 139:4 147:7,10 152:3,4 154:17 <b>billion</b> 138:14 <b>bio</b> 9:8 23:1 80:23 <b>bioinformatics</b> 85:8 <b>biologic</b> 34:8 58:22 74:16 79:25 80:9 85:10 141:24 <b>biologics</b> 19:7 51:1 53:7 56:18 66:25 80:7 81:11 85:5 97:16 99:21 141:11 <b>biology</b> 80:24 85:8 104:24 107:7 <b>biopharmaceuti...</b> 24:19 39:24 111:2 <b>bit</b> 6:10 7:15 16:4 24:8 28:23 44:16 112:22 <b>bla</b> 11:14 21:4 64:23 68:24 98:9 101:15,20 103:11 <b>blas</b> 20:1	<b>board</b> 13:24 145:7 <b>boston</b> 118:6 <b>bottleneck</b> 127:8 127:17 <b>bottom</b> 97:8,17 98:23 101:24 117:22 <b>brad</b> 2:17 129:6 129:10 133:14 <b>break</b> 3:12 25:20 42:23 43:3 94:14 94:18 <b>breakthrough</b> 100:9 137:7,12 146:10 <b>brief</b> 6:7 7:12 138:7 <b>briefing</b> 8:4 48:8 <b>briefly</b> 97:9 <b>bring</b> 22:11 28:10 75:14 141:14 <b>bringing</b> 104:22 141:24 <b>broad</b> 122:12 132:15 <b>broader</b> 37:7,13 110:18 112:22 118:22 131:21 <b>broken</b> 124:3 <b>budget</b> 46:13 <b>build</b> 41:20 53:20 75:11 83:4 85:7 91:13 148:1 <b>building</b> 24:25 41:25 45:17 59:24 61:23 86:19,20 106:23 <b>builds</b> 41:21 53:12 <b>built</b> 34:21 56:2 84:13 147:14 <b>bullet</b> 20:3 <b>bullets</b> 57:13 <b>burden</b> 15:1,6
<b>b</b>			
<b>b</b> 68:15 <b>back</b> 5:5 32:6,6 36:16 38:2 40:19 42:25 43:2,5 51:11 60:17 81:15 85:14 91:21 94:9 94:19 95:7 103:14 148:14 <b>background</b> 3:3 5:12,17 6:1,8 7:12 44:13,16 88:14 125:5 <b>backlog</b> 6:13 <b>bad</b> 81:21 97:15 <b>balance</b> 21:8 <b>bandwidth</b> 5:23 <b>bar</b> 114:19 <b>barriers</b> 69:6,20 69:21 <b>barton</b> 2:11 85:19 85:24 86:3,6 <b>base</b> 6:24 16:10 <b>based</b> 29:14 57:15 67:13 68:8,16 70:4,8 75:3 78:25 79:3 82:19 84:17 98:5 104:23 106:6 114:9 132:1 134:14 143:13 145:25 149:14 151:25 <b>basic</b> 50:22 <b>basically</b> 15:1 19:24 20:1,11 36:4 48:3			

<b>businesses</b> 140:2	<b>captured</b> 34:2	22:20,22,25 30:16	<b>central</b> 64:11
<b>button</b> 117:22,25	<b>capturing</b> 17:15	38:20 39:14 45:20	<b>centralized</b>
<b>c</b>	33:15 51:18 130:4	49:22 66:25 67:25	139:13
<b>c</b> 2:1 3:1 5:1 31:2	<b>care</b> 104:10	69:16 74:25 79:19	<b>centre</b> 78:16
31:8,19 122:12	109:21,22 118:11	79:21 80:21 81:10	<b>centric</b> 25:2
<b>cadence</b> 48:2	129:22 132:10	84:24 85:2,3	<b>century</b> 41:22
<b>calculated</b> 125:22	145:5	91:12 115:11	113:3
<b>called</b> 27:25 28:1	<b>careful</b> 102:20	120:25 121:6,9,10	<b>certain</b> 28:19 69:9
28:4 30:13 31:2	<b>carefully</b> 75:7	121:11,13 126:13	70:1,20 89:9
34:5,14 67:18	<b>caregiver</b> 115:4	126:22,25 127:3,5	96:25 137:11
87:11 109:2 135:7	<b>caregiver's</b> 16:18	127:6,15,19,20	<b>certainly</b> 32:16
135:9,25 136:1,19	<b>caregivers</b> 141:1,4	128:11	35:15 98:19 102:3
137:11	<b>carol</b> 2:9 62:24	<b>cber's</b> 9:23 21:10	137:17
<b>camera</b> 140:14	63:6 71:5,25 73:8	22:3 120:19	<b>certificate</b> 156:1
<b>cancer</b> 104:11	73:13	121:18,20 134:14	157:1
129:21 137:10	<b>cartier</b> 2:3 21:15	<b>cder</b> 38:21 39:14	<b>certify</b> 156:3
152:17	25:7,20 38:3	45:20 49:22 66:25	157:2
<b>cancers</b> 130:7	41:17 43:19 51:7	67:25 68:5 69:15	<b>cetera</b> 61:14 74:24
<b>candid</b> 98:16	53:9,10 54:2	74:25 80:21 85:2	75:11 99:15
<b>capabilities</b> 12:11	60:20 61:18,20,24	86:7 91:12 98:13	101:13
62:1 75:9 76:13	71:4 72:22 81:16	113:23,23 127:5	<b>challenge</b> 5:20
91:9 92:23 106:23	81:18 83:17 91:23	<b>cdrh</b> 113:15	17:5
<b>capability</b> 7:6	92:24	<b>cdrp</b> 67:19	<b>challenges</b> 13:6
19:10 57:8 87:4,6	<b>cartier's</b> 24:25	<b>cell</b> 9:24 11:11,22	16:7 17:10,12,13
87:8,14,18,21	<b>case</b> 48:6 49:19	11:24 12:3,8,13	18:7 32:18 35:22
88:7,22 93:7	50:7,14 69:5,18	12:14,19 13:3,16	36:2 46:6 57:11
127:3	72:11 79:22 97:1	14:19,23 15:20,23	67:5,10 68:5
<b>capacities</b> 84:13	151:19	16:7 17:4,16 18:2	75:14,15 78:2,4
<b>capacity</b> 6:15 7:6	<b>cases</b> 37:12 44:16	18:5 19:1,2 23:3	84:16,18 91:15
9:24 11:21 12:11	57:1,4 65:18	23:13,17 24:24	106:4 119:20
13:5 57:15 74:12	131:1 133:2 152:1	25:3,5 79:25	126:5 127:20
75:8,11,18,22	<b>catalog</b> 46:11 47:1	105:7,19 106:6,6	<b>challenging</b> 15:8
80:21 83:23 84:25	52:19,22	106:11,14,17,25	18:5 32:21 35:15
85:7 86:7,24 87:2	<b>catalogue</b> 122:9	114:9 120:20	39:3 119:15 141:7
87:3,8,11,14,15	<b>catch</b> 146:12	121:1 125:12	<b>championed</b> 112:9
87:17,21,24 88:2	<b>causal</b> 59:20	126:14 127:8	<b>chance</b> 37:1
88:5,6,7,8,19,22	<b>caused</b> 127:8	128:16 134:14	<b>change</b> 14:7 22:20
90:2 109:17 110:4	<b>caution</b> 100:21	<b>cellular</b> 16:20	27:12,18 105:15
111:20 127:3	<b>cautions</b> 100:24	<b>center</b> 3:4 76:7	117:10
<b>caps</b> 138:20 140:2	<b>cber</b> 3:8 9:22	77:20 135:10	<b>changed</b> 27:13,19
<b>capture</b> 32:23	10:12,13,24 11:6	150:15	114:12
102:14 111:14	11:7,21 12:1,5,12	<b>centered</b> 150:16	<b>changes</b> 8:16 16:2
147:11	14:2,9,21 16:5	<b>centers</b> 57:7	56:24 61:12,13
	19:3,7,21 22:5,11	129:21	90:4 132:14 153:4

<p><b>changing</b> 79:16 107:5</p> <p><b>channel</b> 37:23</p> <p><b>channels</b> 50:19</p> <p><b>characteristics</b> 32:25 59:9</p> <p><b>characterize</b> 101:25</p> <p><b>chat</b> 43:1 94:16</p> <p><b>check</b> 21:18 74:3</p> <p><b>chemistry</b> 3:19 10:3 31:6 62:23 63:2</p> <p><b>chief</b> 4:11,14 110:20 118:3</p> <p><b>children</b> 19:19 112:2 134:23 138:6</p> <p><b>children's</b> 118:7</p> <p><b>choppy</b> 81:3,7</p> <p><b>chris</b> 2:2 10:12,19 11:5 21:14,22,24 22:17 23:10,14 79:24</p> <p><b>chronic</b> 104:12 122:18</p> <p><b>circle</b> 103:13</p> <p><b>circumstances</b> 104:24</p> <p><b>citizen</b> 4:5 96:14</p> <p><b>citizens</b> 96:7</p> <p><b>claims</b> 107:20</p> <p><b>clarification</b> 26:20 27:5,9 31:24</p> <p><b>clarifications</b> 32:4</p> <p><b>clarify</b> 90:5</p> <p><b>clarifying</b> 39:20</p> <p><b>clarity</b> 76:14</p> <p><b>class</b> 93:20 94:5</p> <p><b>clear</b> 5:15 21:19 21:20 41:1 56:22 74:5 86:2 100:6 138:15,18 142:8</p>	<p><b>clearance</b> 8:2</p> <p><b>clearly</b> 11:12 13:5 64:5 84:21 112:20 115:7</p> <p><b>click</b> 117:21</p> <p><b>clicked</b> 117:23 138:3</p> <p><b>climate</b> 111:14</p> <p><b>clinical</b> 15:17 16:21 18:18 23:9 23:23,23 27:12 31:5 45:12 52:20 67:3,4,9,9,14,21 67:22 68:6 72:3 74:18,20 75:5,10 76:17 83:5,8,12 106:8,24 107:9 108:6 109:9 114:4 114:5 118:10 120:11,16 122:7 122:12,16 123:3,8 125:24 126:1 130:2,6 136:1,2 137:19 142:3 143:10 152:6</p> <p><b>clinically</b> 100:19</p> <p><b>close</b> 51:5 70:21 101:19 109:23</p> <p><b>closed</b> 148:19 153:9 155:5</p> <p><b>closely</b> 9:20 33:6 119:19</p> <p><b>cloud</b> 77:6,6,18,19 78:2,3,3,24 79:3 84:15,17</p> <p><b>cmc</b> 18:3 23:21,24 63:12,21 64:18,23 67:6,7,10,18,19 67:23,25 68:5,12 68:13,15,16,17 69:1,4 71:13,23 72:7 127:8,13,16 137:14</p>	<p><b>cmcs</b> 18:18</p> <p><b>coalition</b> 4:8 103:23 104:6 110:25 111:2,6</p> <p><b>coas</b> 45:13 122:7 122:10,17</p> <p><b>code</b> 96:20</p> <p><b>codes</b> 147:23</p> <p><b>codify</b> 102:5</p> <p><b>collaborating</b> 76:6</p> <p><b>collaboration</b> 79:6 116:6</p> <p><b>collaborations</b> 15:10 25:8 78:18 101:19</p> <p><b>collaborative</b> 112:24</p> <p><b>collaboratively</b> 119:25</p> <p><b>colleague</b> 24:15 41:15 53:8 61:16</p> <p><b>colleagues</b> 9:8 86:17 110:9 137:10</p> <p><b>collect</b> 45:9 46:4 87:19 130:14</p> <p><b>collected</b> 44:22 45:3,6 107:6 124:12 136:24 137:1</p> <p><b>collecting</b> 53:3 114:1</p> <p><b>collection</b> 56:2 74:20 130:11 132:9,22</p> <p><b>collections</b> 83:2</p> <p><b>collective</b> 117:1</p> <p><b>collectively</b> 51:23 118:9</p> <p><b>color</b> 51:10</p> <p><b>combination</b> 34:8 34:9,12 35:4</p> <p><b>combined</b> 131:6</p>	<p><b>come</b> 28:22 30:6 31:7 33:4,25 43:2 48:13 49:2 50:18 114:18 146:9</p> <p><b>comes</b> 27:23 30:14 63:12 67:6 78:10 145:16 148:1,2,19</p> <p><b>coming</b> 21:18 29:16 42:5 45:17 47:18 80:24 81:2 81:7 83:21 91:19 126:5</p> <p><b>commends</b> 125:12</p> <p><b>comment</b> 8:10 25:1 123:24 124:8 124:12 129:15 155:12</p> <p><b>commentary</b> 51:10</p> <p><b>commenters</b> 155:14</p> <p><b>comments</b> 4:17 8:12,14 21:16 24:15 41:18 43:5 95:16 105:25 107:11 124:2,4,11 124:23 125:4 131:12 134:17 137:21 145:21 149:19 155:19</p> <p><b>commercial</b> 69:10 70:3</p> <p><b>commission</b> 103:9</p> <p><b>commissioned</b> 88:23</p> <p><b>commissioner</b> 150:24</p> <p><b>commit</b> 116:11</p> <p><b>commitment</b> 8:16 9:11 16:13 22:10 24:7 26:15 44:2,9 46:10,21 50:24 51:13 52:12,24 54:18 55:23 56:4</p>
---	---	--	--



56:12 57:13 59:18 60:4,6 61:4,19 63:11,18 68:3 74:11 75:12 76:10 77:17 78:21 79:9 80:13,25 83:21 87:7 93:2,12 96:17 97:4 99:5,9 99:11,22 100:5 101:8,22 102:25 103:8,18 112:19 115:1,6,8 116:17 116:21 117:8 119:7,8 122:8 125:14 127:2,12 130:16 131:21 153:4,4 154:2 <b>commitments</b> 20:25 40:10 54:24 55:17,18 56:15 57:16 58:18 60:9 60:17 61:1,13 63:17 70:22 76:25 84:3,8,14 87:12 87:16 88:1,11 89:2,8 93:9 107:17 108:12,14 109:15 115:14 116:3,4,12 123:11 143:6 <b>committed</b> 49:13 55:3 64:2,10 65:1 75:22 118:18 <b>committee</b> 76:4,5 98:4,6,17 113:14 146:8,9 149:13 <b>committees</b> 8:5 56:25 113:13 <b>common</b> 17:12 33:22 98:2 104:12 <b>communicate</b> 14:12,25 <b>communicated</b> 64:24	<b>communicating</b> 57:20 <b>communication</b> 12:25 32:12 61:5 63:22,25 64:17 65:2,10 68:18 76:18,18 101:11 126:7 146:19 <b>communications</b> 6:25 14:14 63:14 63:20 70:23 78:12 101:17 126:23 <b>communities</b> 83:11 112:24 117:3,4 <b>community</b> 23:12 51:16 52:13 100:18 110:19 112:9 113:6 116:20,22,24 117:1,8 118:23 119:5 123:17 126:18 134:12,19 136:5 <b>companies</b> 23:1 47:17,18 57:4 138:12,17 139:13 139:16,16 141:10 <b>company</b> 32:7 36:17 50:11 65:15 129:20 138:5,13 138:14 139:2,4,5 139:19 <b>comparative</b> 36:23 <b>comparison</b> 35:19 <b>compensation</b> 89:14 <b>compete</b> 140:3,4 <b>competitive</b> 116:8 <b>complain</b> 139:25 <b>complement</b> 107:8 130:2	<b>complete</b> 26:17 27:11 28:15 29:9 55:10 142:7 143:8 153:21 <b>completed</b> 28:21 68:21 142:9 143:3 143:7 <b>completely</b> 32:1 140:23 <b>completing</b> 84:15 <b>complex</b> 7:8 15:16 44:4 48:23 50:21 53:10,18 78:5 81:11 83:25 106:4 126:18 137:18 <b>complexity</b> 57:9 79:25 <b>component</b> 28:19 46:10,22 56:19 <b>components</b> 36:21 49:25 64:11 <b>composed</b> 140:24 <b>comprehensive</b> 12:5 114:2 131:9 <b>comprised</b> 111:1 <b>compromised</b> 101:20 <b>computation</b> 80:24 <b>computational</b> 49:4 85:8 <b>concept</b> 36:9 87:6 <b>concepts</b> 34:1 116:7 <b>concern</b> 55:10 121:19 126:11 127:7 <b>concerned</b> 106:15 142:21 <b>concerning</b> 98:11 <b>concerns</b> 57:2 144:7,11 146:17 153:23	<b>concerted</b> 148:21 <b>concludes</b> 123:21 155:15 <b>conclusion</b> 116:19 128:22 <b>concur</b> 60:23 <b>condition</b> 141:17 <b>conditions</b> 114:13 115:16 122:18 130:6 143:2 <b>conduct</b> 59:8 74:18 93:15 <b>conducted</b> 91:10 91:14 108:8 111:17 152:13 <b>conducting</b> 75:23 113:24 125:23 <b>confident</b> 98:14 155:5 <b>confidentiality</b> 66:10 <b>confirm</b> 94:24 143:4,10 152:15 <b>confirmation</b> 155:10 <b>confirmatory</b> 137:3 143:3,9 <b>confirmed</b> 152:18 <b>conflicted</b> 147:5 <b>conflicts</b> 96:15 125:3 145:10,14 <b>confront</b> 126:5 <b>congress</b> 8:18,20 46:15 97:13 98:21 110:9 114:20 117:4 123:19 134:7 153:6 <b>congressional</b> 8:5 <b>connect</b> 147:14 <b>connected</b> 76:24 116:8 <b>connection</b> 136:6 <b>conscious</b> 76:21
--	--	---	--

<p><b>consequences</b> 145:2</p> <p><b>consider</b> 70:19 73:1 130:23 133:8 139:10,11 140:1</p> <p><b>consideration</b> 8:20</p> <p><b>considerations</b> 57:12 105:20 116:25 117:5 131:17 137:15</p> <p><b>considered</b> 19:3 137:2</p> <p><b>considering</b> 16:23 149:19</p> <p><b>considers</b> 131:12</p> <p><b>consistency</b> 15:4 60:2 76:17 82:16 82:18 109:16</p> <p><b>consistent</b> 58:20 76:18 135:7,18 142:17</p> <p><b>consistently</b> 95:24</p> <p><b>consolidation</b> 77:21</p> <p><b>consortium</b> 122:13</p> <p><b>constantly</b> 132:21</p> <p><b>consult</b> 47:17,18 131:14</p> <p><b>consultants</b> 147:6</p> <p><b>consultation</b> 48:11 120:17</p> <p><b>consumer</b> 143:23 145:24 146:7 148:23 149:1,11 153:7</p> <p><b>contact</b> 103:19</p> <p><b>containing</b> 85:10</p> <p><b>contains</b> 76:23</p> <p><b>contemplating</b> 67:2</p> <p><b>content</b> 78:14,14</p>	<p><b>context</b> 15:7 59:10</p> <p><b>contingent</b> 108:16</p> <p><b>continual</b> 88:4</p> <p><b>continuation</b> 16:8 51:12</p> <p><b>continuations</b> 44:14</p> <p><b>continue</b> 14:15,16 15:9,12 18:13 20:14 22:21 23:1 23:25 42:15 46:18 47:21 49:15 52:7 52:10,14,22 53:14 53:20 55:17 60:10 60:13 61:23 80:2 81:1 84:13 87:21 88:6 91:7 92:12 93:19 94:4,4 105:11 106:9 117:2 123:16 130:12,15 140:1 155:1</p> <p><b>continued</b> 52:19 53:1 54:19 57:14 60:25 86:14 90:24 110:1 112:18,19 113:2,3 122:8 136:8</p> <p><b>continues</b> 11:18 53:21 61:14 66:11 89:4 117:5 125:20 142:5 144:13</p> <p><b>continuing</b> 44:15 47:22 52:21 54:3 54:22 60:15 77:9 87:17 89:1 126:11 140:5 148:16</p> <p><b>contracting</b> 80:21</p> <p><b>contractor</b> 91:10 93:13</p> <p><b>contribute</b> 95:14 132:7 133:11 137:9</p>	<p><b>contributions</b> 108:1</p> <p><b>control</b> 10:21 36:23 97:24</p> <p><b>controlled</b> 149:9 152:2,5</p> <p><b>controls</b> 3:19 10:4 58:5 59:25 62:24 63:2,12</p> <p><b>controversial</b> 153:1</p> <p><b>convene</b> 110:25</p> <p><b>convened</b> 113:10 116:14</p> <p><b>conversation</b> 39:1 123:25</p> <p><b>conversations</b> 72:16 145:6</p> <p><b>convert</b> 39:11</p> <p><b>coordination</b> 82:16</p> <p><b>core</b> 15:24 46:11 52:20 93:1 101:12 112:10 122:9 126:9</p> <p><b>correctly</b> 144:16</p> <p><b>correlated</b> 101:4,5</p> <p><b>costs</b> 89:15,16,20 90:8</p> <p><b>counsel</b> 156:10,13 157:7,10</p> <p><b>country</b> 154:1</p> <p><b>couple</b> 21:23 38:7 72:20 82:4 90:1,1 117:23</p> <p><b>course</b> 12:6,16,18 18:25 19:4 20:22 22:6 24:2 26:17 26:23 27:19 31:17 32:9 34:9 35:8 37:17 79:17 83:12 134:3</p> <p><b>cover</b> 10:11 31:3 90:8</p>	<p><b>covering</b> 21:24</p> <p><b>covid</b> 11:19 65:23 73:2 82:23 83:4 108:3,10 112:7,15 121:8 122:24 123:4 146:5,24</p> <p><b>craft</b> 37:14</p> <p><b>crafted</b> 33:11 37:19</p> <p><b>create</b> 23:7 24:11 35:20 39:23 85:7 103:8 120:2</p> <p><b>created</b> 33:11</p> <p><b>creating</b> 7:6 30:5 35:13 56:4 70:14 76:2</p> <p><b>creation</b> 30:2 128:6 135:13 136:3</p> <p><b>crisis</b> 112:18</p> <p><b>critical</b> 24:21 51:1 54:15 79:20 82:12 90:23 91:1 93:6 94:7 103:12 104:15 113:25 114:11,23 115:20 116:7 119:25 121:3 122:5 125:16 130:4</p> <p><b>criticality</b> 91:5</p> <p><b>criticisms</b> 152:25 153:1</p> <p><b>cross</b> 76:5 117:20 137:24</p> <p><b>crucial</b> 132:6</p> <p><b>crystal</b> 5:15</p> <p><b>culture</b> 22:22 148:17</p> <p><b>curation</b> 132:22</p> <p><b>cure</b> 125:19 141:16</p> <p><b>cures</b> 41:22 46:14 46:14,15,16 113:3 119:22</p>
--	---	---	---

<b>curing</b> 118:19 <b>current</b> 8:22 17:12 24:12 45:15 61:9 66:14 78:13 80:4,16 142:17 145:2 <b>currently</b> 7:4 8:21 96:19 102:22 136:16 <b>customer</b> 149:16 <b>customized</b> 147:11 <b>cutting</b> 126:17 <b>cycle</b> 22:7 24:2 40:15 45:16 63:7 63:23,24 64:19,19 64:21,21 65:17 68:25 72:13 99:13 108:12 121:21 134:16 145:18 <b>cycles</b> 38:12 53:13 92:2 99:14 <b>cynthia</b> 2:13 4:7 96:3 103:22,24 104:4 110:12	84:1,2,24,25 85:5 85:10 87:4,19 100:1 105:22 107:6 108:6,8,25 113:18,22 114:15 114:24 120:1,3,5 120:13 123:6 129:18 130:1,13 130:14 131:5,14 132:10,24 133:2,9 135:20 136:21,24 137:1,1 147:11,17 152:3,4 154:17,21 <b>datasets</b> 28:24 29:4,6 77:5 78:7 108:20 110:5 <b>date</b> 113:11 <b>dates</b> 29:23 <b>day</b> 74:21,21 149:14 155:24 <b>days</b> 48:7 49:20 65:16 <b>deadline</b> 8:17 <b>deadlines</b> 116:13 142:9 <b>deal</b> 35:11 <b>death</b> 144:24 <b>debate</b> 148:8 <b>debated</b> 153:5 <b>decade</b> 32:18 <b>decentralized</b> 74:18 83:5 109:5 123:8 137:19 <b>decision</b> 3:14 7:11 10:2 35:22 36:1 36:14 37:4 43:9 43:12,17 44:20,25 45:2,7 53:5,15 64:9 76:3 82:2,10 88:1,9 98:18 100:13 105:23 109:18 114:6 117:5 128:18 131:18,22 132:23	153:8 <b>decisions</b> 6:16 35:14 37:16,25 97:6 98:15 103:11 131:3 143:14,19 148:11 154:14 155:4 <b>deck</b> 96:5 <b>dedicated</b> 25:6 125:6 127:6 129:21 134:14 <b>deemed</b> 100:17 <b>deepened</b> 113:6 <b>deeply</b> 141:12 <b>defense</b> 97:14 <b>deficiencies</b> 64:7 64:14 <b>deficiency</b> 64:16 <b>define</b> 68:17 72:7 <b>definitely</b> 42:14 155:8 <b>degree</b> 116:10 <b>delay</b> 135:3 <b>delayed</b> 30:24 <b>delighted</b> 118:13 <b>deliver</b> 91:3 128:16 129:21 <b>deliverable</b> 60:6 <b>delivered</b> 104:23 <b>delivery</b> 109:20 <b>demand</b> 11:20 13:6 22:4,13 <b>demands</b> 83:24 85:4 120:20 <b>demonstrate</b> 60:9 97:13 128:25 <b>demonstrated</b> 115:1 <b>demonstrates</b> 142:3 <b>demonstrating</b> 62:4 107:16 <b>demonstration</b> 59:1,8,13 62:14	75:24 79:1 84:19 <b>dependent</b> 21:5 <b>depending</b> 37:3 108:18 <b>depends</b> 75:6 <b>deployed</b> 112:6 <b>deploying</b> 77:24 112:13 <b>derive</b> 130:14 <b>derived</b> 76:3 <b>dermaceuticals</b> 138:4 <b>describe</b> 119:10 <b>described</b> 16:13 46:16 57:24 70:8 86:16 89:24 119:1 <b>describes</b> 122:8 <b>describing</b> 64:12 <b>description</b> 64:13 <b>deserve</b> 110:23 <b>deserving</b> 112:18 <b>design</b> 16:21 26:25 35:1,24 47:14 50:3 55:25 56:2 59:5 60:3 72:3 120:15 <b>designed</b> 87:4 97:25 100:23 132:2 147:7 152:1 <b>designs</b> 7:9 15:16 23:9 44:5 47:12 48:23 49:2,10,16 49:17 50:5,22,22 50:22 53:11,18 59:10 62:10 115:13 131:8 137:18 <b>desire</b> 96:21 146:6 147:1 <b>desperate</b> 153:16 <b>desperately</b> 147:16 <b>desperation</b> 153:17
<b>d</b>			
<b>d</b> 5:1 31:1,13 38:25 115:25 128:6 <b>dap</b> 120:2,8 <b>data</b> 16:23 17:2,16 23:8 25:11 26:20 35:13,16,17,18,18 35:20,25 36:22,22 37:2,3,21 51:19 51:24 52:16 53:4 56:2 57:6,6,7,17 57:19 58:12,23 59:22 61:10 62:11 74:20 75:2,10,10 75:16 76:3 77:15 77:20,22,24,25 78:10 80:14,23 81:14,23 83:1,25			

<b>detail</b> 84:21 119:11	27:7 30:4,8,10,23 31:4,17,20 32:19	<b>dhts</b> 74:17 75:5,14 75:20 76:15 83:14 109:16,18,19,25	<b>disclosures</b> 134:4 <b>discretion</b> 133:4 <b>discuss</b> 29:20 37:12 50:21 58:6 73:1 89:6 91:17 126:15
<b>detailed</b> 26:23 68:11	33:3,6,9,16,20,21 33:24 34:2 35:3	<b>diagnostics</b> 114:10	<b>discussed</b> 18:20 22:18 36:21,24 39:16 46:6 70:16 90:25 126:12
<b>details</b> 63:19	36:18,23 38:12	<b>dialogue</b> 22:23 23:20 38:11	<b>discusses</b> 50:11 <b>discussing</b> 12:4 79:14 112:21
<b>detect</b> 58:17 147:7 147:7,7	42:16 44:3,4,19 44:20 45:14 46:23	<b>diana</b> 2:22 149:23 149:23 150:15 155:7	<b>discussion</b> 22:24 27:5,9 30:21 35:23 39:4 48:9 50:13 60:16 82:3 92:22 102:20 120:16 155:18
<b>determination</b> 34:13 59:4 62:9	47:3,5,8,10,15 48:5,18,20 49:9	<b>dictate</b> 110:5	<b>discussions</b> 15:13 15:13,15 17:18,25 24:4 38:9 41:24 42:8 44:7 68:16 72:7 92:1
<b>determinations</b> 56:24	49:11 51:25 52:9 52:11,19 53:7,11	<b>dictates</b> 75:25	<b>disease</b> 15:23 25:7 26:10 28:8 32:19 33:4,9,13 42:16 42:17 46:25 101:16 106:9 110:19,22,23,24 111:22 112:9,17 113:6 114:19 115:9,18 116:11 116:20 117:8 118:10,16,22 119:9,12,17,22 120:13,16 121:2 121:23 122:12,25 123:17 127:23 134:2,3,11 135:2 135:9 136:1,2,4 136:12
<b>determine</b> 17:2 20:18 27:17 29:9 55:11 56:6,13 128:8 154:6	53:14,22 54:1 58:2,11,20 59:20 60:5 66:24 67:3,5 67:6,8,9,12,18,20 67:22,23 68:6,12 68:14 69:5 71:15 74:16,17 75:17,20 82:13,20 85:13 100:6 101:12 104:18 107:3,12 111:4,10 113:2,9 113:25 114:9 115:11,18 117:6 120:10 121:17 122:1,4,6,23 123:9 125:12 127:14,25 128:18 131:8 132:18 133:1 134:10 136:15,18 137:13 138:5	<b>different</b> 17:5 20:20 31:3,7,9 49:2 57:11 58:23 59:10 68:8 76:25 118:16 126:6 139:13 148:22 150:19	<b>diseases</b> 4:11,14 15:22 23:16 32:17
<b>determined</b> 12:4	67:22,23 68:6,12	<b>difficult</b> 78:7 105:13 109:11 140:4	
<b>determines</b> 34:16	68:14 69:5 71:15	<b>difficulty</b> 78:5	
<b>determining</b> 56:3 57:18 59:15 62:17 135:22	74:16,17 75:17,20 82:13,20 85:13 100:6 101:12 104:18 107:3,12 111:4,10 113:2,9 113:25 114:9 115:11,18 117:6 120:10 121:17 122:1,4,6,23 123:9 125:12 127:14,25 128:18 131:8 132:18 133:1 134:10 136:15,18 137:13 138:5	<b>digital</b> 3:22 10:7,8 73:21 74:1,12,13 76:7 82:1,9,24 83:9 105:22 109:4 123:5,12 131:4 156:8 157:3	
<b>devastating</b> 125:20 128:24	104:18 107:3,12 111:4,10 113:2,9 113:25 114:9 115:11,18 117:6 120:10 121:17 122:1,4,6,23 123:9 125:12 127:14,25 128:18 131:8 132:18 133:1 134:10 136:15,18 137:13 138:5	<b>diligence</b> 143:9	
<b>develop</b> 16:24 32:22 35:25 37:18 55:9,23 58:22 59:14 80:20 97:3 98:5 120:15 122:17 131:24 141:10	104:18 107:3,12 111:4,10 113:2,9 113:25 114:9 115:11,18 117:6 120:10 121:17 122:1,4,6,23 123:9 125:12 127:14,25 128:18 131:8 132:18 133:1 134:10 136:15,18 137:13 138:5	<b>direct</b> 13:2 99:1 133:8	
<b>developed</b> 28:2 33:11,14 35:6 36:2,6,12 37:9 50:5 59:11	104:18 107:3,12 111:4,10 113:2,9 113:25 114:9 115:11,18 117:6 120:10 121:17 122:1,4,6,23 123:9 125:12 127:14,25 128:18 131:8 132:18 133:1 134:10 136:15,18 137:13 138:5	<b>direction</b> 32:2 39:22 127:19	
<b>developers</b> 47:13 120:4 125:23 126:15,16 128:14	104:18 107:3,12 111:4,10 113:2,9 113:25 114:9 115:11,18 117:6 120:10 121:17 122:1,4,6,23 123:9 125:12 127:14,25 128:18 131:8 132:18 133:1 134:10 136:15,18 137:13 138:5	<b>directly</b> 12:22 78:8 132:25	
<b>developing</b> 15:8 36:17 37:1 42:19 45:11 46:12 47:4 75:8 76:15 114:3 122:9 135:3	104:18 107:3,12 111:4,10 113:2,9 113:25 114:9 115:11,18 117:6 120:10 121:17 122:1,4,6,23 123:9 125:12 127:14,25 128:18 131:8 132:18 133:1 134:10 136:15,18 137:13 138:5	<b>director</b> 3:5 86:6 125:1 129:10	
<b>development</b> 7:8 7:10 16:14 18:24 19:15 23:2 25:2,6	104:18 107:3,12 111:4,10 113:2,9 113:25 114:9 115:11,18 117:6 120:10 121:17 122:1,4,6,23 123:9 125:12 127:14,25 128:18 131:8 132:18 133:1 134:10 136:15,18 137:13 138:5	<b>directors</b> 91:11 145:7	
	104:18 107:3,12 111:4,10 113:2,9 113:25 114:9 115:11,18 117:6 120:10 121:17 122:1,4,6,23 123:9 125:12 127:14,25 128:18 131:8 132:18 133:1 134:10 136:15,18 137:13 138:5	<b>disclose</b> 108:17 <b>disclosed</b> 108:23 <b>disclosure</b> 108:18	

32:20 33:15,16,17 33:22,22 42:14,20 67:1 104:12,12,13 110:18,21 111:25 112:4 113:11 114:22 117:14 118:12,18,19 119:15 120:5,7,22 123:1 125:20 128:1,24 133:25 <b>dismissing</b> 147:2 <b>disorders</b> 118:5 128:24 <b>disproportional</b> 139:18 <b>disproportionate</b> 111:25 <b>disregarding</b> 147:2 <b>dissemination</b> 57:21 <b>distances</b> 123:2 <b>distressing</b> 154:19 <b>diverse</b> 109:10 <b>diversity</b> 80:23 83:7 <b>division</b> 113:20 <b>divisions</b> 28:3 45:19 106:20 135:18 <b>dmap</b> 77:23 79:8 <b>docket</b> 8:11,12 43:4 95:15 124:4 155:19 <b>dockets</b> 8:14 <b>doctors</b> 141:19 <b>document</b> 24:8 66:13 70:13,17,18 70:20 72:12 73:14 76:2 88:18 <b>documents</b> 17:11 70:5 113:24 <b>doing</b> 13:11 14:7 16:2 46:23 55:12	60:13 65:6 79:7 79:17 93:5,25 119:21 130:25 <b>dollar</b> 138:14 139:5 <b>domains</b> 46:25 <b>donations</b> 140:21 <b>door</b> 148:19 <b>doors</b> 153:9 155:5 <b>dozen</b> 118:9 <b>dozens</b> 56:23 <b>dr</b> 5:8 118:2 150:14 <b>draft</b> 50:25 52:24 70:5 73:4,9,14 96:17 101:8 119:7 145:19 <b>dramatic</b> 120:23 <b>drive</b> 77:23 <b>driving</b> 148:11 <b>drowned</b> 148:25 <b>dru</b> 2:20 140:10 140:20 144:14 <b>drug</b> 1:4,9 3:4 7:8 7:9 10:1 16:14 23:2 25:2,6 26:7 26:18 28:11 30:4 32:19,24 33:3 34:8 42:16 44:3,4 44:18,20 46:23 47:3,8,10,15 48:5 49:10 50:7 51:24 52:8,11 53:11,14 53:21 54:15,17,20 56:9 58:11 60:10 62:4 74:16,16 82:13 85:13 95:12 98:15 100:5 101:11 104:2,16 104:17 105:2 113:9,24 114:8 115:10 118:11 120:10 121:25 122:4,5,23 123:9	127:25 128:18 130:17 131:7 133:1,4 136:18 140:19 142:24 143:7,14 144:7,23 145:2 146:9 <b>drug's</b> 143:10 <b>drugs</b> 27:25 28:7 29:24 30:5 51:1 53:7 58:12,13,21 66:25 97:15 99:20 114:9 130:3 132:4 141:10,14,20 144:3 146:8 149:5 149:7,9,12 152:17 <b>duchenne</b> 134:25 <b>due</b> 60:7 109:12 143:9 144:24 154:13 <b>duly</b> 156:5 <b>durable</b> 83:15 <b>dystrophy</b> 133:23 135:1,1	<b>easy</b> 77:18 125:15 142:19 <b>echo</b> 25:7 53:10 62:13 72:23 <b>ecosystem</b> 111:10 <b>ed</b> 2:15 4:13 96:3 117:13,15 123:21 <b>edge</b> 126:17 <b>edit</b> 94:18 <b>education</b> 13:13 104:8 118:20 <b>edwin</b> 118:2 <b>effect</b> 144:25 <b>effective</b> 24:1 41:8 71:13,17 72:17 75:16 84:6 110:25 126:10 128:9 141:5,14,20,22 142:11 145:9 146:18 154:6 <b>effectively</b> 77:25 <b>effectiveness</b> 29:21 55:4 56:18 59:23 62:4 99:13 107:5 130:3 135:23 142:6,14 <b>efficacy</b> 17:2,15 25:10 29:4 41:3,6 42:11 119:14 143:15 145:25 151:12 152:15 <b>efficiencies</b> 39:23 64:4 <b>efficiency</b> 15:2,6 15:19 26:5 28:10 47:11 58:1 99:12 109:20 <b>efficient</b> 24:1 31:17 32:13 41:7 78:14 126:9,20 <b>efficiently</b> 14:10 78:1 108:20 <b>effort</b> 55:18 61:23 63:20 64:8 81:24
		<b>e</b>	
		<b>e</b> 2:1,1 3:1 5:1,1 <b>eager</b> 117:2 <b>earlier</b> 28:11,12 29:8,13,13,14,15 29:23,25 30:22 31:18,20 36:7,8 49:10 67:14,21 79:24 86:17 90:25 107:18 120:20 121:18 <b>early</b> 30:8 33:3 38:14,14 68:7 95:17 107:15 108:12 119:20 138:9 <b>earned</b> 143:21 <b>ease</b> 151:3 <b>easier</b> 49:17 <b>easily</b> 147:11	

148:22 <b>efforts</b> 41:24 42:1 53:20 54:3 81:25 82:6 119:4 122:2 125:13 130:21,23 131:4 132:18,19 135:17 136:19 148:6 153:13 154:20 <b>ehr</b> 131:25 <b>eight</b> 48:1,12 49:23 124:14 <b>either</b> 74:19 135:19 146:1 <b>electronic</b> 78:24 <b>electronically</b> 77:2 78:8 <b>element</b> 42:4 <b>elements</b> 26:25,25 28:19,25 35:1 108:17 <b>elicit</b> 53:24 <b>embrace</b> 77:19 <b>emerge</b> 35:19 110:6 <b>emergency</b> 65:23 <b>emerges</b> 30:19 37:3 <b>emerging</b> 35:10 69:15 73:2 82:23 115:22 <b>emmanuel</b> 156:2 156:17 <b>emphasis</b> 17:3 45:20 115:19 151:2 <b>emphasize</b> 25:1 41:18 42:13 53:16 61:19 62:5 73:1,8 99:6 <b>emphasizing</b> 18:14 24:18 <b>employed</b> 67:14 156:11,14 157:8	157:10 <b>employee</b> 156:13 157:10 <b>enable</b> 23:1 38:11 39:18 41:7 54:22 57:25 60:15 74:18 <b>enabled</b> 57:1 113:19 123:6 <b>enables</b> 38:14 <b>enactment</b> 134:6 <b>encourage</b> 8:11 33:10,18 63:17 103:17 104:17 108:13,23 116:3 124:6 127:18 128:1,11 130:22 <b>encouraged</b> 107:16 116:20 121:19 142:13 <b>ended</b> 152:13 <b>endpoint</b> 33:6,9 33:14,24 42:17 100:16 115:9 119:12 127:23 131:7 136:4 <b>endpoints</b> 15:15 32:23,25 33:10,11 33:12,21 34:3 42:19 44:24 100:11 114:6 119:14 120:15 136:6,12 <b>ends</b> 60:16 <b>engage</b> 42:19 121:16 123:24 128:12 132:25 <b>engaged</b> 7:20 95:24 122:11,15 <b>engagement</b> 7:25 22:23 23:20 40:9 54:2 68:7 71:14 84:11 95:25 112:12 113:1,7,14 113:15,20 114:8	115:7,16,23 122:2 123:17 128:15 132:11,15 143:22 <b>engagements</b> 40:14 72:6 111:6 133:8 <b>engaging</b> 23:10 57:19 <b>enhance</b> 14:25 15:3 26:5 28:9 33:19 34:2 47:6 54:20 56:12 60:10 63:14,20 76:16 79:10 81:10,11 83:10 86:23 109:20 132:12 154:16 <b>enhanced</b> 14:14 53:23 54:2 65:9 70:23 92:14 115:23 <b>enhancement</b> 27:15 44:17 47:9 49:12 50:1 <b>enhancements</b> 3:8 3:10,15,17,20,23 3:25 5:14 6:24 7:10,14 8:9 9:11 10:24 25:16,24 26:4,16 43:9,17 43:24 44:1 45:16 51:4 54:6 57:6 61:24 63:3 74:1 85:22 86:16,20 89:1 90:25 105:9 112:21 129:17 <b>enhancing</b> 7:5,7 9:23 75:9 76:17 100:8 115:20 <b>enjoy</b> 140:8 <b>enlightening</b> 51:15 <b>enquiries</b> 61:7	<b>ensure</b> 23:25 38:10,13 40:13,15 42:15 53:5 56:1,9 64:21 65:19 68:19 69:1 71:12,14 83:23 84:5,11,24 85:4,7,12 93:22 104:16 116:23 117:4 126:25 128:20 132:18 135:17 <b>ensures</b> 92:20 <b>ensuring</b> 22:18 40:7 55:13 72:15 86:14 91:1 93:6,7 94:2,6 99:25 100:9 104:23 115:2 117:9 120:19 122:22 128:16 <b>enter</b> 94:11 <b>entered</b> 36:14 <b>entering</b> 50:9 <b>enterprise</b> 85:2 <b>entire</b> 9:15 93:1 <b>entirely</b> 28:15 <b>entitle</b> 142:1 <b>environment</b> 27:13 74:21 77:22 78:2,13 79:3,10 79:22 80:3 148:10 <b>environmental</b> 109:10 <b>epidemiologist</b> 152:3 <b>equally</b> 121:16 143:2 <b>equivalent</b> 90:17 <b>es</b> 156:4 <b>esg</b> 84:15 <b>esham</b> 2:3 21:17 21:21 38:5 51:8 60:22 71:5 81:19 83:18 92:25
--	--	--	---

<p><b>especially</b> 11:11 11:23 15:20 19:19 78:6 114:13 127:25</p> <p><b>essential</b> 29:1,9 104:20 121:13 123:13</p> <p><b>essentially</b> 44:6 65:23</p> <p><b>establish</b> 38:24 87:8,9,15 102:8 102:13 130:18,23 131:4,14</p> <p><b>established</b> 13:20 13:22 39:18 47:24 55:19,19 76:8 89:2 101:18</p> <p><b>establishes</b> 38:21 42:17</p> <p><b>establishing</b> 90:3 90:13 109:15 119:14 127:19</p> <p><b>establishment</b> 90:7</p> <p><b>estimated</b> 112:1</p> <p><b>estimates</b> 125:24</p> <p><b>et</b> 61:13 74:23 75:11 99:15 101:13</p> <p><b>evaluate</b> 14:22 34:22 52:16 58:17 75:21 106:17 130:2 143:14 150:22 151:12</p> <p><b>evaluating</b> 15:14 61:10 75:2</p> <p><b>evaluation</b> 3:4 53:1 60:1 88:21 106:24</p> <p><b>evaluations</b> 52:17 91:14 151:9</p> <p><b>event</b> 147:20</p> <p><b>events</b> 146:19</p>	<p><b>eventually</b> 132:8</p> <p><b>everchanging</b> 148:8</p> <p><b>evergreen</b> 38:9</p> <p><b>everybody</b> 21:18 24:5 26:2 43:22 74:13 86:4 94:19</p> <p><b>everyday</b> 145:2</p> <p><b>everylife</b> 4:10 110:17,20 115:5 116:19</p> <p><b>everyone's</b> 43:3</p> <p><b>evidence</b> 11:14 15:16 18:1 23:9 25:12 26:10 35:8 35:13,21 36:3,19 37:22 41:19 42:2 42:10 44:25 46:1 56:22 60:2 61:11 61:25 62:3 97:24 98:1 100:12,22 105:21 115:12,22 127:23 129:23 130:1,2,4 131:7 135:23 137:4,19 151:11</p> <p><b>evidenced</b> 136:7</p> <p><b>evident</b> 112:20 115:7</p> <p><b>evidentiary</b> 114:19</p> <p><b>evolution</b> 44:9 51:11 111:14 112:25</p> <p><b>evolve</b> 130:15</p> <p><b>evolved</b> 6:10 27:13 101:1</p> <p><b>evolves</b> 40:19,19</p> <p><b>evolving</b> 13:7 15:8 17:9 107:24</p> <p><b>exacerbated</b> 111:23</p> <p><b>example</b> 14:8,16 15:17 18:14 25:11</p>	<p>32:22 53:12 62:7 68:25 82:21 93:11 94:2 96:22 98:12 99:8 116:14 132:4 153:2</p> <p><b>examples</b> 66:18 82:24 92:13 97:8 115:13</p> <p><b>exceed</b> 89:15</p> <p><b>exceeded</b> 11:20</p> <p><b>exceeding</b> 116:13</p> <p><b>excellence</b> 76:7 78:16 135:10</p> <p><b>excellent</b> 21:24 51:9</p> <p><b>exception</b> 108:11 154:9</p> <p><b>exchange</b> 78:18</p> <p><b>excited</b> 40:22 41:12 52:12,24 54:3 73:16 82:6</p> <p><b>excitement</b> 72:23</p> <p><b>exciting</b> 27:23 33:2 35:7 37:20 38:16 39:5 41:10 125:16</p> <p><b>exclude</b> 153:10</p> <p><b>excluded</b> 19:13 20:10 58:10</p> <p><b>excuse</b> 21:1 76:9 122:14</p> <p><b>execute</b> 77:8</p> <p><b>execution</b> 16:21</p> <p><b>exercising</b> 66:3</p> <p><b>existence</b> 20:7</p> <p><b>existing</b> 13:8 15:14 16:23 20:12 56:5 73:7 81:13 110:5</p> <p><b>expand</b> 52:9 74:12 130:12 135:16</p> <p><b>expanded</b> 30:17 66:1 113:19 115:19</p>	<p><b>expanding</b> 41:11 45:18 75:21 107:1</p> <p><b>expansion</b> 37:5 38:19 135:10</p> <p><b>expect</b> 22:14 45:14 130:12</p> <p><b>expectation</b> 146:2</p> <p><b>expectations</b> 16:19 38:22 64:22 76:14</p> <p><b>expected</b> 48:3 55:15 67:20</p> <p><b>expedite</b> 67:19</p> <p><b>expedited</b> 17:18 69:5 137:6,11,13 145:22</p> <p><b>expediting</b> 100:5</p> <p><b>expeditiously</b> 127:15</p> <p><b>expended</b> 45:9</p> <p><b>expense</b> 146:5</p> <p><b>experience</b> 16:22 17:23 37:19 50:3 51:19,24 66:13 70:9 75:1 98:8 113:18,22 114:15 117:4 136:21</p> <p><b>experienced</b> 112:25 121:7</p> <p><b>experiences</b> 62:11 129:23 130:5</p> <p><b>expert</b> 93:20</p> <p><b>expertise</b> 13:22 75:1,8,19 76:13 80:20 86:15 91:3 91:10 92:6 93:14</p> <p><b>experts</b> 147:5</p> <p><b>explaining</b> 64:5</p> <p><b>explanation</b> 64:16</p> <p><b>explicitly</b> 72:24 100:20</p> <p><b>explore</b> 16:6,17 17:6 23:12 46:9 47:13 79:1</p>
---	---	---	---

<p><b>exploring</b> 7:11 15:18 16:22 17:14 100:12</p> <p><b>exposed</b> 58:21</p> <p><b>extensions</b> 44:14</p> <p><b>extent</b> 61:22</p> <p><b>external</b> 15:9 25:8</p> <p><b>externally</b> 79:17 113:9</p> <p><b>extra</b> 72:6 96:4</p> <p><b>extract</b> 19:8,13,23 20:4,5,9,16 77:7 78:9 133:5</p> <p><b>extraordinarily</b> 51:15 83:22</p> <p><b>extremely</b> 132:23</p> <p style="text-align: center;"><b>f</b></p> <p><b>face</b> 17:13 39:11 39:11 67:5 126:19 126:19 141:18</p> <p><b>faced</b> 17:9</p> <p><b>facilitate</b> 13:12 14:14 26:12 30:10 30:23 31:20 33:8 33:16,21 49:16 59:4 62:9 75:15 103:19 108:7 119:24 124:6 135:16</p> <p><b>facilitated</b> 32:13</p> <p><b>facilitating</b> 10:5 107:18 136:20</p> <p><b>facilities</b> 65:17,21 65:25 66:2,16,22 73:5</p> <p><b>facility</b> 138:25 139:2,20,22 144:4</p> <p><b>facing</b> 29:19 37:10 106:16 147:17</p> <p><b>fact</b> 44:13 53:6 109:8 111:22</p> <p><b>factor</b> 34:6,7,9,13 34:25 35:2</p>	<p><b>faculties</b> 118:6</p> <p><b>faers</b> 147:9</p> <p><b>fails</b> 143:10</p> <p><b>faith</b> 143:20</p> <p><b>falb</b> 2:16 124:21 124:25 125:1</p> <p><b>fall</b> 108:13</p> <p><b>fallen</b> 151:1</p> <p><b>familiar</b> 6:5 7:1 9:13 74:13 104:7</p> <p><b>families</b> 145:1</p> <p><b>family</b> 141:2</p> <p><b>far</b> 11:20 30:7 42:22 72:18</p> <p><b>fashion</b> 5:15 32:6 34:24</p> <p><b>fast</b> 101:1 146:10</p> <p><b>faster</b> 24:9,11 67:23 101:3,4 142:25 146:4 151:5</p> <p><b>fda</b> 3:5 6:9 7:21,23 8:3 9:6 25:18 30:9 31:11,17 32:2 33:19 35:11,24 36:5,17,24 39:24 41:3 42:14 46:2 46:12 47:18 48:17 49:7,23 50:6,8,11 50:13,14 51:23 54:9 55:3,14,17 55:20,23 57:1,3,5 57:14,25 58:25 59:24 60:9,24 62:24 64:10,14,17 65:2,9,13,20 66:1 66:11,13 67:12 68:13,18 70:18 73:1,10,14,22 75:6,15,22 77:1 77:25 78:12 79:12 80:6 81:1,11,24 82:7,16,18,22 83:13,23 86:8</p>	<p>91:6,7 92:5 93:3,4 93:12,25 97:3,19 97:23 98:3,6,14 98:16 100:2,2 102:5,12 103:2,6 103:9,13,17 104:1 104:18,20 105:5 106:1,12,13,16,20 107:23 108:13,23 109:2,16,25 110:8 111:9 112:4 113:9 114:18,20 115:1 115:14 116:10,14 118:10 119:7,19 120:2,17 121:3,15 122:3,14 123:10 125:11 128:2,10 130:21 131:12,20 132:25 133:5,7 134:1,17,22 135:8 141:8,13,19,21,23 142:4,7,8,13 143:5,11,13,18,20 143:25 145:24 146:2 148:5,6,18 149:14 151:4,17 151:18 152:16,24 154:14,24 155:1</p> <p><b>fda's</b> 54:16 56:12 56:19 58:9 61:19 75:18 77:14 88:23 94:5 97:6 99:6 101:10,14,25 105:1 107:2 109:17 110:1 115:6 118:24 119:4 122:2,8 131:3,23 132:12 132:18 135:20 143:21 146:7 148:13 149:4 153:24</p> <p><b>fdas</b> 65:14 92:22</p>	<p><b>feasible</b> 50:14 66:1 108:15</p> <p><b>feature</b> 109:9</p> <p><b>february</b> 7:22</p> <p><b>federal</b> 89:24</p> <p><b>fee</b> 1:9 6:9 7:5 46:18 86:25 89:22 89:23 95:12 104:2 138:19 139:3,8 141:25</p> <p><b>feedback</b> 8:10,15 31:20 36:24 59:7 70:11 92:19 133:12</p> <p><b>feel</b> 98:16 151:15 155:5</p> <p><b>feels</b> 65:13</p> <p><b>fees</b> 11:7 20:1,2,20 54:20 60:10 138:8 138:9,16,25,25 139:9,12,12,17 140:3,5,19 141:23 152:20 154:11 155:2</p> <p><b>felt</b> 11:21 12:7 14:1 99:1 111:24</p> <p><b>fewer</b> 134:2</p> <p><b>field</b> 11:16 12:10 13:7,16 15:8 16:5 17:4,9,20 23:25 105:15 115:6 116:16 129:2</p> <p><b>fields</b> 147:12</p> <p><b>fifth</b> 137:5</p> <p><b>fight</b> 128:23</p> <p><b>figure</b> 154:20</p> <p><b>fill</b> 130:4</p> <p><b>filled</b> 59:1</p> <p><b>final</b> 8:7 48:22 60:6 123:23 129:18</p> <p><b>finalization</b> 8:4</p> <p><b>finalize</b> 70:19</p>
---	--	---	---



<p><b>finally</b> 36:6 50:24 59:12 97:22 102:12,16 109:2 117:13 122:21 137:5 148:17 <b>finance</b> 3:25 10:9 85:18,22 91:20 <b>financial</b> 7:5 86:8 86:9,12,19,20,20 86:24 88:20,25 89:3,5,7,10 90:12 90:21 92:11,15,21 96:15 102:3 124:7 125:3 145:10 148:25 <b>financially</b> 156:14 157:11 <b>financials</b> 92:1,10 <b>find</b> 45:4 47:14 49:8 79:23 88:13 120:12 <b>findings</b> 91:13,17 <b>fine</b> 81:22 100:15 140:16 <b>finished</b> 45:15 <b>first</b> 22:16 44:18 48:8 49:21 58:18 79:9 81:20 86:9 87:2 88:3,12 90:17 96:6 97:10 99:13 105:6 134:22 139:7,24 140:17 146:25 <b>firsthand</b> 144:2 <b>firsts</b> 105:6 <b>fiscal</b> 68:3 89:25 90:19 127:4 <b>fit</b> 114:4 <b>fits</b> 138:17 <b>five</b> 38:4 59:8 97:8 153:11 154:11 <b>fixtures</b> 123:9 <b>flag</b> 146:15</p>	<p><b>flatiron</b> 129:11,14 129:20 130:9,21 131:13 132:6,16 132:21,25 <b>flexibility</b> 135:8 <b>flexible</b> 104:20 <b>floor</b> 129:8 <b>focus</b> 6:21 7:4 22:3 23:15 45:19 53:25 57:25 65:5 68:15 71:7 72:7 91:15 105:17 112:23 118:11 132:17 145:22 150:18 <b>focused</b> 7:8 9:23 16:14 25:6 31:14 39:1,4 44:3,18 45:12,22 46:22 47:3,8,10 48:4 49:1 52:8,11 68:16 75:24 86:19 87:17 96:20 104:20 107:23 111:4 113:8,11,24 114:8 115:10 122:4,5 136:18 <b>focusing</b> 43:25 52:8 146:16 <b>folks</b> 5:22 6:25 7:13 95:9 <b>follow</b> 9:20,21 39:15 <b>followed</b> 9:14 91:17 <b>following</b> 6:2 46:16 48:8 49:21 101:9,24 145:21 <b>food</b> 1:4 19:16 20:23 <b>foods</b> 19:18 <b>foot</b> 112:16 139:2 139:22</p>	<p><b>footprint</b> 47:23 <b>forced</b> 111:14 123:1 <b>fore</b> 29:17 <b>forecasting</b> 87:20 <b>foregoing</b> 156:3,4 157:4 <b>foreign</b> 66:8 <b>form</b> 46:7 <b>formal</b> 47:21 113:13 <b>formalization</b> 128:6 <b>formalized</b> 30:14 <b>formally</b> 102:10 <b>format</b> 31:19 138:23 <b>formation</b> 113:14 <b>formats</b> 115:23 <b>forth</b> 13:1 14:12 36:16 76:19 123:11 <b>forum</b> 111:13 <b>forward</b> 25:15 29:16 41:13,25 52:21 54:1 76:1 77:17,18 78:4 104:22 107:22 110:9 116:15 133:11 137:9 144:12 154:9 155:18 <b>forwarded</b> 36:6 <b>foster</b> 120:8 <b>fostered</b> 105:5 <b>found</b> 98:13 <b>foundation</b> 4:10 110:18,21 115:5 116:19 <b>foundational</b> 86:13 87:13 <b>founded</b> 118:15 <b>four</b> 54:24 63:25 64:1,11,12 65:6</p>	<p>95:25 96:2 154:5 <b>fourth</b> 9:1 54:9 136:17 <b>fragmented</b> 80:4 <b>frame</b> 47:6 <b>framework</b> 58:22 59:7,11,13 76:2,8 77:23 109:15 123:13 131:5,24 133:8 154:4 <b>frameworks</b> 107:4 <b>free</b> 99:1 148:7 <b>frequent</b> 74:22 <b>frequently</b> 24:5,7 <b>friendly</b> 147:19 <b>friends</b> 137:10 <b>frontier</b> 128:23 <b>frontiers</b> 130:11 <b>frs</b> 136:9 <b>ftes</b> 52:2,3 106:20 121:12 <b>fulfill</b> 106:2 <b>fulfilled</b> 152:11 <b>full</b> 5:8 49:14 103:13 126:23 132:8 142:4 143:5 155:21 <b>fully</b> 32:2 63:19 74:19 103:2 123:7 128:14 <b>function</b> 99:25 122:19 <b>functions</b> 12:24 <b>fund</b> 147:5 154:11 <b>funded</b> 16:10 120:2 122:14 <b>funding</b> 6:24 14:5 14:11 16:10,11 46:20 90:8 104:16 <b>funds</b> 6:11,14 46:13,18 88:19 89:15 <b>further</b> 37:21 46:6 59:19 79:8,10</p>
--	---	---	---

87:24 95:14 100:20,21 107:13 111:23 112:10 113:18 115:15 116:4 121:7,12 131:18 135:17,25 136:1,20,20 155:19 156:12 157:9 <b>furthering</b> 107:3 <b>furthermore</b> 127:18 134:25 <b>future</b> 24:12 47:4 48:19 53:25 95:19 105:10 107:9 129:18 130:19 131:5 132:2 <b>fy</b> 90:18	114:9 120:21,23 121:1,3,6 125:12 126:14 127:8 128:16 134:14,19 134:22,25 <b>general</b> 37:13 61:6 98:13 <b>generally</b> 19:25 34:3 99:4 <b>generate</b> 131:7 <b>generated</b> 75:2,16 82:3 155:17 <b>generation</b> 26:20 85:11 117:10 <b>generators</b> 131:15 <b>genetic</b> 120:22 130:7 <b>geneticist</b> 118:3 <b>genzyme</b> 118:8 <b>geographic</b> 109:11 <b>germane</b> 98:19 <b>getting</b> 19:20 29:6 75:2 148:22 <b>girdle</b> 135:1 <b>give</b> 5:25 9:3 21:16 30:21 44:12 80:15 96:4,22 97:6 <b>given</b> 22:3,17 32:6 48:12 66:12 108:21 114:22 115:17 122:24 <b>gives</b> 97:19 <b>giving</b> 31:20 <b>glad</b> 154:15 <b>global</b> 111:21 <b>globally</b> 125:24 126:1 <b>globe</b> 66:20 <b>go</b> 6:6,6 7:15 9:3 10:11 38:9 39:22 40:19 44:11 74:8 75:4 77:13 81:21	84:9 86:18 95:6 102:18 117:25 124:17,18 150:6 <b>goal</b> 29:12 44:19 47:20 49:15 50:1 51:21 54:20 56:3 56:13 58:14 64:20 65:14 67:24 72:15 99:11,17,18 100:6 121:20 122:22 131:21,23 135:6 136:24 141:24 142:24 <b>goals</b> 6:18 20:24 29:22 55:12,20 72:25 91:7 92:4 96:18 97:5 100:10 100:14 104:3 105:10,18 119:13 119:23 121:24 122:5,8 123:11,13 128:13 131:20 132:8 145:25 151:1 <b>going</b> 5:4,7,22,25 6:4 16:2 17:22 21:15,22 22:2,10 23:20 24:14 30:2 37:11 38:6,20 39:22,23 40:2 41:15 42:23 43:16 43:25 44:12 51:11 52:5 54:8,10,23 62:22 63:16 71:24 72:20 73:20 75:4 80:1,2 81:20 84:1 85:17 86:9 95:7 95:21 96:4 98:23 105:14,16 116:12 123:22 124:20 139:24 149:20 150:3,18 151:15 152:2,6 155:8,10	<b>gold</b> 97:24 149:7 <b>good</b> 5:19 11:1,4 21:8,17 24:16 26:2 40:23 41:10 43:22 45:24 55:12 63:5 64:17 86:4 96:13 97:14 103:25 121:2 124:25 129:9 133:19,21,22,22 140:17 144:17,20 144:21 148:3 149:17 150:13 <b>government</b> 8:3 138:11 <b>graham</b> 2:6 5:19 7:16 8:8 11:1 19:6 26:1 38:2 43:21 54:13 60:18 71:1 74:3 81:15 85:15 85:24 91:21 94:9 104:4 <b>grant</b> 126:19 <b>granted</b> 128:11 <b>grateful</b> 111:19 116:22 119:7 121:22 141:9 <b>gratified</b> 115:19 <b>great</b> 11:4 18:10 21:21,22 24:23 26:1 30:3 32:20 32:20 35:9,11 38:6 83:19 86:3 92:3,9 103:25 120:21 123:2 144:21 149:4 150:14 151:6 155:23 <b>greater</b> 36:4 37:1 131:16 <b>greatest</b> 48:18 <b>grew</b> 87:6 <b>gross</b> 139:18
<b>g</b>			
<b>g</b> 5:1 <b>gain</b> 41:6 131:15 <b>gained</b> 17:23 18:22 40:10 <b>gaining</b> 50:3 <b>gaps</b> 58:25 59:9 106:22 130:4 <b>gate</b> 141:21 <b>gatekeeper</b> 102:1 <b>gateway</b> 78:24 <b>gather</b> 95:10 <b>gathering</b> 25:4 108:6 <b>geared</b> 26:9 <b>gene</b> 9:24 11:11 11:22,24 12:3,8 12:13,14,19 13:3 13:16 14:19,23 15:20,23 16:7,16 16:20 17:4,16 18:2,5 19:2 23:3 23:13,17 24:24 25:3,5 80:1 105:7 105:20 106:6,7,11 106:14,17,25			

<p><b>group</b> 11:7 17:7 86:8,12 96:8 129:12</p> <p><b>groups</b> 9:21 35:19 36:23 111:2 140:25 149:1</p> <p><b>grow</b> 11:24</p> <p><b>growing</b> 13:7,9 57:9 71:11 83:24 109:8</p> <p><b>grown</b> 49:14</p> <p><b>growth</b> 26:10 126:3 130:8,10 139:12</p> <p><b>guardian</b> 141:21</p> <p><b>guidance</b> 23:21 24:9 32:10,11 35:4 40:4 45:12 47:4 48:19 50:25 52:25 53:19 54:1 55:7 59:14 66:13 73:4,9 107:12,21 113:24 121:17 130:21</p> <p><b>guidances</b> 18:24 27:20 34:2 37:19 45:23 55:6 56:5,5 70:14 75:25 76:14 109:19 114:7 115:21 136:23</p> <p><b>guide</b> 76:2</p>	<p><b>hard</b> 116:23 120:12 139:19 152:3 155:5</p> <p><b>harm</b> 103:11</p> <p><b>harmed</b> 141:3 151:8 153:14,19</p> <p><b>harmonize</b> 14:23</p> <p><b>harmonizing</b> 81:13</p> <p><b>harmony</b> 63:25 64:1,12 65:6</p> <p><b>harms</b> 146:19 147:1 154:13</p> <p><b>harness</b> 125:18</p> <p><b>harnessed</b> 107:8</p> <p><b>harvard</b> 118:7</p> <p><b>hash</b> 103:6</p> <p><b>health</b> 3:22 4:6 10:7,8 54:16,21 58:9 60:14 65:23 73:21 74:1,12,14 76:7 82:1,9,24 83:9 94:8 96:7,14 97:5,7 99:19 103:12 104:9 105:22 106:3 108:24 109:4 112:14,18 117:10 123:5,12 129:11 129:20,20 131:4 131:11 132:10 141:8,17 143:19 143:24 145:5 150:16,17 153:7 154:3,25 155:1,3 155:6</p> <p><b>healthcare</b> 34:11 55:5 74:14,15</p> <p><b>healthier</b> 141:11</p> <p><b>hear</b> 5:24 8:9 11:2 18:25 21:20 74:4 74:5 85:24 86:1 93:24 95:1,22 117:19,21 133:16</p>	<p>133:17,19 138:1 143:21 144:18 149:11,24,25 153:13 154:15,19</p> <p><b>heard</b> 9:16 25:5 39:20,21 79:23 104:14 120:20 128:21 150:20</p> <p><b>hearing</b> 5:21 149:20</p> <p><b>heavily</b> 8:5 9:23</p> <p><b>heightened</b> 57:11</p> <p><b>held</b> 7:23,23 46:8 71:16</p> <p><b>hello</b> 43:21 118:2</p> <p><b>help</b> 25:9 35:2 42:18 45:2 47:12 55:7,25 56:1 57:8 57:14 59:21 64:8 65:19,21 67:1 85:9 87:4 90:12 101:12 107:9 119:23 120:8 126:7 127:17,25 129:2 130:4 132:14,18 141:11 151:15 152:21</p> <p><b>helped</b> 55:9 141:2 141:23 151:7</p> <p><b>helping</b> 6:12 37:22 116:16 129:21</p> <p><b>helps</b> 75:14 77:17 151:22</p> <p><b>hereto</b> 156:14 157:11</p> <p><b>hhs</b> 8:3 98:12</p> <p><b>hi</b> 86:4 124:25 137:25 138:1,3 150:14</p> <p><b>high</b> 22:4,4 46:1 61:7 71:24 120:18</p> <p><b>highlight</b> 92:14 97:9 98:24 102:21 109:24</p>	<p><b>highlighted</b> 106:1 135:21 145:12 146:5</p> <p><b>highlights</b> 9:6 90:21</p> <p><b>highly</b> 90:9 139:18</p> <p><b>hill</b> 138:4</p> <p><b>hire</b> 6:14 91:2</p> <p><b>hires</b> 127:4</p> <p><b>hiring</b> 3:25 10:10 12:25 16:2 85:22 86:11,11 89:11,19 90:7,9,23,23 91:1 91:6,7,9,20 92:1 92:10 93:16</p> <p><b>historic</b> 60:25</p> <p><b>historically</b> 58:10 83:11</p> <p><b>history</b> 6:8 15:17 25:12 104:24 119:17</p> <p><b>hold</b> 59:2 73:10 74:15 120:21 127:24</p> <p><b>holding</b> 75:22</p> <p><b>holistic</b> 61:21</p> <p><b>hope</b> 24:9 31:19 33:12,12,25 37:7 37:23 70:22 84:21 93:17 135:5,17 136:12,13 140:14 141:16,16,18 143:11,23</p> <p><b>hopefully</b> 5:14 15:4 30:22 71:6 72:14 94:4 135:4 141:20</p> <p><b>hoping</b> 150:11</p> <p><b>hospital</b> 118:7 147:21</p> <p><b>hospitalized</b> 108:9</p> <p><b>host</b> 117:24</p> <p><b>hosting</b> 109:17</p>
<b>h</b>			
<p><b>half</b> 43:13 113:11 145:11</p> <p><b>hamburg</b> 150:24 154:24</p> <p><b>hand</b> 81:15</p> <p><b>handful</b> 136:9,15</p> <p><b>happen</b> 150:3</p> <p><b>happened</b> 147:24</p> <p><b>happening</b> 22:16 40:14 71:14 72:16</p> <p><b>happy</b> 153:13</p>			

<b>hour</b> 94:13	128:12 134:8	<b>improved</b> 59:25	50:7 56:24 57:6
<b>house</b> 57:2	<b>implemented</b> 37:1	78:11 81:12,14	63:21 65:12 66:3
<b>hr</b> 7:5 91:11	76:8 84:13 86:21	<b>improvement</b>	66:7 69:8 72:24
<b>human</b> 10:1 34:6	87:12	60:11 88:5	77:3 83:4,7 87:13
34:7,9,13,25,25	<b>implementing</b>	<b>improvements</b>	88:15 100:6 105:6
35:2 58:12 93:14	57:5	57:25 91:15 106:8	105:12 114:22
97:7	<b>imply</b> 79:21	109:24 142:18	116:12 135:11
<b>humans</b> 30:7	<b>import</b> 39:2 60:23	<b>improving</b> 122:6	137:7,12,18
<b>husband</b> 144:24	71:12 84:23	134:23	153:18
<b>hybrid</b> 74:19	<b>importance</b> 22:18	<b>inappropriately</b>	<b>inclusion</b> 76:16
<b>i</b>	24:18 25:1,4,8	101:19	109:14 110:3
<b>iceberg</b> 101:17	26:15 35:9 51:17	<b>inaudible</b> 8:25	114:14 119:12
<b>ich</b> 68:11	58:4 62:13 82:15	19:3 46:20 48:10	136:23
<b>idea</b> 28:6,14 33:8	93:6 94:6 104:2	72:25 150:7	<b>incorporate</b> 55:24
36:5,8,20 46:21	145:15	<b>incentivize</b> 116:5	68:9 128:17
78:25 146:20	<b>important</b> 13:17	<b>inception</b> 138:9	<b>incorporated</b>
<b>ideally</b> 45:5	14:1,1 15:21	<b>inceptions</b> 19:12	128:3
<b>identification</b>	19:14 21:25 26:9	<b>include</b> 21:1 32:10	<b>incorporating</b>
38:14	27:2,14 28:8	33:23 36:15 42:3	114:5 121:25
<b>identified</b> 64:5,7	32:12 37:15 40:8	45:18 59:5 62:10	<b>incorporation</b>
64:25 120:5	40:9 46:22 52:8	64:12 66:18 68:7	19:7 131:2
142:23	62:6 65:11 71:7	68:23 69:5,13,25	<b>increase</b> 6:23,24
<b>identify</b> 55:25	72:9 77:7 83:22	70:11,13,17 73:4	11:10,18 12:11
58:25 65:7 114:2	93:18 99:24 102:6	88:2 92:4 101:23	13:25 32:16 42:9
<b>identifying</b> 53:25	106:10 109:7	105:19 109:10	76:11 80:2,2,22
64:3 84:18 118:19	114:3,17 121:16	131:10 137:20	110:4 120:23
<b>ignores</b> 152:24	123:24 125:15	147:22 151:9,24	121:6,7,12 139:12
<b>ii</b> 6:17	126:4,15 128:7,15	153:6,14	<b>increased</b> 11:13
<b>iii</b> 6:19 97:25	128:17 132:24	<b>included</b> 7:22	11:20 22:4,12
149:8 152:2	141:7 143:2	19:25 20:2 23:14	41:19 42:4 61:25
<b>impact</b> 56:22	147:10 148:6,23	47:1 55:6,23	66:6 67:25 68:18
74:14 97:5,7	152:6,12 153:10	69:24 86:24 87:7	75:3 82:2 83:2
134:20,20 141:17	153:18	105:9 130:5 134:9	105:3 123:7
<b>impactful</b> 137:2	<b>importantly</b> 42:3	136:13 137:15	143:22
<b>implement</b> 59:14	53:23 114:12	148:20	<b>increases</b> 75:18
86:16 90:25	<b>improve</b> 10:1	<b>includes</b> 8:3 9:22	<b>increasing</b> 13:6
127:16 154:3	47:11 54:21 57:8	21:1 24:20 28:24	19:18 34:20 54:21
<b>implementable</b>	60:13 61:5 81:2	56:17 58:19 62:5	60:14 80:1 83:7
92:5	81:10 93:19 94:4	64:2,22 68:4	106:17 109:17
<b>implementation</b>	96:17 126:7	82:17 84:14	126:13
62:16 69:9 70:1	128:25 129:24	107:17 126:6	<b>increasingly</b> 49:9
73:12 75:5,20	130:18 132:19	127:12 128:19	106:4
76:6 84:9 88:3,12	153:13	<b>including</b> 7:11 8:4	<b>ind</b> 11:13 30:12
88:15,17 113:17		10:1 11:8 23:3	67:20 116:9

<b>independence</b> 102:6	143:25 146:2 149:2,17 153:15	<b>infrequent</b> 98:10	133:5,11 153:6 155:17
<b>independent</b> 88:21 91:10 93:13 129:11 140:23 145:8 154:12	<b>industry's</b> 72:23 <b>ineffective</b> 99:20 150:23 153:25 <b>inefficiencies</b> 77:3	<b>initial</b> 6:3 7:18 28:18,24 59:7 148:20	<b>inputs</b> 90:6 <b>insights</b> 93:18,23 104:1 109:22 114:15 120:6 130:14 132:12
<b>indicated</b> 28:12 134:1	<b>infancy</b> 113:2 <b>infectious</b> 104:12	<b>initially</b> 6:11 36:9 46:14	<b>insist</b> 143:6
<b>indicates</b> 11:6 152:22	<b>inference</b> 59:20	<b>initiating</b> 16:1 58:1	<b>inspected</b> 65:18
<b>indication</b> 29:10 37:5	<b>inflation</b> 89:16	<b>initiative</b> 56:16,17 57:10,18 58:19 59:6,19 60:12 61:9,15 131:24 142:16	<b>inspection</b> 65:11 65:20 66:5,8,19
<b>indications</b> 29:25 42:12 49:1 152:17 152:19	<b>influenced</b> 56:23	<b>initiatives</b> 62:6 77:16 79:18 92:3 104:18 105:4 126:9 127:16 128:20	<b>inspections</b> 65:16 144:4 148:14 154:5,7,10
<b>indirect</b> 13:2,9 99:2	<b>influx</b> 134:13	<b>innovations</b> 24:19 26:6 30:3 33:10 79:3 104:17 115:20 135:25 136:2 150:25	<b>inspector</b> 98:13
<b>individual</b> 50:2	<b>inform</b> 18:23 34:24 45:2 58:12 58:15 87:5 117:5 129:24	<b>innovation</b> 24:19 26:6 30:3 33:10 79:3 104:17 115:20 135:25 136:2 150:25	<b>instance</b> 75:18 77:6,12,21 78:15 78:18
<b>individual's</b> 107:7	<b>informatics</b> 3:22 10:8 73:22 74:1	<b>innovative</b> 7:9 10:6 15:16 23:9 29:15 30:19 33:20 44:5 48:23 50:3 53:10,14 63:15 67:17 69:10,19,21 70:1,24 72:3 73:12 115:13,18 131:8 137:14,18	<b>instantiates</b> 30:13
<b>individuals</b> 17:13 18:16 141:9	<b>information</b> 15:19 18:22 24:10 25:11 27:3 28:17 29:19 31:5,6 45:1,6,10 46:4 48:17 50:13 50:16 53:24 57:3 61:5 63:21 64:5,6 65:3,7 66:4,7,22 68:21 71:23 76:23 77:7 78:18 80:24 83:14 88:14 97:6 103:19 108:22 113:16 124:10 126:7 136:21 142:18 143:16 147:12 154:22	<b>input</b> 9:8 23:17 25:5 30:9 31:11 32:6 36:8 37:13 42:8 44:21 46:4 46:24 52:14,22 53:24 69:12 70:12 70:19 73:11 82:11 92:19 95:10,14 114:2 131:10	<b>institute</b> 120:1
<b>inds</b> 20:1 21:4 120:24 121:1,6,7 121:10,10	<b>informational</b> 15:19 18:22 24:10 25:11 27:3 28:17 29:19 31:5,6 45:1,6,10 46:4 48:17 50:13 50:16 53:24 57:3 61:5 63:21 64:5,6 65:3,7 66:4,7,22 68:21 71:23 76:23 77:7 78:18 80:24 83:14 88:14 97:6 103:19 108:22 113:16 124:10 126:7 136:21 142:18 143:16 147:12 154:22		<b>instituted</b> 101:7
<b>industries</b> 13:18 13:20,21 96:21	<b>informative</b> 126:21		<b>instituting</b> 114:24
<b>industry</b> 7:21 9:7 12:1,6 13:13,18 14:2 16:5 17:7 18:10,16 19:21 21:10,16,16 25:19 35:11 40:6 42:1 42:14 44:7 45:22 54:11 58:4 60:20 61:19 62:10 65:9 65:10 69:17 71:18 73:1 75:19 79:12 81:25 82:5,5,22 83:3,13 85:12 99:2 102:2,4 103:2,5 108:25 115:14 119:8 125:13 134:18 141:10,13 142:7,9	<b>informed</b> 7:9 44:4 47:10 53:11,21		<b>instructed</b> 136:25
	<b>informing</b> 114:8		<b>instructions</b> 142:8
	<b>infrastructure</b> 110:2 111:5		<b>insufficiencies</b> 58:3
			<b>integral</b> 56:19
			<b>integrate</b> 14:3 55:5 82:13 87:24 88:8
			<b>integrated</b> 28:22 53:6
			<b>integrating</b> 137:13
			<b>integration</b> 14:6 51:24 113:21
			<b>integrity</b> 101:20
			<b>intend</b> 68:2 69:4
			<b>intended</b> 31:13 35:21 66:25 68:19 75:7 132:22
			<b>intense</b> 49:5
			<b>intensive</b> 77:8

<p><b>intent</b> 28:6 30:17 33:18 <b>intention</b> 148:4 <b>interact</b> 14:24 30:13 38:19 109:1 115:24 128:5,9 <b>interaction</b> 33:19 49:6 67:11 <b>interactions</b> 13:13 14:15 15:11 32:13 36:4,16 102:9 <b>interactive</b> 101:11 101:17 126:22 <b>interest</b> 9:22 18:10 35:9 37:23 46:25 145:10,15 <b>interested</b> 127:22 156:15 157:11 <b>interests</b> 111:3 124:7,9 148:25 149:2 <b>interference</b> 145:15 <b>interfering</b> 155:3 <b>internal</b> 14:18,21 15:11 18:16 135:20 <b>internally</b> 45:19 <b>international</b> 14:17 125:6 <b>internationally</b> 13:14 140:3,4 <b>introduce</b> 78:25 <b>introduced</b> 6:23 57:11 <b>introducing</b> 9:25 <b>introduction</b> 10:7 <b>intuitive</b> 147:18 <b>invaluable</b> 119:19 <b>investigate</b> 147:1 <b>investigational</b> 74:23 <b>investment</b> 45:8</p>	<p><b>investments</b> 147:6 <b>invitation</b> 118:24 <b>invited</b> 95:23 <b>inviting</b> 110:17 <b>involve</b> 18:20 48:4 49:4 <b>involved</b> 12:18 44:9 47:17,25 102:8 138:8 148:22 <b>involvement</b> 16:21 18:21 153:12 <b>involves</b> 59:19 60:4 <b>involving</b> 70:9 <b>issuance</b> 53:23 68:4 92:15 <b>issue</b> 20:16 38:14 38:15 39:3,3,16 48:17 50:24 53:19 54:14 64:15 66:13 73:14 127:13 <b>issued</b> 70:5 75:24 113:23,23 <b>issues</b> 5:4,7 26:19 30:6,8 31:3,4,7,9 31:12,14,16,23 32:5 33:15 35:17 38:9 46:9 48:5,10 64:4,7,13,24 82:8 109:1 115:22 126:16 145:14 146:15 150:19,19 <b>issuing</b> 46:3 73:9 75:24 <b>it'd</b> 149:4 <b>it'll</b> 88:7 <b>item</b> 97:16,22 103:7 <b>iterative</b> 24:13 84:12 <b>iv</b> 6:19,21 54:17</p>	<p><b>j</b> <b>janet</b> 54:13 <b>janet's</b> 5:8 9:16 <b>january</b> 8:18,19 55:7 <b>jerry</b> 2:19 137:24 138:3 140:9 <b>job</b> 1:23 21:24 55:12 <b>jobs</b> 93:5 <b>join</b> 86:5 <b>joining</b> 12:16 50:12 118:5 <b>joneckis</b> 10:12 11:1,4,5 <b>jordan</b> 2:17 129:6 129:7,9,10 <b>josh</b> 85:19 86:6 91:23,24 92:16,25 <b>joshua</b> 2:11 <b>journey</b> 51:12 <b>judge</b> 102:2 <b>july</b> 118:25 <b>jump</b> 6:7 8:24</p>	<p>152:20 <b>kinds</b> 37:12 47:7 49:9 93:17 98:22 154:17 <b>kish</b> 3:4 5:11,19 <b>know</b> 5:22 7:13 10:15 11:15 13:11 22:17 29:3,24 38:8 42:24 45:14 45:24 48:2,8 61:3 67:1,23 74:13 79:16 81:3 90:23 93:1 94:17 97:7 109:23 110:13 117:18 125:15 138:12 139:19 140:5 143:18,20 149:5,11 151:15 152:12,12 153:20 <b>knowledge</b> 18:9 18:12,17 23:22,23 23:24 50:4 58:25 59:9 75:9 81:12 144:3 156:9 157:6 <b>knowledges</b> 18:17 <b>known</b> 39:8 152:18 <b>knows</b> 122:2 134:19 146:17</p>
		<p><b>k</b> <b>k</b> 100:7 <b>k.v.</b> 157:2,15 <b>keep</b> 17:11 47:23 80:11 119:4 124:1 <b>keeps</b> 121:4 <b>kennedy</b> 2:14 4:10 96:3 110:13,16,19 <b>key</b> 14:13 23:10 24:10 26:25,25 36:20 55:25 77:16 77:16 147:13 <b>kick</b> 7:19 29:1,7 29:14 <b>kickoff</b> 6:4 <b>kim</b> 2:21 144:15 144:22 149:22 <b>kind</b> 15:5 37:14 48:11 151:14,21</p>	<p><b>l</b> <b>label</b> 28:13 29:10 37:5 <b>labeling</b> 52:17 56:24 58:13,16 61:13 107:20 <b>lack</b> 119:15 151:11 <b>landscape</b> 106:5 113:5 114:11 <b>language</b> 99:5,9 99:16 142:19 <b>large</b> 13:20 14:3 17:3 77:5 78:7 81:12 83:25 110:5</p>

<b>largely</b> 29:3 87:16	102:25 103:6,8,18	<b>little</b> 7:15 24:8	<b>loved</b> 111:18
<b>lastly</b> 23:19 24:3	104:4 105:10,18	28:23 39:7 42:22	<b>lower</b> 114:18
52:23 85:6 139:23	115:8 116:13,21	44:12,16 81:3	<b>lucy</b> 2:4 21:15
149:3	119:7,13 121:24	96:4 136:6	24:15,17 25:19
<b>late</b> 64:19,21	122:8 123:11	<b>live</b> 124:1 145:1	38:4 41:16 43:19
<b>launch</b> 122:12	125:14 127:12	<b>lived</b> 111:15	51:7 53:8 60:20
<b>launched</b> 76:7	130:17 131:21	<b>lives</b> 114:12 129:1	61:17 71:4 72:21
<b>lead</b> 9:5 11:6,7	143:23 153:4,4	134:23 141:11	81:16,17,20,21
26:3 131:1	154:2	<b>living</b> 111:25	83:18 91:23 92:25
<b>leaders</b> 23:11	<b>letting</b> 110:8	<b>load</b> 96:6	<b>lunch</b> 4:2 85:18
<b>leadership</b> 79:13	<b>level</b> 16:18 27:16	<b>loaded</b> 10:20	94:11,13,15 95:7
111:8,17 127:18	108:18 113:19	110:14	<b>m</b>
<b>leading</b> 120:6	120:5,13	<b>long</b> 77:1 97:4	<b>main</b> 105:17
125:5	<b>leverage</b> 18:16	112:8	<b>maintain</b> 22:22
<b>lean</b> 117:2	61:22 82:22 83:4	<b>longer</b> 47:22	60:24 80:17
<b>learn</b> 40:6 66:12	108:20 147:4	94:14 142:3	143:11
93:19 94:4 149:12	<b>leverages</b> 104:19	<b>look</b> 6:4 14:5 15:2	<b>maintained</b> 11:19
<b>learned</b> 51:16	<b>leveraging</b> 18:9	15:21 17:14 30:4	52:7 90:15 122:24
69:6,14 70:8 73:2	23:22 79:11	35:19 41:13 44:2	<b>maintaining</b> 57:16
82:23 83:14	<b>license</b> 65:15	52:21 54:1 75:12	61:9
122:23 128:2	<b>licensed</b> 20:4,9	77:13 102:21	<b>major</b> 12:9 16:12
<b>learnings</b> 29:20	<b>lieu</b> 66:5	110:9 133:11	19:6 58:8
37:12,17 41:6,13	<b>life</b> 63:24 107:5	144:12 155:18	<b>majority</b> 12:18
42:5 72:11 83:15	<b>lifecycle</b> 63:23	<b>looked</b> 9:12	22:15 28:16
130:20 133:5	117:6	<b>looking</b> 15:23	100:18
<b>leaving</b> 109:19	<b>lifestyle</b> 107:7	16:23,25 17:5,10	<b>making</b> 7:11
<b>led</b> 51:20 86:7	<b>lift</b> 80:8,15,15	17:22 29:16 41:25	10:16 14:6 16:4
113:9,10 118:10	<b>light</b> 145:14	67:7 78:20,20	18:3 35:22 44:21
119:25	<b>likewise</b> 79:19	79:7,8 84:17 98:8	44:25 45:2,7,25
<b>left</b> 117:22 124:20	<b>limb</b> 135:1	105:3	53:5 64:23 76:4
<b>legislation</b> 8:6	<b>limitations</b> 108:21	<b>looks</b> 5:6 10:19	77:18 82:2,10
<b>legislative</b> 110:11	<b>limited</b> 12:23,23	36:11 150:4	88:1,9 98:18
<b>lessons</b> 37:8 69:6	16:3 58:11 68:15	<b>lost</b> 150:5	100:13 105:23
69:14 70:8 73:2	74:25 78:17	<b>lot</b> 10:11 13:20	109:19 114:6
82:23 83:13	119:17 136:14	15:22 16:1,8	117:5 128:19
122:23 128:2	<b>limiting</b> 72:1	17:13 22:18,24	131:18,22 132:23
136:14	<b>limits</b> 100:16	35:23 49:6 72:18	153:8
<b>letter</b> 8:17 9:11	<b>line</b> 119:22 122:11	74:15 76:23 77:3	<b>manage</b> 77:7,25
16:13 40:11 44:2	<b>linkages</b> 57:6	77:10 82:3 83:3,6	80:22 90:12
46:21 63:18 83:22	<b>listed</b> 60:4 78:22	88:13	<b>management</b> 7:6
84:4 96:17 97:4	101:24	<b>loud</b> 21:20 74:5	14:7 22:20 32:11
99:5,9,11,22	<b>listen</b> 114:25	86:1	40:4 75:11 81:13
100:5,7,21 101:9	<b>listening</b> 122:3	<b>love</b> 148:15	81:14 109:6
101:22 102:7,12		149:11 152:3	132:13

<b>managing</b> 89:20 <b>mandated</b> 152:10 <b>manner</b> 24:13 40:15 58:17 84:4 84:22 107:23 141:25 143:3,7 <b>manufacturer</b> 147:21 <b>manufacturers</b> 18:15 140:22 <b>manufacturing</b> 3:19 10:4,5,6 18:6 31:6 62:23 63:2 63:12,15 65:13,19 65:25 66:16 67:17 69:7,8,11,21 70:3 70:10,24 72:24 73:5,13 106:24 138:5 144:4,5 154:5 <b>mapp</b> 59:14 68:9 <b>mapps</b> 27:20 70:14 <b>march</b> 8:1 <b>marked</b> 32:16 121:5 <b>marker</b> 142:23 <b>market</b> 3:10,17 6:20,22 7:2 9:25 10:3 25:16,24 26:3,7 40:13,17 54:6,9 57:15 59:4 59:16 60:8,17 61:12 62:8,10 99:21 142:2 143:6 143:8 144:7 146:4 146:16,21,22 147:10 151:16 152:5,7,7 <b>marketed</b> 101:6 <b>marketing</b> 26:17 26:22 27:1 58:15 62:18 101:5 152:10	<b>marking</b> 57:5 <b>marks</b> 53:1 <b>mary</b> 2:10 10:9 73:23,23 81:19,23 83:5,19 <b>massive</b> 121:7 <b>match</b> 120:19 <b>materials</b> 48:8 49:21 145:20 <b>matter</b> 47:14 <b>matters</b> 51:17 144:23,25 <b>maturation</b> 92:22 113:4 <b>mature</b> 87:17,22 88:6 92:12 <b>maturing</b> 11:16 <b>maximum</b> 45:25 <b>mda's</b> 134:16 <b>meaningful</b> 42:8 100:19 105:15 113:12 114:25 136:7,11 143:1,4 <b>means</b> 20:16 <b>meant</b> 69:1 125:19 <b>measured</b> 98:20 <b>measurement</b> 122:20 <b>measurements</b> 60:3 132:1 <b>measures</b> 20:8 46:12 92:21 96:18 96:19,23 97:1,2,5 97:9,11 98:5,22 103:15 150:22 <b>mechanism</b> 90:3 123:24 132:24 145:16 <b>medical</b> 4:14 54:23 60:15 67:2 100:18 104:24 105:13 114:10 118:3,4,7 141:17 145:9,16	<b>medicare</b> 57:7 <b>medication</b> 141:16 <b>medications</b> 97:21 141:3,6,15,24 142:11,22 <b>medicinal</b> 74:16 75:17 <b>medicine</b> 4:7 103:23 104:6,11 105:11,16,24 106:10 107:10 109:7 125:2,17 128:22 <b>medicines</b> 17:20 105:1 125:7 141:22 <b>medwatch</b> 142:15 147:9 <b>meet</b> 13:6 16:7 56:4 57:16 67:2 75:15 83:24 85:4 93:8,9 94:7 129:3 <b>meeting</b> 1:8 6:4 7:18,19 8:7,8 9:14 9:17,20 10:16,17 16:14 24:6 30:25 30:25 31:1,10,13 31:19,22 32:5 37:11 38:25 40:4 40:4 47:17 48:6,9 48:25 49:19,19,21 50:6,18,19,19 55:12 56:3,13 63:11 64:21 65:17 89:6 91:17 92:17 93:23 95:10,17,18 95:19,20 102:20 106:3 115:25 118:25 123:22 124:13 125:5 126:19 128:5,6,13 134:12 140:8 144:12 145:20 152:16 155:13,16	155:21 <b>meetings</b> 7:23 11:13 13:8 16:6,8 17:6 18:9,22,23 25:6 30:2,12,18 31:2,2,8 32:3,9 33:7 38:23 39:13 39:15 40:3,8 48:4 48:14 51:15 57:22 64:20 68:15 71:14 71:16 72:17 75:23 79:12 103:2,5 113:9,10 116:15 119:3 121:14 122:4 133:3 136:23,25 142:15 143:25 148:15,19 148:21 153:9 <b>meets</b> 21:9 <b>melmeyer</b> 2:18 133:15,17,21,23 <b>member</b> 98:17 118:22 126:16 <b>members</b> 98:7 104:9 116:22 125:10 141:2,4 <b>mention</b> 47:2 139:4 153:24 <b>mentioned</b> 8:8 9:2 22:17 23:10,14 39:15 40:1,12 41:23 42:5 52:21 53:23 54:14,16 61:20,25 63:6,10 69:18 71:25 72:4 73:14 83:5 90:22 92:16 104:4 <b>met</b> 35:23 64:22 <b>methodologic</b> 50:25 <b>methodological</b> 45:12 46:5,9 55:21 131:16
--	--	--	--



<p><b>methodologically</b> 44:22 45:3</p> <p><b>methodologies</b> 61:6 87:20 112:5</p> <p><b>methodology</b> 51:1 59:24 87:10,15 90:6</p> <p><b>methods</b> 45:21 59:20 60:5 114:2 126:17 130:13</p> <p><b>metrics</b> 55:25</p> <p><b>michael</b> 2:12 4:5 96:2,5,7,13 103:22</p> <p><b>mid</b> 64:19,21 65:17</p> <p><b>midd</b> 47:10,11 48:18 115:24</p> <p><b>middle</b> 99:10 148:24</p> <p><b>milestones</b> 41:22 68:17 72:8</p> <p><b>million</b> 111:24 118:17 139:2,21 148:1</p> <p><b>mind</b> 95:5 124:1</p> <p><b>minded</b> 149:19</p> <p><b>minimize</b> 5:22 99:14 102:13</p> <p><b>minimizing</b> 99:19</p> <p><b>minimum</b> 90:13 90:14,16</p> <p><b>minute</b> 43:13 94:14,23 136:8</p> <p><b>minutes</b> 9:14,17 9:20 25:21 38:4 94:13,14 96:5 105:16 124:15</p> <p><b>missed</b> 95:9,17</p> <p><b>missing</b> 53:22</p> <p><b>mission</b> 54:16 58:9 93:2 94:7 101:13 104:21 106:2 155:3,6</p>	<p><b>missteps</b> 97:20</p> <p><b>mistakes</b> 97:20</p> <p><b>model</b> 7:9 44:3 47:10 53:11,21</p> <p><b>modeled</b> 40:24 72:2</p> <p><b>modeling</b> 115:23</p> <p><b>models</b> 47:19 115:25</p> <p><b>modern</b> 68:9,10 77:6 85:13</p> <p><b>modernization</b> 14:22 60:11 77:14 77:15 79:11,20 80:7,12,15 81:23 84:10 85:1 110:1 121:20 131:10 132:19</p> <p><b>modernize</b> 23:2 78:23 79:4 87:9</p> <p><b>modernized</b> 77:22 80:4</p> <p><b>modernizing</b> 6:22 7:4 135:20</p> <p><b>modifications</b> 56:6 90:1,5</p> <p><b>modified</b> 99:17 101:23</p> <p><b>modifying</b> 114:4</p> <p><b>moment</b> 112:23</p> <p><b>monetization</b> 84:3</p> <p><b>money</b> 14:20 154:18</p> <p><b>monitor</b> 78:23 142:5 143:13 144:5</p> <p><b>monitoring</b> 58:7 74:22 79:13 123:5 142:17</p> <p><b>month</b> 28:20 29:13 115:8</p> <p><b>months</b> 28:20,23 29:13 97:1 111:12 118:6</p>	<p><b>morning</b> 5:19 11:1 11:5 21:13,17 24:16 26:2 43:22 86:4 104:14 133:22</p> <p><b>motivation</b> 148:2 148:3</p> <p><b>move</b> 5:11 6:17,20 10:21 25:15 29:23 29:23 42:23 43:16 51:7 54:8 56:14 62:22 76:20 85:17 95:8,21 107:22 123:22 127:15 155:11,12</p> <p><b>moved</b> 7:3</p> <p><b>moves</b> 110:10 123:18</p> <p><b>moving</b> 66:17 73:20 76:1 77:16 79:2 137:12 154:9</p> <p><b>mullin</b> 2:7 43:18 43:21,22</p> <p><b>multi</b> 138:14 139:21,21</p> <p><b>multibillion</b> 139:5</p> <p><b>multiple</b> 18:12,17 33:23 36:16 42:6 69:10,11 70:2,3 78:15,22 82:24 122:3</p> <p><b>multitude</b> 140:25</p> <p><b>muralidharen</b> 157:2,15</p> <p><b>muscular</b> 133:23 134:24 135:1,1</p> <p><b>mutations</b> 130:7</p> <p><b>mute</b> 95:5</p> <p><b>mutual</b> 58:3 66:9 68:20</p> <p><b>myriad</b> 76:19</p> <p><b>mythological</b> 45:23</p>	<p><b>n</b></p> <p><b>n</b> 2:1 3:1,1 5:1</p> <p><b>name</b> 11:5 63:6 86:5 124:25 129:9 140:19 144:21 155:8</p> <p><b>named</b> 66:2,16 73:5</p> <p><b>names</b> 139:4</p> <p><b>narratives</b> 147:22</p> <p><b>narrower</b> 31:15</p> <p><b>nation</b> 111:18</p> <p><b>national</b> 4:13 14:17 117:13 118:4 150:15 154:3</p> <p><b>nationally</b> 13:14</p> <p><b>natural</b> 15:17 119:17</p> <p><b>nature</b> 25:12 114:22</p> <p><b>nda</b> 64:23 68:24 98:9 101:1,20 103:11 138:19,22</p> <p><b>near</b> 95:19 108:13 132:13</p> <p><b>nearly</b> 8:13</p> <p><b>necessary</b> 8:16 12:7 13:2 49:6 56:8 71:15 91:2 99:14 106:23 142:10</p> <p><b>necessity</b> 59:15 62:17 83:1 108:5</p> <p><b>need</b> 12:2 13:23 16:23 22:3,9,25 27:1,18 28:8,9 30:9 32:20,21,22 34:17,18 36:1 51:22 58:25 59:1 64:6 65:17 75:11 75:25 79:15,20 80:11,20 93:21 94:12 100:24</p>
--	--	--	--

103:5 106:5,16 114:21 139:11 141:5 143:18 145:12 146:12,14 146:18,22 147:4,9 147:19,25 148:6,7 148:14 149:3,14 149:17,17 150:22 152:12 <b>needed</b> 11:21 22:6 34:14 35:1 51:21 54:22 56:8 60:15 64:14,16 84:25 85:3 86:15 106:1 108:7 116:17 131:10 147:16 154:8 <b>needs</b> 12:4 21:9 23:15 46:6 67:2 80:8 83:13,24 85:5,8,13 87:5,10 87:19 90:4 93:3,4 105:13 110:5 116:23 119:8 121:18 137:14 143:20 146:25 147:12,18 150:25 153:21 <b>negative</b> 58:5 59:25 <b>negotiated</b> 136:16 153:9 <b>negotiation</b> 7:19 9:15 103:1 148:21 <b>negotiations</b> 7:20 12:1 22:2 71:9 87:7 119:5 129:16 144:1 153:8 <b>negotiators</b> 9:5 14:2 63:7 125:13 134:18 <b>neilan</b> 2:15 4:13 96:3 117:13,17,20 117:23 118:2	<b>neither</b> 156:10 157:7 <b>network</b> 77:20 140:21 141:7 145:8 <b>network's</b> 144:11 <b>neuromuscular</b> 133:25 134:11 135:9 136:12 <b>neuropathy</b> 136:9 <b>new</b> 7:6 9:25 10:1 10:3,7 14:4 15:14 15:18 16:24 18:6 19:7,15 20:1 22:21 23:12 26:4 27:6,21 28:12 29:10,25 30:2,3,4 30:5,20,25 37:5,6 37:18 38:18,25 39:5 40:12 45:19 51:3 56:4 57:6 58:18 59:18,20 62:13 63:11,13 66:23 67:17 68:4 70:14,22 71:8 73:6,16 75:16,24 77:24 86:16 87:10 87:15 90:7 96:24 100:10 105:1 106:17 107:19 110:6 112:13 113:19 115:24 118:10 120:6 121:12 122:12 126:17 128:13 130:12,24 131:1,1 151:1 <b>newer</b> 13:21 20:22 21:3 <b>newly</b> 39:18 152:22 <b>news</b> 121:2 <b>nice</b> 39:12,17 95:7	<b>nishan</b> 155:8 <b>non</b> 20:14 23:23 46:18 108:25 147:5 <b>nonprofit</b> 104:8 140:24 <b>nonproprietary</b> 18:12 <b>nontraditional</b> 108:5 <b>nord</b> 118:4,5,13 118:15,24 119:2 119:11,21 120:1 121:19,22 122:1 122:10,11,15,21 123:9,16 <b>nord's</b> 119:1,6 123:15 <b>normal</b> 48:13 <b>northwestern</b> 122:15 <b>notable</b> 105:5 <b>notary</b> 156:1 <b>note</b> 22:1 24:3 34:4 114:17 119:20 124:7 <b>noted</b> 8:11,21,22 89:18 121:18 <b>notice</b> 89:24 <b>notification</b> 20:6 43:1 94:16 <b>notify</b> 50:15 <b>notifying</b> 65:14 <b>novel</b> 16:25 17:1,8 18:6 25:10,12 30:6 33:5,20 35:16 39:3,8 50:22 53:17 76:15 <b>november</b> 113:18 <b>nuanced</b> 114:21 <b>nucoat</b> 122:16 <b>number</b> 7:10 9:10 12:14,23 14:4 22:12 27:11 31:8	31:15,23 32:16 34:20 68:16 84:10 99:14 102:15 103:7 105:2 106:17 109:8 120:23 128:10 134:16 147:4 149:5,7 154:2,4 154:11 <b>numbers</b> 11:13,20 106:20 <b>numerous</b> 113:8 114:7 <b>o</b> <b>o</b> 3:1 5:1 135:11 <b>objective</b> 103:10 154:12,21 <b>objectivity</b> 102:6 <b>obligations</b> 152:11 <b>observational</b> 132:3 <b>observe</b> 65:20 143:25 <b>observed</b> 65:14 <b>obtain</b> 15:19 <b>obtained</b> 41:14 <b>obtaining</b> 25:10 <b>obviously</b> 29:18 30:3 76:11 81:9 146:5 <b>occasionally</b> 20:15 <b>occur</b> 15:7 34:16 48:7 133:9 <b>occurred</b> 31:3 <b>occurs</b> 13:14 67:23 <b>oce</b> 135:17 <b>october</b> 8:13 19:25 20:4,10 <b>offer</b> 97:7 134:5 142:25 <b>offering</b> 39:5,12 <b>offers</b> 99:23 141:16
--	--	---	---

<p><b>office</b> 3:5 12:20,20 14:8 27:25 98:12 <b>officer</b> 4:15 118:4 156:2 <b>offices</b> 12:21 28:3 <b>oftentimes</b> 24:4 67:5,12 126:15 <b>oh</b> 76:21 81:7,20 117:24 150:4,5 <b>okay</b> 6:7 9:10 42:21 43:15,21 54:4,13 62:20 73:18 74:6,11 85:16 94:10,25 95:21 100:14 101:14 103:21 129:9 138:3 140:17 149:25 150:2,7,14 <b>old</b> 80:17 <b>oldest</b> 6:9 <b>omb</b> 8:3 <b>onboard</b> 14:3 22:21 93:4 94:5 <b>onboarding</b> 14:6 22:15,15,19 <b>once</b> 40:17 102:21 145:22 <b>oncology</b> 27:25 28:1 40:25 41:5 78:16 135:10,11 <b>ones</b> 16:12,24 44:8 111:18 <b>ongoing</b> 27:24,24 56:21 61:23 109:8 109:12 119:21 126:1 142:16 149:4 <b>online</b> 124:12 <b>ood</b> 27:25 <b>oops</b> 145:21 <b>open</b> 8:11,13 103:2 123:23 149:18</p>	<p><b>opened</b> 95:15 <b>opening</b> 7:16 9:16 <b>openness</b> 148:18 <b>operate</b> 81:10 <b>operating</b> 90:11 90:14 <b>operation</b> 77:22 78:25 90:17 <b>operational</b> 56:20 86:23 87:25 88:9 <b>operationalized</b> 128:8 <b>operations</b> 65:20 79:2 90:19 91:11 93:14 <b>opinion</b> 146:14 <b>opioid</b> 153:25 <b>opioids</b> 154:4 <b>opportunities</b> 82:7 103:9 110:6 112:8 113:12 116:24 133:12 <b>opportunity</b> 36:16 42:7 50:18 63:13 73:11 77:10 78:11 92:18 102:5 104:1 119:19 123:15 125:4 129:15 133:10 140:18 144:10 150:17 <b>opposed</b> 97:25 <b>optimal</b> 22:23,23 59:4 <b>optimization</b> 15:2 60:12 <b>optimize</b> 15:6 56:15 58:19 59:19 131:23 <b>optimized</b> 27:8 <b>optimizing</b> 132:21 133:6 <b>options</b> 48:14 148:15</p>	<p><b>orbis</b> 78:16 <b>order</b> 12:15 46:1 124:19 <b>organization</b> 4:13 104:8,21 110:22 117:1,14 118:5 125:6 144:23 <b>organizational</b> 76:5 <b>organizations</b> 108:25 111:1 116:7 118:17,22 131:14 132:6,11 132:16,24 133:9 <b>organize</b> 14:10 <b>original</b> 88:15 152:25 <b>otat</b> 12:20 14:8 <b>outcome</b> 38:16 45:13 46:11 52:20 75:10 114:4,5 122:7,16 151:3 156:15 157:12 <b>outcomes</b> 12:9 58:21 62:15 71:20 100:19 106:8 107:8 117:10 122:13,20 132:20 <b>outdated</b> 136:10 <b>outline</b> 70:6 73:15 88:4 <b>outlined</b> 38:18 70:18 130:16 131:20 134:17 <b>outputs</b> 75:21 <b>outreach</b> 13:11 14:18 45:22 <b>outside</b> 48:19 132:25 135:11,16 147:5 <b>outweigh</b> 55:14 56:9 <b>overall</b> 21:7 24:18 88:6 155:13</p>	<p><b>overcome</b> 18:7 119:20 <b>overcoming</b> 67:10 <b>overhaul</b> 153:21 <b>overseen</b> 91:11 <b>oversight</b> 154:4 <b>overused</b> 111:11 <b>overview</b> 3:3 5:13 5:17 9:4,6 10:9 21:22 25:15 43:16 <b>owners</b> 138:4</p> <p style="text-align: center;"><b>p</b></p> <p><b>p</b> 2:1,1 5:1 <b>p.m.</b> 94:15,19 <b>pace</b> 125:21 133:7 <b>package</b> 8:4,6 56:12 77:19 <b>page</b> 3:2 <b>paid</b> 107:2 154:1 <b>pair</b> 48:4 53:22 <b>paired</b> 47:17 48:25 49:18 50:6 50:17 <b>pandemic</b> 66:17 73:3 82:25 83:15 83:16 108:4 109:13 111:19,21 111:23 112:6,15 122:24 123:4 145:11 148:13 154:8 <b>paradigm</b> 19:11 <b>parallel</b> 7:22 79:22 109:20 <b>part</b> 14:13,21 15:3 16:5,10 17:8 19:6 26:14 30:15 54:16 54:25 55:2 58:8 63:25 64:1,12 65:6 72:4 84:8 94:1 95:9,17 102:17 114:16 119:21 124:2,13 135:19 137:2</p>
--	---	---	---

153:7 <b>partially</b> 10:7 123:7 <b>participants</b> 74:21 <b>participate</b> 15:10 50:17 96:1 110:8 123:3 <b>participated</b> 119:3 145:19 <b>participating</b> 68:12 83:8 <b>participation</b> 83:11 108:7,15 113:13 133:2 <b>particular</b> 9:7,22 18:2 23:16 28:7 28:21 32:22 33:9 33:13 39:2,2 55:13 <b>particularly</b> 6:21 9:24 10:4 18:4 31:22 76:6 82:8 106:5,15 115:19 142:21 <b>parties</b> 156:11,14 157:8,11 <b>partner</b> 102:2,3 149:16 <b>partners</b> 18:10 66:9,20 111:2 117:2 119:8 <b>partnerships</b> 14:17 15:11 18:20 <b>parts</b> 41:7 74:19 <b>party</b> 65:1 71:22 88:21 91:8 103:9 <b>pass</b> 92:24 <b>passage</b> 8:20 17:24 <b>path</b> 119:25 122:12 <b>pathway</b> 131:14 132:5 137:8,8 142:23 146:10	<b>pathways</b> 101:2,3 137:7,12 <b>patient</b> 7:8 16:14 16:15,18,22,22 17:7 23:8 25:2,4,6 32:23 34:11 44:3 44:18,21 45:1 46:22 47:3,5,8 51:14,18,24 52:8 52:11,16,25 53:3 53:6 54:21 60:14 61:19 67:15,21 76:16 82:11 83:7 104:22 108:7 111:1 113:1,7,8 113:14,15,17,21 113:24 114:8,8,15 114:15,23,25 115:3,7,10,15 116:6 117:3,4 118:16,20 120:5 120:13 121:25 122:2,4,5,19 128:15,17,19,20 129:1,23 132:19 136:7,17,20,21 140:20,23 141:6 143:22 144:11 145:4,7,8 147:20 147:22 148:22,24 149:1 150:16 153:12,18 <b>patient's</b> 44:20 45:8 <b>patients</b> 19:22 21:10 24:19,22 28:12 29:24 51:18 53:15 54:23 104:11 105:12 108:2,10 109:11 109:12 114:3 115:16 117:11 118:12 119:9 121:2 122:25	129:4,22 130:5 136:10 141:1,4,14 141:19 143:1 150:22 151:7,15 153:6,14,15,16,19 <b>patterns</b> 108:9 <b>paul</b> 2:18 133:15 133:15,23 137:23 <b>pay</b> 139:3 140:5 <b>paying</b> 141:25 <b>pc&amp;b</b> 89:15 <b>pdufa</b> 1:9 3:3 5:12 5:17 6:1,8,8,17,19 6:19,21,23 7:12 7:14 8:22 10:3,7 11:8 12:10,16 14:5 15:25 16:11 16:13 19:1,8,9,10 19:20,24 20:10,14 21:1,2 22:7 24:2 24:18,20 26:3,14 35:10 38:2,9 39:5 39:12 40:11 41:20 41:21 42:16 43:24 44:15 45:11 46:8 46:11 47:16,20,24 48:24 51:4,11,13 51:13,20 52:2,3,5 52:7 53:12,13,20 53:21 54:17,25 55:3,17,18 56:11 60:7 61:2,21 62:5 62:16 63:7 71:8 72:13,24 73:3,17 76:1 79:18 81:12 82:6,17 86:13,14 86:16,18,21,22,23 87:5,7,12,16,23 88:3,11,13 89:2,4 89:21 90:3,10,24 91:6,14 92:3,11 92:12 93:2 95:13 96:17 101:3,7,18 102:17,24 104:3	104:14 105:10,14 105:18 106:1,19 106:21 107:2,13 107:17 108:12 109:3,14 110:3,10 112:10,20 113:2,3 115:7 116:14,21 118:14 119:2 120:9,19 121:11 121:21,24 122:22 123:15,18 125:14 125:21 126:3,24 128:19 129:2,16 130:16 131:12,20 132:7 133:12 134:6,16 138:8 143:22 145:18 148:19 150:21 151:5 155:16,22 <b>pdufa's</b> 19:12 <b>peanut</b> 19:17 <b>pediatrician</b> 118:3 <b>peer</b> 15:3 <b>peggy</b> 150:24 154:24 <b>pending</b> 66:16 73:6 <b>people</b> 10:15 14:24 17:19 50:9 94:17 100:3 124:14 130:6 141:11 <b>percent</b> 98:14,25 101:1 105:1,3 112:1,3 127:6,10 <b>percentage</b> 96:24 112:1 139:17 151:9,19,24 152:9 152:11 <b>percentages</b> 149:5 <b>perform</b> 65:4 141:23 <b>performance</b> 20:24 55:20 59:9
---	--	---	--

72:25 75:7 96:18 97:3 98:5,19 103:15 115:15 122:20 143:12 145:24 149:3 150:21 151:1,8,22 151:24 <b>performing</b> 55:15 <b>period</b> 8:10 45:17 51:2 70:20 115:15 155:12 <b>permanent</b> 123:9 <b>permit</b> 121:15 <b>person</b> 144:4 148:14 154:5,10 <b>person's</b> 104:23 <b>personalized</b> 4:7 103:23 104:6,10 104:25 105:11,15 105:24 106:10 107:10 109:7,21 <b>personnel</b> 89:14 89:16,21 93:21 94:6 111:9 <b>perspective</b> 23:8 52:16 53:4 60:20 71:11 113:7 115:3 128:21 145:5 <b>perspectives</b> 4:4 16:15 69:17 95:22 96:11 98:17 153:10,18 <b>peter</b> 2:5 25:18,21 38:5,18 39:15 40:1,12 41:23 42:4 <b>peter's</b> 41:18 <b>pezoa</b> 156:2,17 <b>pfdd</b> 113:10 116:15 136:25,25 <b>ph</b> 25:12 91:25 115:24 117:14 155:9	<b>pharma</b> 9:8 139:4 <b>pharmaceutical</b> 23:1 68:10 71:11 75:19 140:22 <b>pharmacology</b> 31:5 <b>phase</b> 97:25 107:15 110:11 149:8 152:2 <b>phases</b> 49:10 111:19 <b>phasing</b> 50:25 <b>philosophy</b> 101:10 <b>phrma</b> 24:17 <b>physical</b> 122:19 <b>physician</b> 147:20 <b>piece</b> 47:4 50:4 <b>pieces</b> 154:22 <b>pilot</b> 10:2 27:23 30:15 33:2 36:3 36:15 37:20 40:24 41:3,5,10 42:2,3 47:16,19,21,22 48:24 49:14,18 50:5,10 67:17,18 67:24 68:13 69:12 69:14 71:25 72:1 72:4,5,6 107:18 108:11,17,22 115:9,10 119:13 119:18,23 120:9 120:17 127:14,16 127:19,23,23,24 130:17 131:23 136:4,13,14,16 <b>pilots</b> 108:16 115:21 128:3 <b>pipeline</b> 135:2 <b>pipelines</b> 117:9 <b>pivot</b> 148:13 <b>pivoting</b> 112:13 <b>place</b> 61:24 69:2 76:4 80:12 92:6 92:12,20 115:2	152:19 <b>placebo</b> 149:8 <b>placed</b> 120:20 <b>places</b> 100:4 <b>plan</b> 29:7 40:16 55:9 56:7 58:22 65:21 77:14,15 79:15 88:3,12,15 88:17 89:5,6,10 89:13,20 91:18 92:15 94:11 <b>planned</b> 65:4 69:4 <b>planning</b> 7:6 46:7 55:24 86:7,24 87:3,3,8,11,14,15 87:18,21,24 88:2 88:5,6,7,8,19,22 90:2 92:23 <b>plans</b> 26:23 47:18 50:13,21 79:11,13 79:14 <b>platform</b> 30:20 120:1 <b>platforms</b> 30:5 73:7 109:6 131:6 <b>play</b> 130:10 132:9 <b>playing</b> 97:14 146:24 <b>please</b> 5:21,22 12:9 19:5 25:17 30:1 34:4 44:12 47:9 48:21 55:2 63:9 65:22 66:24 69:3 74:10 76:21 77:13 89:21 90:20 94:24 96:16 98:3 99:4 100:4 101:8 102:15 118:15 119:11 120:18 121:22 122:21 123:14 124:3 <b>pleased</b> 105:17 115:5 116:1 118:24 119:5	127:2,11 134:13 135:12 136:3,22 137:9,15 143:21 <b>pleasing</b> 96:21 <b>pleasure</b> 43:23 63:9 <b>plenty</b> 137:17 <b>plug</b> 43:4 <b>plus</b> 41:24 <b>pmc</b> 58:15 104:6,7 107:1,6,11 109:2 110:3,8 <b>pmc's</b> 104:25 <b>pmr</b> 27:18,19 <b>pmrs</b> 27:5,8,11,14 27:16 58:15 59:16 <b>point</b> 20:3 33:5 102:22 106:11 109:22 139:10 <b>points</b> 21:25 63:22 68:22,23 114:24 <b>policies</b> 37:18 56:5 56:21 115:12 153:5,5,8 <b>policy</b> 4:9,11 13:1 13:15 34:1 53:25 82:19 104:5 110:20,22 111:3 116:11 119:1 121:17 125:1 129:11,24 <b>political</b> 145:15 148:10 <b>politics</b> 148:10 149:15 <b>pompe</b> 135:2 <b>poorly</b> 155:8 <b>population</b> 37:6 57:15 <b>populations</b> 15:23 17:3 62:7 76:16 83:8 109:11 114:23 119:16
--	--	---	---

<p><b>portion</b> 89:16</p> <p><b>portions</b> 123:22</p> <p><b>posed</b> 106:4</p> <p><b>position</b> 79:19</p> <p><b>positive</b> 71:20,20</p> <p><b>possess</b> 130:7</p> <p><b>possibilities</b> 61:10</p> <p><b>possibility</b> 66:23</p> <p><b>possible</b> 18:11 22:14 32:14 38:15 61:22 66:12 84:7 110:1 116:10 127:17 142:15 144:6</p> <p><b>possibly</b> 139:11 140:1</p> <p><b>post</b> 3:17 6:20,22 7:2 10:2 11:16 17:15 21:4 26:16 26:21 27:1 40:13 40:17 43:17 51:14 54:6,9 57:4,14 58:14,23 59:2,4 59:16 60:8,16 61:12 62:8,9,18 68:25 95:17 132:3 143:6 146:22 147:10 151:16 152:7,10</p> <p><b>posted</b> 9:14,17,20 42:6 92:16 155:22</p> <p><b>posting</b> 5:8</p> <p><b>posture</b> 78:3,4</p> <p><b>potency</b> 20:7,17 20:19</p> <p><b>potential</b> 15:14,24 18:1 75:13 76:15 83:4,10 106:7 109:24 120:10 125:18 129:3,17 132:8</p> <p><b>potentially</b> 33:22 35:14 37:2,3 93:19</p>	<p><b>potentials</b> 83:6</p> <p><b>power</b> 128:25 143:5</p> <p><b>practice</b> 128:4</p> <p><b>practices</b> 32:11 40:5 65:2 66:14 69:14 114:1</p> <p><b>practitioner</b> 34:11</p> <p><b>pre</b> 3:10 9:25 25:16,24 26:3,7 30:12 65:15,15 102:9 116:8 144:7 146:16,21 152:7</p> <p><b>precedent</b> 39:7 119:16</p> <p><b>preclinical</b> 18:18</p> <p><b>preclude</b> 64:25</p> <p><b>predictable</b> 6:15</p> <p><b>predicted</b> 22:6</p> <p><b>predictive</b> 100:18</p> <p><b>prefer</b> 10:22 11:23 124:10</p> <p><b>preference</b> 16:22 45:1 47:5 52:25 136:21</p> <p><b>preferences</b> 153:12</p> <p><b>pregnancies</b> 58:21</p> <p><b>pregnancy</b> 58:5 58:13,14,16,24 59:16 62:15,18</p> <p><b>pregnant</b> 58:10 59:3 62:6,8</p> <p><b>premarket</b> 6:11 151:8</p> <p><b>preparation</b> 99:24</p> <p><b>prepare</b> 38:23</p> <p><b>prepared</b> 8:25 38:23 157:3</p> <p><b>preparing</b> 40:7</p> <p><b>prescription</b> 1:9 95:12 97:15 104:2 140:19 141:3</p>	<p><b>present</b> 9:6 22:4 110:17 118:25 139:1</p> <p><b>presentation</b> 5:24 9:9,19 54:15 72:5 83:19 103:14,17 123:21</p> <p><b>presentations</b> 56:25</p> <p><b>presented</b> 25:18 50:6 69:19 98:20</p> <p><b>presenter</b> 43:18 54:10 62:24 73:22 85:19</p> <p><b>presenting</b> 7:13 10:13</p> <p><b>presently</b> 99:8</p> <p><b>president</b> 4:8 28:18 104:5 119:1 140:20 150:15</p> <p><b>pressure</b> 146:6</p> <p><b>pressures</b> 99:2</p> <p><b>prevented</b> 57:3</p> <p><b>previous</b> 9:2 42:13 53:13 69:18 91:14 92:2 136:18 146:20</p> <p><b>previously</b> 8:22 19:13 21:5 124:15 126:12 149:13</p> <p><b>price</b> 139:3 154:1</p> <p><b>primarily</b> 86:12 89:1</p> <p><b>primary</b> 99:17,18 100:11 102:1</p> <p><b>principles</b> 34:1 68:10</p> <p><b>prior</b> 18:16 23:22 27:4 32:5 40:18 68:24 72:13 107:11 118:5,25 120:11 156:5</p> <p><b>priorities</b> 77:16 116:1,23 119:2,6</p>	<p>119:10 121:23</p> <p><b>prioritization</b> 39:6,10</p> <p><b>priority</b> 46:24 48:19 81:24 101:2 120:18 126:24 127:7 134:16 145:21,22 146:11</p> <p><b>private</b> 14:16 15:10 18:20</p> <p><b>proactive</b> 146:22 147:8</p> <p><b>probability</b> 99:20</p> <p><b>probably</b> 17:19 81:8 111:11</p> <p><b>problem</b> 101:22</p> <p><b>problems</b> 5:21 45:4 154:6</p> <p><b>procedure</b> 68:4</p> <p><b>procedures</b> 14:24 20:24 56:6 64:10 70:14 82:19 102:8</p> <p><b>proceeding</b> 30:8 157:4</p> <p><b>proceedings</b> 156:3 156:4,6,8 157:6</p> <p><b>process</b> 5:13 6:1 7:17,19,23,25 8:2 9:15,18 10:1 24:11 25:4 27:6 32:3 39:17,18,24 40:19 53:17 59:15 62:17 64:18 65:13 65:19 71:13,24 77:3 78:5 80:11 86:13 87:1 89:23 89:23 90:2,12 95:15,25 98:2 99:13 102:7,18,24 103:1 106:1 110:10 114:16 116:2 120:17 123:18 124:6,13 126:10 133:13</p>
---	---	--	---

<p>144:12 149:20  <b>processes</b> 14:23  24:1 27:21 38:11  40:12 51:25 56:20  57:18 82:14 84:11  85:14 88:1,10  98:18 106:25  115:2 122:1  <b>processing</b> 77:5  <b>produce</b> 44:23  72:6 123:6  <b>produced</b> 125:14  <b>product</b> 17:16  20:5,9,19 40:14  55:13 58:1,4  59:21,23 62:2  63:23,24 65:3  67:12 68:14 69:2  74:17 100:11  107:16 117:6  127:9 128:14  138:25 139:8,9  142:2,3 144:5  147:3  <b>production</b> 144:3  <b>productive</b> 40:8  71:16 72:17  <b>products</b> 11:15  12:13 13:4 16:16  18:5 19:3,4,8,10  19:13,15,23 20:4  20:12,14,16,18,20  20:23,25 21:2,3,8  21:11 34:8,9 35:4  38:21 54:23 58:8  58:22 60:15 67:4  67:15,20 68:1,5  69:11 70:3 75:17  101:6 102:2  106:18 113:16  114:13,19,21  127:20 138:6  139:6 142:6  145:17,24 146:3</p>	<p>150:23,25 151:4  151:25 152:4,9,15  153:23  <b>professional</b>  118:11  <b>proffer</b> 97:4  <b>program</b> 3:6 5:12  6:9,20,25 7:1 8:22  11:22,24 12:3,8  13:9 14:7,12,22  17:20 19:2,8,20  27:22,23 28:2  29:20,22 30:1,6  30:13,14,15,16  33:2 34:4,21 35:8  36:3,3,15,15  37:20 38:2,19  39:8 40:23,24  41:1,3,5 42:2,17  44:10 47:22,22  48:10 49:3,15,18  49:19 50:5,6,10  50:12,18 55:8  56:20 67:18 71:25  72:1,4 81:12  86:14,22,23 87:5  88:13 89:4 90:10  90:13,18,24 91:3  95:13 96:19 98:20  99:12,17,18  100:10 104:3,15  107:18 119:13,23  120:10 123:12  127:14 130:17  133:1 135:14  136:4 146:12  <b>programmatic</b>  92:21  <b>programs</b> 10:2  17:18,21 26:5,8  26:11,14 30:20  32:17 41:11 47:15  48:12 53:22 56:21  66:24 69:16 70:15</p>	<p>118:20 130:18,24  130:25 135:10  136:15 137:13  138:11  <b>progress</b> 16:4 77:9  77:10 88:17 120:6  133:6  <b>project</b> 62:14  78:16 120:2  122:11,14 135:16  154:16  <b>projected</b> 22:5  <b>projects</b> 58:2 59:1  59:8,14 60:5  75:24 79:1 84:19  <b>prolonged</b> 142:1  <b>prominent</b> 99:9  <b>promise</b> 74:15  115:17 117:9  120:21 121:3  125:7 126:23  127:24 128:17  <b>promised</b> 152:14  <b>promising</b> 36:11  108:15  <b>promote</b> 71:22,23  79:3 82:18 99:12  104:18 106:3  <b>promoting</b> 94:8  109:15  <b>prompt</b> 45:19  <b>pronounced</b> 106:5  <b>pronouncing</b>  144:15  <b>proposal</b> 33:4  36:10 137:9  <b>proposals</b> 48:1  115:24 120:15  123:16  <b>proposed</b> 3:8,10  3:14,17,20,22,25  5:14 8:6,9,16 9:11  10:24 25:16,24  43:9,24 44:17</p>	<p>54:6 59:10,12  63:2 70:17 74:1  85:22 95:11 96:19  107:18 115:24  118:14 119:12  120:9 121:11  135:12 136:3  137:6 155:16  <b>proposes</b> 77:23  <b>proposition</b> 146:1  <b>protect</b> 58:9 99:19  106:3 111:18  112:14 141:8  <b>protected</b> 150:23  <b>protecting</b> 94:8  <b>protection</b> 54:22  60:14  <b>protocol</b> 26:24  36:6,19,25 55:21  <b>protocols</b> 28:25  29:6 37:9 109:4  <b>proud</b> 130:10  <b>proven</b> 142:11  153:21  <b>provide</b> 9:8 10:9  11:21 13:2,10,23  14:3,11 15:4 19:9  26:6 27:3 31:11  31:11 36:7 37:7  37:13 42:8 44:25  51:9,22 52:22  57:13 62:16 68:13  72:10 73:11 76:13  88:16 89:3 90:8  92:19 93:3,18  108:24 109:21  119:18 124:10,11  125:4 129:16  151:18  <b>provided</b> 22:19  31:18 36:25 52:1  52:3,6 61:1 64:3  68:22 85:6 89:15  93:11 105:25</p>
--	--	---	---

125:11 <b>provider</b> 133:3 <b>providers</b> 123:3 <b>provides</b> 24:10 80:13 104:16 <b>providing</b> 5:12 29:18 63:21 64:11 68:14 79:13 86:15 113:25 120:10 130:20 <b>proving</b> 151:11 <b>provisions</b> 24:21 24:25 41:20 42:13 61:21 72:24 73:17 82:17 92:7 93:6 101:23 116:21 134:9 138:12 <b>psychopharmac...</b> 146:8 <b>public</b> 1:8 4:4,5,9 4:17 7:18,19 8:7,8 8:10,11,15 9:1,14 14:16 15:10 17:18 18:8,17,20,21 25:4 29:19,19 32:8 33:23 37:10 37:11 40:3 42:4 43:4 50:20 52:14 53:17,17 54:16,21 57:20,21,22 58:9 59:2 60:5,14 61:6 62:7 65:23 69:3 70:12,19 73:10 75:23 82:8 89:6,9 91:17 92:9,17,22 93:23,24 94:8 95:11,15,23,23,25 96:7,11,14 97:5 97:14,15 98:21,25 99:19 103:3,12 104:5 106:3 107:20 112:18 115:21 123:23,25 124:3,4,23 125:4	131:12 136:23 141:8,14,25 142:20 143:16,19 143:19,24 145:23 147:17 148:20 149:16 150:16 153:7 154:3,24 155:1,3,6,12,14 155:15,19 156:1 <b>public's</b> 112:14 146:6 <b>publication</b> 61:4 84:9 <b>publicly</b> 42:6 50:16 108:16 153:5 <b>publish</b> 24:7 <b>published</b> 55:7 72:13 88:12,23 89:24 91:16 152:22 <b>publishing</b> 88:2 89:5 <b>pulled</b> 31:9 <b>purpose</b> 95:10 114:4 <b>purposes</b> 42:11 61:12 62:12 107:15 130:9 <b>pursuant</b> 20:6 <b>pursue</b> 102:17 <b>pushing</b> 130:10 <b>put</b> 22:5 24:8 26:21 61:23 92:11 116:15 137:9 140:6 <b>putting</b> 76:4 140:2	65:3 99:25 107:19 130:19 132:12 151:3 <b>quantify</b> 103:10 115:3 154:12 <b>quantity</b> 57:17 <b>quarter</b> 48:2 49:22 <b>question</b> 24:6,8 30:19 <b>questions</b> 24:5 32:4 39:20 59:21 59:23 126:18 <b>quick</b> 5:13,25 9:4 <b>quicker</b> 39:19,19 146:18 <b>quickly</b> 108:9 127:17 145:13 146:3 147:2 <b>quite</b> 6:10 16:4 41:23 <b>quote</b> 99:11 100:7 101:9 154:24 <b>quoting</b> 99:10	111:4,22,25 112:4 112:9,17 113:6,11 114:13,19,22 115:9,16,18 116:11,20 117:8 117:14 118:5,9,12 118:16,18,19,22 119:9,12,14,22 120:5,13,16,22 121:2,23 122:12 122:18,25 123:1 123:17 127:23 128:1 130:6,7 133:25 135:9 136:1,2,3 <b>rarely</b> 146:18 153:21 <b>rcp</b> 87:14 <b>rdca</b> 119:22 120:1 120:2,8 <b>rdea</b> 119:13,18,23 120:9,17 <b>read</b> 63:18 84:20 <b>readily</b> 78:9 <b>readiness</b> 10:5 23:21 67:18,25 68:13,16 69:1 72:7 127:14 <b>reading</b> 8:15 100:7 <b>ready</b> 18:3 25:22 43:12,20 54:12 62:25 73:24 85:20 96:9 103:24 110:15 117:15 123:16 <b>real</b> 15:16 18:1 23:8 25:11 26:10 28:1,4 35:8,12,13 35:16,20,20 36:3 36:19 37:21,21 41:19 42:2,9 59:22 60:2 61:11 61:25 62:3,11
			<b>r</b>
		<b>r</b> 2:1 5:1 <b>rachel</b> 118:25 <b>raise</b> 126:17 <b>ran</b> 7:22 <b>randomized</b> 97:24 100:23 152:2,5 <b>range</b> 31:3,7,12 49:1 105:12 122:18 <b>rapid</b> 131:2 <b>rapidly</b> 13:7 15:7 17:9 80:3 130:25 <b>rare</b> 4:11,14 15:21 15:22 17:3 23:16 26:10 32:17,18,19 33:4,13,15,16,17 33:21 42:14,15,17 42:20 110:18,18 110:21,22,23,24	
	<b>q</b>		
	<b>q&amp;a</b> 17:11 <b>q12</b> 68:11 <b>qualified</b> 90:9 156:7 <b>quality</b> 45:4 46:1 47:7 57:16 60:24		



63:8 100:12,21 105:21,22 108:8 108:20 109:21 115:12,22 123:6 127:22 129:18,23 130:1,1 135:13 137:18 143:15 145:4 146:24 148:23 <b>realize</b> 121:2 132:8 <b>realized</b> 67:15 103:10 126:24 128:14 <b>realizing</b> 125:7 <b>really</b> 5:25 6:7,11 6:12,19 9:4,4 18:6 21:8 23:24 26:9 29:7 30:14 32:4 36:11 38:10 39:8 39:18 40:8 41:4 41:25 42:8 45:17 46:9 47:11 49:1,2 49:7 51:10,10,16 51:21 61:8,14 62:15 63:11,13,16 64:20 65:4 67:7 69:1 71:23 72:14 86:13 87:6 89:10 91:1 92:2 93:1,5 104:15 105:13 147:24 151:2,15 152:6,12 153:16 <b>reason</b> 71:10 135:15 152:5 154:7 <b>reasons</b> 151:12,21 <b>reassert</b> 102:5 <b>reassuring</b> 106:21 <b>reauthorization</b> 1:9 5:13 6:1 8:21 55:3 102:17,24 103:1 110:10 123:18 144:1	155:16 <b>reauthorized</b> 125:22 <b>recalls</b> 151:17 <b>recast</b> 99:5 <b>receive</b> 78:5,8 121:12 <b>received</b> 39:9 46:13 121:10 <b>receiving</b> 47:8 48:7 49:20 120:25 155:18 <b>recess</b> 43:7 94:21 <b>recognition</b> 66:10 91:5 <b>recognize</b> 19:14 27:10 44:21 107:23 <b>recognized</b> 12:2 114:20 <b>recognizes</b> 80:13 80:19 126:3 <b>recognizing</b> 75:13 <b>recommend</b> 98:4 128:10 <b>recommendation</b> 9:4 <b>recommendations</b> 1:8 7:14 9:1 91:18 94:1 95:11 101:25 118:14 129:17 <b>recommended</b> 103:15 <b>record</b> 66:21 124:3,3,9 156:9 157:5 <b>recorded</b> 13:12 156:6 <b>recording</b> 10:17 95:18 155:20 156:8 157:4 <b>records</b> 66:4 <b>recruit</b> 93:20 127:1	<b>recruited</b> 153:15 <b>redesign</b> 147:9 <b>reduce</b> 15:1,5 47:12 141:17 <b>reduced</b> 156:6 <b>refer</b> 31:1 63:24 138:24 <b>reference</b> 46:20 <b>references</b> 80:19 <b>referred</b> 30:12 <b>refers</b> 46:10 <b>refined</b> 87:20 <b>refinement</b> 116:4 <b>refining</b> 115:11 <b>reflect</b> 17:11 32:23 37:19 104:3 112:23 136:10 <b>reflected</b> 11:13 60:25 84:21 112:10 116:2,25 119:6 121:24 <b>reflecting</b> 79:15 <b>reflection</b> 111:5 <b>reflects</b> 22:8 <b>reforms</b> 92:11 137:11 <b>regard</b> 103:16 <b>regarding</b> 16:19 20:7 61:6 97:17 98:15 128:9 139:17 140:19 <b>regardless</b> 124:11 <b>regards</b> 82:19 <b>regenerative</b> 17:20 125:2,7,17 128:22 <b>regions</b> 109:11 <b>register</b> 89:24 <b>registration</b> 124:13 <b>regular</b> 79:12 97:23 98:21 128:4 143:16	<b>regulated</b> 20:14 58:8 66:25 68:1,5 96:21 99:2 127:20 <b>regulation</b> 12:12 12:19 13:1 21:9 <b>regulator</b> 71:17 78:17 85:12 <b>regulators</b> 42:19 78:15 <b>regulatory</b> 3:14 7:1,7,11 10:2 13:10,22 14:25 15:3,6 23:5,6,6 35:14,21 36:1,14 37:4,16,25 42:9 43:9,12,17 44:25 45:2 51:4 53:5,15 56:20,22,23 61:12 64:8 66:8,20 68:10 69:7,17,20 69:23 76:3,11 77:2 79:5 80:25 82:2,10,14,16 83:25 98:2 99:6,7 102:7,14 105:6,21 105:23 106:4 107:4 109:16,18 111:4 113:22 114:6 119:16 121:4 122:1 126:10 128:18 129:11 130:9,21 131:2,18,22 132:23 135:8,18 136:22 137:3 145:12 154:4 <b>rehkopf</b> 2:9 62:25 63:5,6 <b>rejected</b> 97:12 151:10 152:23 <b>related</b> 12:24,25 34:5,15,23 35:1,8 35:17 54:25 62:6 64:19 65:11 66:14
--	---	---	--

70:15 89:18,20 92:17 98:3 113:1 121:8 124:8 147:2 156:11 157:7 <b>relating</b> 31:4 52:12 <b>relative</b> 20:19 156:13 157:9 <b>relatively</b> 71:8 <b>released</b> 115:8 <b>relevant</b> 27:17 35:5 70:15 79:18 111:3 113:21 <b>reliable</b> 44:23 <b>relying</b> 144:8 146:14 <b>remain</b> 8:13 20:10 153:1 154:5 <b>remaining</b> 55:10 91:15 108:12 <b>remains</b> 54:21 <b>remark</b> 154:23 <b>remarkable</b> 125:21 <b>remarks</b> 5:8,9 7:17 9:16 111:5 <b>remember</b> 139:7 <b>remind</b> 95:9 <b>reminder</b> 155:20 <b>remiss</b> 111:16 <b>remit</b> 86:12 <b>remote</b> 83:1 123:5 148:15 154:7 <b>remove</b> 142:10 <b>rems</b> 54:25 55:4,8 55:9,12,15,16,17 55:21,22,24,25 56:2,3,7,7,8,11,12 56:13 60:11 144:9 146:12,15,17 149:9 153:20,21 153:22,25 <b>rep</b> 149:11	<b>repeat</b> 24:23 <b>replacement</b> 41:2 <b>report</b> 37:10 60:7 88:20 89:14 91:7 91:19 92:19 97:23 98:13 128:2 135:21 143:8 147:14 <b>reported</b> 122:19 147:19,20,21 <b>reporting</b> 37:9 87:9,13 89:13 92:14 103:12 113:15 <b>reports</b> 28:22 66:8 66:19 147:1,13,22 <b>represent</b> 118:13 140:25 141:1 <b>representative</b> 13:19 114:2 146:7 <b>represented</b> 145:5 <b>representing</b> 125:9 138:4 <b>represents</b> 118:16 145:1 <b>request</b> 10:21 39:11 46:4 48:16 53:24 65:3 66:4 71:24 133:7 <b>requests</b> 24:6 34:20 39:7 57:4 63:21 65:8 66:21 66:21 78:19 124:12 126:14,20 128:10 131:13 <b>require</b> 26:19 35:23 85:3 102:12 <b>required</b> 68:24 84:6,24 108:6 152:14 <b>requirement</b> 27:2 <b>requirements</b> 26:17,22 40:13,17 40:20 61:13 89:13	132:4 <b>requires</b> 67:11 <b>requiring</b> 57:4 74:22 <b>research</b> 3:5 96:8 100:25 101:4 118:20 129:25 137:10 150:16 <b>researcher</b> 4:6 96:14 <b>researchers</b> 108:24 120:4 <b>reserve</b> 90:11 <b>reserves</b> 90:14 <b>resolution</b> 38:15 64:6 146:16 <b>resolve</b> 22:10 57:2 <b>resolved</b> 144:7 153:23 <b>resource</b> 21:5 57:12 62:12 77:8 86:6,24 87:2,3,5,8 87:14,17,19,21,24 87:25 88:7,8,9,22 92:23 93:14 120:3 <b>resourced</b> 104:20 <b>resources</b> 16:3 19:9,20 21:2 22:3 22:19,25 23:4 34:22 38:24 45:9 51:22 52:1,6,9 57:23 59:5 61:1 78:23 80:14,20,22 83:24 84:5,23 85:3,6 86:15,22 92:5 93:3,4 106:2 106:22 107:12 110:4 115:20 126:25 127:11 134:13,18 135:5 138:21 139:20 147:5 <b>respect</b> 60:2 109:25 154:25	<b>respectfully</b> 131:13 133:7 <b>respond</b> 132:14 145:13 <b>responding</b> 124:1 <b>response</b> 39:10 73:3 146:19 <b>responses</b> 126:14 <b>responsibilities</b> 99:7 <b>responsibility</b> 99:8 100:2 103:13 <b>responsible</b> 8:5 146:21 <b>rest</b> 155:23 <b>resubmitted</b> 152:24 <b>result</b> 70:23 72:12 97:18 106:16 151:17 <b>resulted</b> 51:25 101:18 112:7 151:5 154:13 <b>resulting</b> 103:11 <b>results</b> 59:13 98:11 120:19 <b>resumed</b> 144:6 <b>retain</b> 91:2 93:20 127:1 <b>retaining</b> 90:9 <b>retention</b> 10:10 89:11,19 90:8 91:6,9 93:16 148:5 <b>returning</b> 94:15 <b>revealed</b> 101:16 <b>revenues</b> 139:18 <b>review</b> 3:8,10 6:12 6:18,24 9:1,22 10:1,13,24 11:6 12:12,15,19,21,22 13:3 15:5 19:10 21:3 24:1 25:16 25:24 26:3,7,18
--	--	--	--

27:5,16 28:1,5,10 29:2,4,7,14 34:21 38:12,21 40:15 41:8 51:25 53:7 55:20 56:20 63:23 64:20 65:10 68:19 68:25 71:15 73:22 75:16 76:12,17 79:5 82:14 83:25 85:5,14 87:10,20 90:4 92:19 98:18 99:13,14 101:2,14 105:20 106:6 110:5 113:20,22 114:21 121:15 122:1 126:10 127:8,11 135:13 137:7 138:22 146:11 <b>reviewed</b> 8:14 21:5 27:14,15 40:20 <b>reviewer</b> 98:3 <b>reviewers</b> 98:6,9 98:14,25 127:1 <b>reviewing</b> 8:6 17:23 55:20 98:9 99:3 106:13 114:16 134:19 135:3,8 145:19 <b>reviews</b> 13:8 85:9 96:21 101:21 102:10 104:17 113:16 121:4 134:15 135:18 142:7 149:3 151:4 <b>revise</b> 103:1,18 <b>revised</b> 99:5 100:15 <b>revisions</b> 56:7 <b>right</b> 5:6 7:4 21:17 25:14 37:14 43:14 51:6 57:23 67:24 72:16 74:9 78:3	79:23 80:3 81:15 83:1 85:17,24 86:3 91:22 93:2 94:11,14 99:6 101:9 110:14 117:15,24 123:20 129:8 138:2 147:23 148:9 <b>rightly</b> 143:21 <b>rigor</b> 112:11 <b>rise</b> 140:5 <b>risk</b> 7:8 34:5,15,23 52:17 67:13 68:8 70:4 <b>risks</b> 16:19 23:13 34:16,17 55:14 56:10 90:13 102:14 <b>rmat</b> 17:20 <b>robert</b> 2:16 124:20 125:1 129:5 <b>robust</b> 37:8 42:15 98:1 110:25 114:15 <b>robustness</b> 37:15 60:1 <b>roche</b> 129:12,12 <b>role</b> 26:15 61:9 99:6,7 102:1 130:10 131:17 132:9 <b>roth</b> 2:19 137:24 137:25 138:2,3 <b>routine</b> 56:19 132:11 <b>rtor</b> 40:25 41:2 135:12 <b>running</b> 80:11 <b>rwd</b> 107:24,25 108:14 109:1,25 130:11 131:19,25 132:7,17 133:6	<b>rwe</b> 7:11 107:17 107:19,20,21,24 107:25 108:14,17 109:1,25 123:12 130:9,12,17,19,20 130:22 131:1,2,15 131:17,22 132:5,9 132:19,22 <b>rwee</b> 107:14 <b>s</b> <b>s</b> 2:1,19 3:1 5:1 <b>safe</b> 101:6 110:24 141:6,14,20,22 142:12 144:3 145:9 <b>safety</b> 3:17 6:22 7:2 15:19 17:2,15 25:10 29:4 42:11 54:6,9,15,17,20 56:18 57:2 58:1,5 58:7,8,12,14,16 58:17,24,24 59:3 59:21 60:8,10,17 60:24 61:20 62:2 62:6,8 74:22 98:15 107:4,16 130:3 142:6,14,17 142:18 143:15 144:7,23 145:3,16 145:25 146:5,13 146:15,16,22,25 147:10 148:3 151:11 152:15 153:22 <b>salient</b> 153:2 <b>sanofi</b> 118:8 <b>saved</b> 114:12 <b>saw</b> 40:25 41:4,11 154:24 <b>saying</b> 109:23 <b>says</b> 20:11 42:25 117:24 <b>scales</b> 136:9	<b>scarcity</b> 122:25 <b>schedule</b> 42:22 94:12 <b>school</b> 118:7 <b>science</b> 7:2 40:18 55:8 67:13 68:8 70:4 104:19 107:23 115:1 121:4 148:8 149:15 <b>scientific</b> 4:15 22:22,23 23:11 27:12 38:11 56:21 57:21 58:2 70:15 90:9 91:2 112:11 118:4 125:17 <b>scientifically</b> 100:17 <b>scope</b> 90:6 133:1 <b>scores</b> 102:11 143:12 <b>scratchy</b> 74:7 <b>search</b> 147:13 <b>second</b> 5:2 48:6 49:19 59:18 82:15 97:16 98:24 102:22 135:7 <b>secret</b> 103:5 <b>secretary</b> 20:7 <b>section</b> 9:9 43:23 44:1 63:11,12 70:22 100:7,8 <b>sections</b> 9:5,6,7 19:1 83:21 <b>sector</b> 125:9,17 126:3 128:22 <b>sectors</b> 104:9 131:12 <b>secure</b> 77:20 79:6 <b>see</b> 5:4,10,24 6:19 14:9 26:8 40:23 41:12 43:5 55:19 57:12 75:13 76:24 78:21 81:2 82:24
--	--	---	---

<p>94:19 97:11 98:25 105:17 115:6,19 116:1,10 119:12 121:22 123:2 134:13 135:12,15 136:3,22 137:15 138:2 140:15 142:4 144:18 147:19,23 148:15 148:21 150:8,10 150:12 155:1</p> <p><b>seed</b> 139:24</p> <p><b>seeing</b> 29:16 34:20</p> <p><b>seeking</b> 46:24</p> <p><b>seeks</b> 36:4</p> <p><b>seen</b> 32:16 77:12 113:6</p> <p><b>sees</b> 149:15</p> <p><b>selecting</b> 114:3</p> <p><b>self</b> 109:6 143:13</p> <p><b>send</b> 43:1 94:16</p> <p><b>sending</b> 57:3</p> <p><b>senior</b> 4:5,8 96:14 104:5 129:10</p> <p><b>sense</b> 48:25 71:11 97:19</p> <p><b>sensing</b> 109:5</p> <p><b>sensitive</b> 126:16</p> <p><b>sensors</b> 109:10</p> <p><b>sentinel</b> 56:16,16 56:17,22 57:7,10 57:17,25 58:2,19 59:5,6,19,24 60:12 61:6,9,15 62:1,2,11,13 131:23,24 142:16 154:16</p> <p><b>sentinel's</b> 57:8</p> <p><b>sentinels</b> 54:25</p> <p><b>separated</b> 139:8</p> <p><b>separately</b> 103:5</p> <p><b>separates</b> 102:8</p> <p><b>separating</b> 146:20</p>	<p><b>september</b> 1:13 7:21 8:2,19,23</p> <p><b>sequencing</b> 85:11</p> <p><b>series</b> 16:6 33:7 45:12 51:14 53:17 75:23 113:23</p> <p><b>serious</b> 28:8 67:1 143:1</p> <p><b>seriously</b> 151:8</p> <p><b>serve</b> 23:25 104:5 110:19 133:24 141:8</p> <p><b>served</b> 11:7 26:2 118:6</p> <p><b>serves</b> 99:25</p> <p><b>service</b> 113:13</p> <p><b>services</b> 77:19 118:21</p> <p><b>servicing</b> 149:16</p> <p><b>session</b> 25:20 43:11 54:9 62:23 73:21 85:18 95:22 123:23</p> <p><b>sessions</b> 122:3 155:15</p> <p><b>set</b> 6:13,15 27:6,6 30:17 57:11 96:18 103:24 116:12 123:11 133:20 142:8 150:1</p> <p><b>sets</b> 52:20 83:25 122:9 154:21</p> <p><b>setting</b> 38:10,13 86:25 89:22,23</p> <p><b>share</b> 8:9 26:4 50:13 72:10 104:1 118:13 123:15 126:6 143:16 144:11</p> <p><b>shared</b> 23:7 52:15 53:2,2 66:8 111:3</p> <p><b>shareholder</b> 129:13</p>	<p><b>sharing</b> 50:15 78:14 130:19</p> <p><b>sheet</b> 36:9</p> <p><b>sher</b> 118:25</p> <p><b>shift</b> 78:24 79:15</p> <p><b>shifted</b> 113:5</p> <p><b>shined</b> 145:13</p> <p><b>short</b> 97:4 151:1</p> <p><b>shortcuts</b> 100:22</p> <p><b>shortening</b> 6:18</p> <p><b>shortly</b> 124:17</p> <p><b>shown</b> 101:4 104:25 153:25</p> <p><b>shows</b> 34:10 100:25</p> <p><b>side</b> 8:3 65:22 103:4 144:25</p> <p><b>sides</b> 71:17</p> <p><b>signals</b> 58:17</p> <p><b>signature</b> 156:16 157:14</p> <p><b>signed</b> 7:24 124:14</p> <p><b>significant</b> 12:11 22:1,9,11 52:1 61:1 71:6 72:21 83:20 84:5 106:20 107:25 127:3</p> <p><b>significantly</b> 51:12 116:16</p> <p><b>similar</b> 33:15,15 48:25 88:11</p> <p><b>similarly</b> 45:1 135:15,16</p> <p><b>simple</b> 39:19</p> <p><b>simplistic</b> 96:20</p> <p><b>site</b> 74:23</p> <p><b>sites</b> 69:11 70:3</p> <p><b>sits</b> 141:18</p> <p><b>situation</b> 27:12 79:24</p> <p><b>situations</b> 49:5</p> <p><b>six</b> 73:21 118:10 136:8</p>	<p><b>size</b> 106:16 108:21 138:17 139:18</p> <p><b>sizes</b> 13:19 114:23 139:14</p> <p><b>skills</b> 156:10 157:6</p> <p><b>skipping</b> 103:7</p> <p><b>slack</b> 2:10 10:9 73:23 74:3,6 81:7</p> <p><b>slide</b> 6:6 7:15 8:24 9:2,3 11:5 12:9 19:5 26:13 27:22 30:1 32:15 34:4 35:7 38:1 42:24 42:24 43:15 44:11 47:9 48:21 51:7 55:2,19 57:13,23 57:24 58:6 59:18 60:4 63:9 66:24 69:3 74:9,9 76:20 76:21,24 86:18 88:25 89:12,21 90:20 91:4 96:16 96:22 97:8,8,16 97:22 98:3,23 99:4,10 100:4,8 101:8,10 102:15 102:15,23 103:8 103:19,24 117:15 118:15 119:11 120:18 121:22 122:21 123:14 124:19</p> <p><b>slides</b> 10:16,19,21 25:17 54:24 56:14 94:17 95:18 96:6 101:24 110:14 155:21</p> <p><b>slowed</b> 108:3</p> <p><b>slower</b> 133:6</p> <p><b>slowing</b> 139:11</p> <p><b>small</b> 6:23 13:19 17:3 23:16 119:16 138:5,12 140:2</p>
---	---	--	---

<p><b>smaller</b> 31:15 139:20</p> <p><b>solicited</b> 69:13</p> <p><b>solid</b> 40:16,16</p> <p><b>solution</b> 147:11</p> <p><b>solutions</b> 84:18 147:25</p> <p><b>soon</b> 22:14 144:6</p> <p><b>sophistication</b> 57:10</p> <p><b>sops</b> 27:20 70:14</p> <p><b>sorry</b> 5:20 50:10 63:23 76:22 81:20 145:21</p> <p><b>sort</b> 9:25 22:5 29:1 30:13 36:7,9 36:17 38:8 41:7 44:23 51:23 53:1 71:21 72:10 84:12 146:10</p> <p><b>sorts</b> 97:1,2</p> <p><b>sought</b> 31:18</p> <p><b>sound</b> 44:23 45:3 74:3 81:6 140:16</p> <p><b>source</b> 36:21 104:15</p> <p><b>sources</b> 35:18 57:7 108:8 130:13 131:6 146:23</p> <p><b>sourcing</b> 130:11</p> <p><b>space</b> 40:25 41:5 63:14 65:7 116:8 148:7 152:7,8</p> <p><b>spaces</b> 79:6</p> <p><b>speak</b> 77:15 86:9 86:10 89:10,19 118:23 124:15 139:17 140:18 150:18</p> <p><b>speaker</b> 43:18 54:11 124:14</p> <p><b>speakers</b> 25:19 96:2 124:7,18,19</p>	<p><b>speaking</b> 87:2 95:5 139:16 144:22</p> <p><b>specialists</b> 122:25</p> <p><b>specific</b> 20:17 30:18 53:4 55:16 62:7 68:13 70:6 70:18 73:15 80:7 80:9 84:14 85:3 88:1 93:13 101:25 116:9 128:19,20 151:12 153:11</p> <p><b>specifically</b> 25:3 42:16,20 53:13,16 61:24 62:14 68:11 82:1 83:1 92:14 138:25 149:4</p> <p><b>specified</b> 26:24</p> <p><b>speed</b> 143:13 146:1,6 150:21 151:2 152:21</p> <p><b>speedy</b> 145:23</p> <p><b>spend</b> 13:8 121:13</p> <p><b>spending</b> 80:16</p> <p><b>spent</b> 154:18</p> <p><b>spinal</b> 134:24</p> <p><b>spirit</b> 67:16</p> <p><b>split</b> 28:4,4 135:13</p> <p><b>sponsor</b> 30:18,21 31:10,10,23,25 33:3,19 36:5 48:10 50:2,15 100:2 126:21,22 133:4 143:8</p> <p><b>sponsored</b> 78:17</p> <p><b>sponsoring</b> 65:2</p> <p><b>sponsors</b> 6:25 24:10 30:4 35:23 36:8 37:22 39:7 39:11,25 42:18 48:15 49:7 50:17 55:9 57:20 61:5 68:7,12 75:6 76:14 78:12 99:23</p>	<p>101:11,20 102:10 102:14 116:6 117:3 119:18 120:11,14 121:14 126:8 130:18 132:17 133:1</p> <p><b>square</b> 139:2,22</p> <p><b>squarely</b> 141:18</p> <p><b>staff</b> 6:14 11:20,21 12:11,14,16,24 13:5,25 14:4 22:12,21 33:19 57:19 68:19 86:7 90:10 93:16 98:16 102:8,10,13,20 121:16 127:3 146:21 148:5</p> <p><b>staffing</b> 105:19 106:22 107:12 121:13</p> <p><b>stage</b> 49:8 80:16 119:20</p> <p><b>stages</b> 36:18,18</p> <p><b>stakeholder</b> 4:4 7:24 13:13 17:6 41:23 42:6 46:24 53:24 54:2 69:12 95:25 96:11 102:19 103:4 112:12 119:3,4 132:15</p> <p><b>stakeholders</b> 7:24 14:16 16:9 18:21 23:11 35:12 42:7 45:20 46:5 48:19 73:11 82:7 92:18 95:23,23 108:19 108:25 111:3 112:6,9,25 113:21 114:1 131:11</p> <p><b>standard</b> 20:17 46:11 52:20 79:2 91:25 97:24 122:9 144:5 149:8</p>	<p><b>standardization</b> 55:18</p> <p><b>standardize</b> 20:5 20:15 55:4 59:15</p> <p><b>standardized</b> 62:17</p> <p><b>standards</b> 15:5 18:13 75:10 100:24</p> <p><b>stands</b> 79:21 123:16</p> <p><b>star</b> 28:5 40:24 115:10 127:24</p> <p><b>start</b> 6:19 19:24 24:17 25:21 26:16 36:7 43:20 63:10 68:3 74:11 85:20 90:16 91:25 109:2 110:14 111:7 112:22 120:11 134:12</p> <p><b>started</b> 6:3,9 7:17 41:13,21 51:12 54:14 95:6 105:3 134:12 139:7 144:23 152:13</p> <p><b>starting</b> 7:21 16:1 68:2 124:19</p> <p><b>state</b> 99:22 124:9</p> <p><b>stated</b> 99:18,21 100:20 116:13 124:15</p> <p><b>statements</b> 100:15</p> <p><b>states</b> 101:9 125:25 140:6</p> <p><b>statistical</b> 29:6 120:14</p> <p><b>status</b> 64:22 89:3 149:12</p> <p><b>statute</b> 8:25 19:14</p> <p><b>statutory</b> 8:17</p> <p><b>stayed</b> 152:19</p> <p><b>steadily</b> 75:3 105:2</p>
---	--	---	--

<p><b>stein</b> 2:5 25:19 26:1</p> <p><b>step</b> 9:1 90:18 136:19</p> <p><b>steps</b> 109:3 123:10 126:4</p> <p><b>stick</b> 137:20</p> <p><b>stop</b> 25:13 42:20 62:19 81:15 83:16 92:23 146:14</p> <p><b>stopped</b> 65:24 117:24</p> <p><b>story</b> 147:24</p> <p><b>stranger</b> 136:5</p> <p><b>strategic</b> 3:6 89:11 89:18 90:7</p> <p><b>strategies</b> 33:24 69:7,9,23,25 127:12 144:9 153:20</p> <p><b>strategy</b> 70:5,13 70:16,20 72:12 73:14 77:24 84:3 84:10 85:1 146:15</p> <p><b>streamline</b> 14:22 78:9</p> <p><b>streamlined</b> 77:21 78:11</p> <p><b>strengthen</b> 52:22 127:2 142:13</p> <p><b>strengthened</b> 7:1</p> <p><b>stress</b> 82:11,15 128:7</p> <p><b>stretched</b> 111:20</p> <p><b>strikes</b> 21:8</p> <p><b>string</b> 147:15</p> <p><b>strong</b> 12:7 57:14 127:18 134:5 145:12,16 149:14 154:17</p> <p><b>stronger</b> 85:7</p> <p><b>strongly</b> 81:25 98:16 116:25 121:24 131:3</p>	<p>148:5</p> <p><b>structure</b> 7:5 63:24</p> <p><b>structured</b> 9:19 63:21 71:23 114:24</p> <p><b>structures</b> 14:9</p> <p><b>struggling</b> 118:18</p> <p><b>studied</b> 50:7</p> <p><b>studies</b> 15:17 16:16 25:12 34:6 35:20 37:8,24 45:4 50:7,14 52:25 57:5 58:15 58:24,24 59:3,16 62:8,18 69:5,18 72:11 103:10 108:6 120:12 132:3 136:25 137:1 142:9 143:9 152:1,10 154:12</p> <p><b>study</b> 16:21 27:1 28:21 34:7,10,14 34:18,19,25 35:2 35:24 36:6,12 37:8,14 40:16,20 55:21 59:5,10 60:3 62:10 143:9 152:22</p> <p><b>studying</b> 59:23</p> <p><b>subgroup</b> 63:8</p> <p><b>subject</b> 30:11 149:6 152:10</p> <p><b>submission</b> 28:15 28:17,24 41:7 68:24 69:9,25 102:9 108:17 132:12 137:3 138:19</p> <p><b>submissions</b> 11:14 11:14 21:4,4 37:10 47:7 69:19 70:9 75:3 77:2 78:14,24 79:5,25</p>	<p>80:25 85:9 121:15 130:20 136:22</p> <p><b>submit</b> 8:12 43:4 52:15 95:16 124:4</p> <p><b>submitted</b> 20:5,13 28:16,20 32:5 46:2 78:10 134:17</p> <p><b>submitting</b> 50:2</p> <p><b>subsequent</b> 18:23</p> <p><b>subsequently</b> 152:23</p> <p><b>substantial</b> 6:12 11:10 12:13 130:8 135:23</p> <p><b>substantially</b> 103:18 127:2 134:3,23</p> <p><b>success</b> 56:1 86:14 90:24 100:9 119:24 120:9 129:15 132:18 151:6</p> <p><b>successes</b> 41:21 53:12</p> <p><b>successful</b> 38:20 47:20 72:2 75:5</p> <p><b>successfully</b> 41:25 82:13</p> <p><b>sufficient</b> 27:3,8 34:17 35:25 36:13 37:15 56:1</p> <p><b>suggest</b> 139:25</p> <p><b>suggesting</b> 98:22</p> <p><b>suggestion</b> 97:23 98:7</p> <p><b>suggestions</b> 96:16 153:11</p> <p><b>summaries</b> 28:22</p> <p><b>summarize</b> 63:17 105:14</p> <p><b>summary</b> 38:1,6 51:9</p> <p><b>summer</b> 6:3 7:17</p>	<p><b>sunset</b> 8:22</p> <p><b>super</b> 110:16</p> <p><b>supplant</b> 100:23</p> <p><b>supplement</b> 28:7</p> <p><b>supplements</b> 41:3 41:6 65:12</p> <p><b>support</b> 3:8 9:23 10:13,24 11:6,22 11:23 12:3,12,14 12:22,24 13:3,10 13:23 14:3 18:8 19:1,2,6,20 26:11 31:10 35:14,14,21 36:1 37:4,5,15,24 42:11,15 52:16,17 57:14 59:20 62:2 62:15 74:17,22 76:5 77:17 78:13 78:17 80:14,22 81:11 85:9 105:19 105:23 106:23 115:12,15 118:21 125:11 129:18 131:3,7 132:3 134:5,6 140:21 142:16 143:22 146:20 148:5</p> <p><b>supported</b> 38:24 63:8 100:25 107:11 149:1</p> <p><b>supporter</b> 154:17</p> <p><b>supporting</b> 36:13 76:18</p> <p><b>supportive</b> 52:18 92:5 107:19 126:8 127:13 137:6</p> <p><b>supports</b> 42:2 58:19 81:1,25 110:3 122:10,22</p> <p><b>sure</b> 5:3,23 9:12 9:16 14:6,13 18:3 22:13,20,25 23:4 31:25 32:12 38:5 39:20 52:6 61:22</p>
--	---	---	--

64:23 77:12 81:4 82:12,17 92:2,8 92:10 111:12 141:19 145:4 150:3 155:2 <b>surge</b> 134:18 <b>surrogate</b> 15:15 100:11,16 142:23 <b>surveillance</b> 57:15 146:22 147:8 151:16 <b>surveyed</b> 98:13 <b>surveys</b> 98:6,10 <b>sustain</b> 57:14 <b>sustainability</b> 86:22 <b>sustained</b> 11:10 12:8 100:9 <b>sworn</b> 156:5 <b>system</b> 6:22 38:11 38:13 54:20 55:5 56:17,18 60:11,24 77:3 142:16 145:3 147:9,17 <b>systematic</b> 51:23 <b>systems</b> 77:24 121:20 131:25 135:20	<b>takes</b> 80:12 103:13 126:4 141:13 <b>talk</b> 26:15 30:2 33:24 48:22 69:4 117:20 137:24 <b>talking</b> 70:10 138:20 <b>tallies</b> 97:17 <b>tank</b> 150:17 <b>target</b> 26:9 <b>targeted</b> 19:16,22 20:23 91:8 93:15 127:4 130:20 <b>targeting</b> 32:17 128:1 <b>targets</b> 30:5 <b>team</b> 69:15,16 122:16 <b>teams</b> 65:10 <b>tech</b> 129:20 <b>technical</b> 5:20 7:20 54:14 69:20 90:10 91:3 92:6 99:23 <b>techniques</b> 49:5 <b>technological</b> 131:17 <b>technologies</b> 10:6 63:16 66:23 67:17 69:7,10,22,24 70:2,10,25 73:13 74:12,14 77:6 82:1,9 83:2 84:17 109:4,6 112:5 123:6 <b>technology</b> 69:15 69:16,19 73:7 77:7,14 80:14 81:23 82:25 83:10 84:1,2 85:1 123:12 131:4,6,9 131:11 132:14 147:6,24	<b>teleconference</b> 126:19 <b>tell</b> 5:3 <b>term</b> 97:4 111:11 111:12 132:13 <b>terms</b> 52:10 79:6 89:13,22 90:2 <b>terry</b> 2:8 <b>terry</b> 54:10,11 60:21,22 <b>test</b> 20:7 136:8 <b>testifying</b> 156:5 <b>thank</b> 5:19 11:4 21:12,21,21 25:14 26:1 38:5 41:17 42:21 43:14,21 51:7,8 54:4 60:18 60:21,22 62:20 63:5 65:22 71:1,4 71:5,5 74:3,10 81:17,19 83:18,18 85:15,16 91:22,24 94:9,10,19 95:5 103:20,21 110:11 110:12,16,16 111:8,8 112:15,15 112:16 117:7,11 117:12,25 123:14 123:19,20 129:4,5 129:14 133:10,14 133:21 137:22,23 140:7,9,18 144:10 144:13 149:20,22 155:14,22 <b>thanks</b> 10:18 21:14 53:9 54:13 61:18 72:22 73:18 86:3,4 92:25,25 95:2 103:25 110:7 118:1 144:14 155:6,7 <b>themes</b> 112:10 <b>therapeutic</b> 15:24 23:23 111:10	134:14 <b>therapies</b> 9:24 12:21 16:7,20 17:21 23:3,13 25:3 80:1 105:7,7 105:8 106:7,12,14 106:25 107:5 110:24 114:10 120:21 121:1,3 125:8,12,19 126:24 128:1,16 128:24 134:11,19 134:20,21,22,25 135:4,9 <b>therapists</b> 25:5 <b>therapy</b> 11:11,22 11:24 12:3,8,13 12:14,19 13:3,16 14:19,23 15:20,24 16:16 17:4,16 18:3,5 19:2 23:17 24:24 32:24 100:10 105:20 106:6,18 111:4 112:5 120:24 121:6 125:23 126:14 127:9 128:14 137:7 146:11 <b>theresa</b> 2:7 43:13 43:18,19,22 51:8 52:21 53:10,22 72:4 <b>thing</b> 40:1 47:2 93:10,11 147:16 154:15 <b>things</b> 12:25 13:11 16:17 21:23 23:8 23:21 24:23 29:5 38:7 48:3 66:18 66:21 68:7,23 69:15,25 72:20 76:19 78:22 80:7 80:9 84:2 97:5
<b>t</b>			
<b>t</b> 3:1,1 <b>table</b> 103:4 113:18 <b>take</b> 15:1 17:10 27:11 29:3,13 41:4 43:23 55:14 60:19 61:20 70:7 73:16 77:13 80:5 94:17 102:20 109:3 112:23 123:1 141:15 147:25 154:9 <b>taken</b> 44:2 48:12 80:9 151:20 156:3 156:12 157:9			

100:21 145:14 151:22 152:21 <b>think</b> 11:9 13:17 17:19 21:7,25 22:8 23:22,24 26:5,8,11 27:22 29:15 32:15 35:7 37:20 38:1,15 39:1,17 40:23 41:10 42:22 51:10 51:17,18,21 52:10 60:9 61:3,7 65:24 67:3 71:19,19,24 72:19,20 78:15 82:21 83:3,6,23 84:20 85:11 94:12 95:6 97:3,17 98:16 101:16 103:8 111:10 116:5 150:17 154:25 155:11 <b>thinking</b> 17:12 18:23 23:6,6 24:12 25:9 40:19 52:10,14 53:2 61:8 66:14 107:24 148:7 <b>third</b> 20:3 44:4 48:21 65:1 71:22 88:21 91:8 97:22 103:9 135:25 145:18 <b>thompson</b> 5:2 10:14 11:3 21:14 21:20 25:14 38:3 42:21 43:11 51:6 54:4,8 60:19 62:20,22 71:3 73:18,20 74:5 81:6,17 85:16 86:1 91:22 94:10 94:22 95:1,4 103:21 110:12 117:12,19,21	123:20 129:5,8 133:14,19 137:23 138:1 140:9,12,15 144:14,19 149:22 149:25 150:4,9,12 155:7 <b>thoughtful</b> 84:4 84:22 <b>thoughts</b> 9:9 137:21 <b>thousand</b> 139:22 <b>thousands</b> 141:1 145:1 <b>three</b> 43:25 44:7 44:13 56:14 97:10 105:17 154:2 <b>thrilled</b> 119:11 <b>thrive</b> 129:21 <b>throat</b> 74:8 <b>time</b> 6:13 13:8 27:2,3,8,10 28:1,4 28:4,15,18 45:8,9 47:6 49:6 51:2 58:13 63:22 68:22 68:23 70:20 72:16 76:21 79:17 80:17 87:9,13 96:4,25 102:18 107:25 110:7 113:5 121:14 123:1 124:17,17 125:16 132:15 135:13 137:20,22 139:1,8 140:7 146:24 149:10,18 152:13 <b>timeframe</b> 50:23 <b>timeline</b> 7:16 35:3 39:19 96:20 108:14 142:2 <b>timelines</b> 6:15 27:7,21 31:16 34:22 38:22 67:4 67:9 68:6 70:17	<b>timeliness</b> 104:16 <b>timely</b> 19:19 21:3 32:6 34:24 35:3 55:11 58:17 101:10 126:22 141:25 142:7,10 143:3,7 <b>times</b> 6:18 71:15 117:23 <b>tip</b> 101:16 <b>tireless</b> 111:17 117:7 <b>tissue</b> 105:7 <b>tissues</b> 12:20 <b>tmap</b> 79:8 <b>today</b> 5:24 7:13 8:7 9:19 18:25 40:3 48:22 63:9 63:16 74:8 86:5 86:17 91:1 93:21 96:2 110:17 111:7 111:13 112:6,21 113:4 116:18 118:23 125:24 129:15,22 134:12 137:5,22 140:18 145:6 150:18 154:15 155:11 <b>today's</b> 8:8 117:9 123:22 145:20 155:18 <b>toigo</b> 2:8 54:10,13 <b>told</b> 141:15 <b>tomorrow</b> 93:22 129:22 <b>tompson</b> 2:6 <b>tool</b> 82:20 147:10 <b>tools</b> 3:14 7:7 10:2 16:23 43:9,12,17 45:21 51:4 53:15 57:18 66:2,15,19 68:10 73:5 82:13 83:3,10 105:22 109:7 113:25	120:14 123:5 126:6 142:18 147:18 <b>top</b> 96:22 101:10 104:9 121:5 124:20 126:24 <b>topic</b> 9:21 25:18 54:10 62:24 63:13 71:8 73:23 82:3 85:19 86:11 88:15 <b>topical</b> 138:6 <b>topics</b> 69:13 70:16 86:10,11,19,24 89:7,9 90:22 <b>total</b> 49:23 <b>touch</b> 7:16 <b>tough</b> 78:8 <b>toxicology</b> 31:6 <b>track</b> 101:2 128:10 <b>tracking</b> 146:10 <b>traditional</b> 24:9 48:14 50:19 74:19 74:23 101:2 107:8 <b>train</b> 45:21 127:1 <b>training</b> 13:12 32:9 45:18,19,22 56:21 57:20,22 64:11,17 71:22 102:13 <b>trains</b> 80:11 <b>transcribed</b> 124:2 <b>transcriber</b> 157:1 <b>transcript</b> 10:17 95:18 155:21 157:3,5 <b>transcriptionist</b> 156:7 <b>transfer</b> 49:13 <b>transform</b> 107:9 <b>transformations</b> 107:14 <b>transformative</b> 134:20
---	---	---	---



<b>transformed</b> 114:11	<b>trials</b> 32:21 51:1 58:11 74:18,20	116:17 128:6	112:17,20 113:7
<b>transition</b> 84:15	75:6 76:17 83:5,6	<b>types</b> 17:1 18:22 34:15 35:17 58:23	119:17 125:18
<b>transitioning</b> 10:14 49:14	83:8,12 97:24,25	96:23 98:1 148:22	131:16
<b>translate</b> 49:13 83:14 129:23	100:23 107:9,15	<b>typewriting</b> 156:7	<b>understandings</b> 50:9 131:1
<b>transmit</b> 8:18	109:5,9 118:10	<b>typically</b> 30:11,19 130:5	<b>understood</b> 32:1,2 32:25 33:1 111:21
<b>transparency</b> 42:4 86:25 88:25 89:3	120:16 123:3,8	<b>u</b>	<b>undertaken</b> 135:19
92:9,20 93:8 94:3	125:24 126:1,2	<b>u.s.</b> 1:4 125:1	<b>underway</b> 153:13 154:20
108:19 112:11	130:2,6 136:1,2	<b>ultimate</b> 72:15 119:24 145:23	<b>undisclosed</b> 144:24
113:20 132:16	136:13 137:19	<b>ultimately</b> 36:12 36:25 37:24 100:1	<b>unfortunately</b> 148:9 155:4
148:18 151:14	143:3 149:9 152:2 152:6	108:23 149:15	<b>unique</b> 23:15 79:19 114:22
<b>transparent</b> 79:10 124:6	<b>true</b> 156:9 157:5	<b>ultra</b> 15:22 17:3 23:16	127:20
<b>travel</b> 65:23	<b>truly</b> 128:9	<b>uncertainties</b> 47:12,13	<b>united</b> 125:25 140:6
109:12 123:2	<b>trust</b> 141:19 143:11,20	<b>uncertainty</b> 108:22	<b>university's</b> 122:15
<b>treat</b> 114:13	<b>trusted</b> 66:8,20	<b>uncommon</b> 31:21	<b>unmet</b> 28:9 32:21 67:2 105:13
<b>treating</b> 118:19	<b>try</b> 35:19 61:20 140:4 150:7	<b>undergoing</b> 38:21	146:12
<b>treatment</b> 101:15 107:7 108:9	<b>trying</b> 17:10 29:22 80:17 117:17	<b>underline</b> 22:1	<b>unnecessary</b> 135:3
110:24 118:12	150:2 154:16,20	<b>underscore</b> 21:23 23:19 38:7 40:2,5	<b>unprecedented</b> 106:8 111:11
129:24 134:1,2	<b>tuesday</b> 1:13	52:23 61:4 71:21	<b>unsafe</b> 99:20 150:23
141:16 153:17	<b>turn</b> 10:12,20 21:15 24:14 38:2	83:20 84:2,23	<b>update</b> 29:10 59:12 79:13 91:25
<b>treatments</b> 19:17 23:18 32:21	41:15 47:21 53:8	93:10 112:7	149:9
104:22 108:2	60:17,19 61:16	<b>underscoring</b> 72:20	<b>updated</b> 17:11 32:10,10 40:4
129:3 137:14	71:1,3 85:14	<b>understand</b> 13:17 16:15 18:11 23:5	64:18 75:25
141:3,6,22,24	91:21 94:9 117:17	24:12 42:18 46:5	<b>updates</b> 79:14 88:16 89:22 90:1
142:25 145:9	141:1	48:17 63:18 64:15	90:11 92:16
<b>tremendous</b> 111:7 112:25	<b>turning</b> 19:5 140:11	66:12 108:9	107:20
<b>trend</b> 108:3	<b>two</b> 8:4 22:16 28:20,23 29:13	141:12 151:22	<b>updating</b> 17:23 27:20 56:5 64:10
<b>trends</b> 65:7 105:4	30:2 31:14 41:7	153:17	70:13 86:25
<b>triage</b> 78:9	46:7 48:2 49:22	<b>understandable</b> 142:19	
<b>trial</b> 7:9 23:9 27:1 31:5 44:5 47:11	55:6 60:5 68:14	<b>understanding</b> 16:18 23:7 40:10	
48:23 50:5 53:10	89:10 102:21	45:25 50:12 52:15	
72:3 74:21 109:20	136:18 149:8	53:2 59:22,25	
114:23 115:13	151:25 155:15	68:20 108:1	
119:16 131:8	<b>type</b> 31:1,2,8,13 31:19 38:25 59:16		
137:18	62:17 68:15		
	108:18 115:25		

<p><b>upgraded</b> 147:6  <b>upside</b> 77:1  <b>urge</b> 126:18  127:15  <b>urgency</b> 71:12  111:21,24 116:24  141:5  <b>urgent</b> 112:18  <b>urras</b> 34:21  <b>usa</b> 140:20 141:6  144:11 145:7  <b>use</b> 7:7 10:5 15:14  17:25 18:1 28:12  28:13 30:9 34:5,7  34:12,15,23 35:12  35:16 37:6 41:19  45:8 46:1 49:16  50:25,25 52:25  54:19 58:12,16  60:10 61:10,25  62:2 63:15 66:1,7  66:15,22 67:13,16  70:24 73:4 74:17  75:7,14,16 76:3  77:5,19 80:18  82:2,9 83:2 87:4  100:10,16 103:17  105:21,22 107:14  107:24 109:9,18  111:13 113:15  115:12 123:4  129:18 130:8,12  130:22 131:1,18  131:19,22,25  132:7,9,19,22  133:6 135:7 136:5  136:8,20 142:4  143:5 144:8 152:4  <b>useful</b> 45:5,7  98:24 154:22  <b>user</b> 1:9 6:9 7:5  11:7 19:25 20:2  34:10 54:19 60:10  95:12 104:2 138:8</p>	<p>138:16 140:19  141:25 147:19  152:20 154:11  155:2  <b>users</b> 45:23  141:23  <b>uses</b> 97:24 138:21  <b>usual</b> 43:19  <b>utilization</b> 73:12  123:7  <b>utilize</b> 23:7 35:20  93:12 132:17  <b>utilized</b> 37:24 53:4  57:19 61:11 73:6  88:19  <b>utilizing</b> 37:21  126:16</p> <hr/> <p style="text-align: center;"><b>v</b></p> <hr/> <p><b>v</b> 6:23 51:11,13,13  55:3 113:2 116:14  <b>vaccines</b> 146:24  148:9  <b>valid</b> 44:23 153:1  <b>validate</b> 77:4  122:17  <b>validated</b> 100:17  <b>validation</b> 34:6,7  34:10,14,25,25  35:2  <b>valuable</b> 122:22  128:8  <b>value</b> 61:7,14  71:24 122:2  155:17  <b>values</b> 104:24  141:7  <b>variable</b> 60:3  <b>variant</b> 10:8  <b>variety</b> 13:18  14:18 85:10 131:5  146:23  <b>various</b> 14:23  15:10 17:1 18:14  18:21 21:10 50:21</p>	<p>63:17  <b>varying</b> 135:22  <b>venues</b> 14:17  108:24  <b>verbally</b> 124:16  <b>vereshchagina</b>  53:9 61:18 72:22  81:22 91:24  <b>vereshchanga</b> 2:4  24:16,17 41:17  <b>verify</b> 39:21  <b>versus</b> 147:1  <b>vi</b> 7:3 35:10 41:21  44:15 45:11 47:16  47:24 48:24 51:20  52:2,3,7 53:13,20  55:17 86:21 87:7  87:12 88:11,13  89:2 90:4 91:14  92:11 113:3  125:21  <b>vice</b> 4:8 104:5  119:1  <b>video</b> 5:8,23 95:2  117:18,22 140:13  144:19  <b>view</b> 61:21 72:2  136:11 147:13  <b>viewing</b> 85:1  <b>views</b> 118:14  123:15  <b>vii</b> 7:14 12:17  15:25 19:24 24:20  26:3,14 38:2  41:20 42:16 43:24  46:8 47:20 51:4  52:5 53:12,21  55:1,18 56:11  60:7 61:21 62:5  62:16 72:25 73:3  73:17 76:1 82:6  82:17 86:13,16,18  87:16,23 88:3  89:21 91:6 92:3</p>	<p>92:12 104:3  105:10,14,18  106:1,19,21 107:3  107:13,17 108:12  109:3,14 110:3  112:20 115:7  116:21 118:14  119:2 120:9,19  121:11,24 123:15  123:18 125:14  126:3,24 128:19  129:2,16 130:16  131:13,20 132:8  133:12 134:6  143:23 155:22  <b>vii's</b> 122:22  <b>virtual</b> 46:11 47:1  52:19 122:9  <b>visible</b> 150:3  <b>visits</b> 74:23  <b>vital</b> 94:6 126:23  144:3  <b>vitally</b> 125:15  <b>voice</b> 44:20 51:14  53:5 74:7 81:3  114:25 121:25  125:9 140:23  145:1,8  <b>voices</b> 128:18  148:23,25  <b>volume</b> 22:4,12  79:24 80:23  <b>voluntary</b> 146:15  146:17 153:20  <b>volunteer</b> 144:8</p> <hr/> <p style="text-align: center;"><b>w</b></p> <hr/> <p><b>waiting</b> 15:25  <b>walk</b> 26:13 54:24  136:8  <b>waning</b> 111:22  <b>want</b> 22:13 23:19  31:25 39:3 40:5  42:15 43:4 65:4,7  92:2,10 93:22</p>
---	--	--	--

107:22 138:15 140:17 141:10 144:10 154:14 155:2 <b>wanted</b> 12:5,6 18:11 22:9 23:4 52:5,9 92:8 <b>wanting</b> 71:12 <b>wants</b> 48:10 142:13 <b>warnings</b> 97:18 149:6 151:17 <b>watchdog</b> 100:3 102:1 149:17 <b>way</b> 14:10 22:21 30:14 37:20 45:3 78:10 84:7 97:13 114:25 125:5 151:6 154:6 <b>ways</b> 17:5 23:12 44:22 65:24 104:11 105:14 132:7 <b>we've</b> 14:15 16:3,9 18:19 27:6 28:2 30:12 32:3,15 36:2 45:11 47:16 54:19 64:4 95:15 106:15 111:15 113:6,12,16 116:2 150:19 154:1 <b>wearable</b> 83:2 <b>wearables</b> 109:9 <b>webinars</b> 13:11 <b>webpage</b> 29:19 155:22 <b>website</b> 5:9 88:14 88:23 91:7 95:19 <b>weeks</b> 90:17,19 <b>welcome</b> 95:6 131:19 <b>went</b> 72:19 83:21 <b>west</b> 2:20 140:10 140:11,13,17,20	<b>whereabouts</b> 91:25 <b>who've</b> 116:22 153:19 <b>wide</b> 13:17 14:18 31:3,7 49:1 85:2,2 105:12 <b>widely</b> 120:3 <b>willing</b> 48:1 <b>willingness</b> 108:16 <b>wish</b> 95:16 <b>wishes</b> 31:24 <b>witczak</b> 2:21 144:15,17,21,22 <b>withdraw</b> 143:7 <b>withdrawals</b> 97:18 149:7 151:18 <b>withdrawn</b> 151:10 <b>witness</b> 156:4 <b>witnessing</b> 146:23 <b>women</b> 58:10,21 59:3 62:9,15 <b>wonderful</b> 74:6 <b>woodcock</b> 54:14 <b>woodcock's</b> 5:9 <b>woody</b> 144:22,25 <b>word</b> 147:13 <b>words</b> 147:15 153:3 <b>work</b> 11:17 33:5 35:11 41:11 44:14 44:15 46:21 48:18 52:8 53:19 57:1 71:21 72:18 82:7 83:20 92:6 111:17 116:4 117:2,7 119:19,21 120:8 121:16 122:10 123:2 125:15 129:1 134:12 141:7,13 148:7 149:4 153:21	<b>worked</b> 41:4 111:15 116:23 118:8,9 122:3 <b>workforce</b> 107:2 <b>working</b> 37:22 87:24 104:10 110:9 150:5 151:23 <b>workload</b> 87:10 87:20 90:4 106:16 <b>works</b> 150:11 151:16 <b>workshop</b> 29:20 32:8 37:11 50:20 59:2,7 60:5 62:8 69:3,13 70:7,11 70:16 73:10 107:20 109:18 <b>workshops</b> 33:23 42:7 46:8 52:13 53:17 72:11 75:23 82:8 115:21 <b>world</b> 15:16 18:1 23:8 25:11 26:10 35:8,13,13,16,20 35:21 36:3,19 37:21,21 41:19 42:2,9 59:22 60:2 61:11,25 62:3,11 66:9 93:20 94:5 100:12,22 105:21 105:22 108:8,20 109:21 115:12,22 123:6 127:22 129:18,23 130:1,1 137:19 145:4 148:24 <b>worldwide</b> 125:10 <b>worthwhile</b> 49:7 <b>woven</b> 131:19 <b>writ</b> 81:11 <b>written</b> 39:10 43:5 95:16 126:13 137:21	<b>wrong</b> 39:22 <b>y</b> <b>yau</b> 155:9 <b>yeah</b> 94:18 118:1 124:5 140:15 144:19 150:4,9 155:9 <b>year</b> 8:1,18 22:16 44:8 48:1,13 49:24 68:3 88:3 88:12 89:5,5,7,9 89:13,25 90:15,18 90:19 92:15 97:12 99:1 105:2 106:15 121:1 127:4 134:7 139:24 145:11 <b>year's</b> 35:10 88:20 <b>years</b> 11:12 16:9 17:24 18:15 27:11 39:17 41:24 56:16 81:25 82:4 88:17 105:4,5 111:6 112:24 118:8,8 120:22 126:6 148:1 151:20 152:18,20 154:18 <b>yep</b> 86:1 <b>yield</b> 105:11 106:7 <b>z</b> <b>zolgensma</b> 134:21 <b>zuckerman</b> 2:22 149:23,24 150:2,7 150:10,14,15
---	---	---	--