FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

JOINT MEETING OF THE ANESTHETIC AND ANALGESIC AND DRUG SAFETY AND RISK MANAGEMENT ADVISORY COMMITTEES

(AADPAC and DSaRM)

Tuesday, December 18, 2018

8:05 a.m. to 3:49 p.m.

Day 2

FDA White Oak Campus

Building 31, the Great Room

10903 New Hampshire Avenue

Silver Spring, Maryland

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C O N T E N T S

P R O C E E D I N G S

(8:05 a.m.)

Call to Order

Introduction of Committee

DR. BROWN: Good morning. I would like to remind everyone to please silence your cell phones, smartphones, and any other devices if you have not already done so. I'd also like to identify the FDA press contact, Lyndsay Meyer. If you are present, please stand so that we can see you, but not here.

My name is Rae Brown. I'll be chairing today's meeting. I will now call the Joint Meeting of the Anesthetic and Analgesic Drug products Advisory Committee and the Drug Safety and Risk Management Advisory Committee to order.

We'll start by going around the table and introducing ourselves. We're going to start with the FDA to my left.

DR. THROCKMORTON: Good morning. I'm Doug Throckmorton. I'm the deputy director for regulatory programs, CDER, FDA.

DR. HERTZ: Sharon Hertz, director for the

Division of Anesthesia, Analgesia, and Addiction Products in CDER.

DR. STAFFA: Good morning. Judy Staffa, associate director for public health initiatives in the Office of Surveillance and Epidemiology in CDER.

DR. SECORA: Good morning. Alex Secora, Division of Epidemiology, CDER, FDA.

DR. AMIRSHAHI: Good morning. Maryann Amirshahi, emergency medicine physician, Washington, D.C.

DR. DASGUPTA: Good morning. I'm Nabarun Dasgupta, pharmacoepidemiologist at the University of North Carolina Chapel Hill.

DR. GERHARD: Tobias Gerhard, pharmacoepidemiologist at Rutgers University.

DR. BOUDREAU: Denise Boudreau, pharmacoepidemiologist from Kaiser Permanente, Washington.

DR. MEISEL: Steven Meisel, director of medication safety, Fairview Health Services in Minneapolis.

DR. BESCO: Kelly Besco, medication safety officer for Ohio Health Healthcare System in Columbus, Ohio.

DR. SHOBEN: Abby Shoben. I'm a biostatistician at the Ohio State University.

DR. HERNANDEZ-DIAZ: Sonia Hernandez-Diaz, pharmacoepidemiologist, Harvard Chan School of Public Health.

LCDR SHEPHERD: Jennifer Shepherd, designated federal officer, FDA.

DR. BROWN: Rae Brown. I'm a pediatric anesthesiologist at the University of Kentucky.

DR. ZACHAROFF: Good morning. Kevin Zacharoff, expertise in anesthesiology and pain medicine, faculty and clinical instructor at Stony Brook School of Medicine in New York.

DR. McCANN: Mary Ellen McCann, pediatric anesthesiologist at Boston Children's Hospital and Harvard Medical School.

DR. BATEMAN: Brian Bateman, anesthesiologist at Brigham and Women's Hospital, Harvard Medical School.

DR. GOUDRA: Basavana Goudra, anesthesiologist at Penn Medicine, Philadelphia.

MS. ROBOTTI: Suzanne Robotti, founder of MedShadow Foundation and executive director DES Action.

MS. NUMANN: Sabrina Numann, patient representative out of New Albany, Indiana, and advocate for the National Fibromyalgia and Chronic Pain Association. Thank you.

DR. CICCARONE: Good morning, everyone. Dan Ciccarone, addiction medicine and family medicine professor at UCSF.

DR. KREBS: Erin Krebs, general internal medicine and health services researcher at the Minneapolis VA and University of Minnesota.

DR. PISARIK: Paul Pisarik, urgent care medicine, Tulsa, Oklahoma.

DR. GARCIA-BUNUEL: Good morning. Martin Garcia-Bunuel, primary care physician, deputy chief of staff and director of quality and safety improvement at the VA Maryland Healthcare System.

DR. MACHER: Jeff Macher, professor of

strategy, economics, and policy at Georgetown University in D.C.

DR. BALLOU: Jordan Ballou, clinical assistant professor of pharmacy practice at the University of Mississippi, specializing in community practice.

DR. BRAND: Paul Brand, community pharmacist in Florence, Montana.

DR. FAUL: Good morning. Mark Faul, Center for Disease Control, senior health scientist.

DR. HERRING: Good morning. I'm Joe Herring, a neurologist and associate vice president of clinical neuroscience at Merck and the industry representative to the AADPAC committee.

DR. BROWN: Thank you for being here.

For topics such as those being discussed at today's meeting, there are often a variety of opinions, some of which are quite strongly held. Our goal is that today's meeting will be a fair and open forum for discussion of these issues and that individuals can express their views without interruption. Thus, as a general reminder,

individuals will be allowed to speak into the record only if recognized by the chair. We will look forward to a very productive meeting.

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine Act, we ask that the advisory committee members take care that their conversations about the topic at hand take place in the open forum of the meeting.

We're aware that members of the media are anxious to speak with the FDA about these proceedings. However, FDA will refrain from discussing details of this meeting with the media until its conclusion. Also, the committee is reminded to please refrain from discussing the meeting topic during breaks and lunch.

Now I'll pass it to Lieutenant Commander Jennifer Shepherd who will read the Conflict of Interest Statement.

Conflict of Interest Statement

LCDR SHEPHERD: Good morning. The Food and Drug Administration is convening today's Joint

Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and Drug Safety and Risk Management Advisory Committee under the authority of the Federal Advisory Committee Act of 1972. With the exception of the industry representative, all members and temporary voting members of the committee are special government employees or regular federal employees from other agencies and are subject to federal conflict of interest laws and regulations.

The following information on the status of this committee's compliance with federal ethics and conflict of interest laws, covered by but not limited to those found at 18 U.S.C. Section 208, is being provided to participants in today's meeting and to the public. FDA has determined that members and temporary voting members of these committees are in compliance with federal ethics and conflict of interest laws.

Under 18 U.S.C. Section 208, Congress has authorized FDA to grant waivers to special government employees and regular federal employees

who have potential financial conflicts when it is determined that the agency's need for a special government employee's services outweighs his or her potential financial conflict of interest or when the interest of a regular federal employee is not so substantial as to be deemed likely to affect the integrity of the services which the Government may expect from the employee.

Related to the discussions of today's meeting, members and temporary voting members of this committee have been screened for potential conflicts of interest of their own as well as those imputed to them, including those of their spouses or minor children and for purposes of 18 U.S.C. Section 208, their employers. These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties, and primary employment.

Today's agenda involves input and advice on strategies to increase the availability of naloxone products intended for use in the community. The

committees will be asked to consider various options for increasing access to naloxone, weighing logistical, economic, and harm reduction aspects and whether naloxone should be co-prescribed with all or some opioid prescriptions to reduce the risk of overdose death.

Because of the potential significant costs and burdens that may be associated with naloxone co-prescribing -- for example, economic costs to consumers and health systems, adjusting to manufacturing volume growth, drug shortages -- the committees will also be asked to consider the potential burdens that may be associated with naloxone co-prescribing for all or some prescription opioid patients.

This is a particular matters meeting during which general issues will be discussed. Based on the agenda for today's meeting and all financial interests reported by the committee members and temporary voting members, no conflict of interest waivers have been issued in connection with this meeting. To ensure transparency, we encourage all

standing committee members and temporary voting members to disclose any public statements that they have made concerning the topic at issue.

With respect to FDA's invited industry representative, we would like to disclose that Dr. Joseph Herring is participating in this meeting as a nonvoting industry representative acting on behalf of regulated industry. Dr. Herring's role at this meeting is to represent industry in general and not any particular company. Dr. Herring is employed by Merck and Company.

We would like to remind members and temporary voting members that if the discussions involve any other topics not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participants need to exclude themselves from such involvement, and their exclusion will be noted for the record.

FDA encourages all other participants to advise the committee of any financial relationships that they may have regarding the topic that could be affected by the committees' discussions. Thank

you.

DR. BROWN: We will now proceed with the FDA's introductory remarks from Dr. Sharon Hertz.

FDA Opening Remarks - Sharon Hertz

DR. HERTZ: Good morning, Dr. Brown, members of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee, invited guests, welcome back today so that we can continue our discussion about the use of naloxone in attempting to reduce the morbidity and mortality associated with opioid overdose.

I went into a fairly long introduction yesterday. I will not repeat it. But I am really looking forward to today. We're going to here, I'm sure, some interesting comments from our open public hearing, from our speakers, and we heard a lot of information yesterday about a variety of programs that have been successful to varying degrees. But really the question at hand is, how can we help facilitate the delivery and availability of naloxone in the community where it's needed?

I find that when it comes to anything opioid related, anything that sounds like a simple obvious solution should be very, very carefully thought about before pursuing because unintended consequences are very challenging to undo, and many efforts to improve public health with what seemed like very good potentially obvious solutions don't necessarily end up achieving the goal.

As we consider the different approaches for maximizing the availability of naloxone, one of which that we're considering is co-prescription to some extent that would go potentially in labeling versus emphasizing other strategies that you've heard about yesterday, we'd like to hear, as you'll see when we go through the questions, your thoughts in a very broad sense, but also, let's please always remember that we want to avoid the unintended consequences and maximize the public health benefit. Thank you.

Open Public Hearing

DR. BROWN: Thank you, Dr. Hertz.

Both the Food and Drug Administration and the public believe in a transparent process for

information gathering and decision-making. To ensure such transparency at the open public hearing session of the advisory committee meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement to advise the committee of any financial relationship that you may have with the sponsor, its product, and if known, its direct competitors.

For example, this financial information may include the sponsor's payment for your travel or lodging or other expenses in connection with your attendance at the meeting.

Likewise, the FDA encourages you at the beginning of your statement to advise the committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

The FDA and this committee place great importance in the open public hearing process. The

insights and comments provided can help the agency and this committee in their consideration of the issues before them.

That said, in many instances and for many topics, there will be a variety of opinions. One of our goals today is for this open public hearing to be conducted in a fair and open way where every participant is listened to carefully and treated with dignity, courtesy, and respect. Therefore, please only speak when recognized by the chairperson. We thank you for your cooperation.

Will speaker number 1 step up to the podium and introduce yourself? Please state your name and any organization that you're representing for the record.

MS. WHEELER: Good morning. My name is Eliza Wheeler. I'm from the Harm Reduction Coalition. We're based out of Oakland, California and New York. I will be speaking today from my role as overdose response strategies at the Harm Reduction Coalition, and I have no financial conflicts, and I'm nervous.

I'm going to do something a little different

today from what you've heard so far. I want to first thank my colleagues and friends who presented yesterday, Drs. Davidson, Walley, and Coffin, for giving a little bit of context and history around what we're talking about today.

None of us would be here today, including industry who are developing products related to naloxone, to the community, without this person. My colleagues mentioned him yesterday. This is Dan Bigg. He founded the Chicago Recovery Alliance, and he was the first person in the world to distribute naloxone to the community.

Naloxone was first distributed to the community, specifically people who use drugs, off of this van in Chicago starting in 1996. Prior to that, naloxone had been used for about 25 years in hospital and in pre-hospital settings.

In 1996, Dan and his colleagues from Chicago Recovery Alliance realized that people who used drugs were witnessing overdoses at an extremely common rate and that their participants at their program were dying from overdose, so they essentially liberated

the drug from the medical system and started giving it out to people off of this van.

For many years, probably I would say until maybe the late 2000s, 2010, this was considered pretty controversial. It was primary just harm reduction programs that were distributing naloxone at this time. Some of the foundational research on naloxone distribution was done during this time, most of which by people who are in this room, and we started seeing naloxone access laws starting to get passed in the early 2000s, which we heard about yesterday.

It wasn't until 2012 that the CDC published a report documenting how many naloxone distribution programs actually existed in the United States, and at that point, there was 188 different sites that were providing access to naloxone to laypeople, specially to people who use drugs.

It wasn't until 2014 that we started seeing co-prescription and pharmacy access starting to emerge, so much of which we're talking about here today and yesterday has happened in the last four

years.

As Dr. Davidson talked about yesterday, when we last did the CDC MMWR report in 2014, this was the landscape of naloxone access. Dr. Davidson and I and our other colleagues produced this map and produced the data for this map, and the majority of these programs are syringe exchange programs that are distributing naloxone to people who use drugs with a few exceptions that included some pharmacies.

What we're talking about when we're talking about those syringe exchange and harm reduction programs is what we keep referring to in the last two days as community-based overdose education and naloxone distribution. I understand that we're here to really talk about co-prescription, but what I'm here to talk about is the model that we know works.

The model that we know works to reduce mortality, and that is from the evidence that has been produced by the researchers in this room and elsewhere over the last 25 years, is community-based distribution.

This was never intended to be a medical

model, and that's why it's so difficult for everyone in this room and everyone else to figure out how to make it work through co-prescription and through pharmacy, because what we know works is the distribution of naloxone directly to people who use drugs and their community by people who are trusted in the community with low threshold/low barrier program models.

What we see here, when we're talking about community-based overdose education programs, this is what we're talking about. We're talking about programs that are distributing high volumes of naloxone directly to people who use drugs -- that's the acronym you see there -- and other high utilizers of naloxone. That might be a family member, friend, or other community of someone who uses drugs.

Programs operate under standing orders. This is different than the standing orders you hear referenced in relation to pharmacy access. The standing orders that we operate under authorize nonmedical staff, volunteers, and peers, meaning other people who use drugs, to provide direct access

to naloxone, meaning that the program that I run, which is one of the largest single city-based naloxone programs in the world in San Francisco, we distributed 60,000 doses of naloxone directly to people who use drugs this year. That is done by other people who use drugs, syringe exchange workers, outreach workers, and other volunteers and staff of programs working directly in the community.

Naloxone is purchased or obtained, stored, and distributed by our programs, and we operate under a low-threshold/low-barrier model. We do minimum 5-, 10-minute trainings. We don't collect much data. Programs are anonymous. We do unlimited refills, no appointments. The photos on the bottom are three examples of naloxone distribution programs.

We heard a little bit yesterday about the role of injectable naloxone. The role of injectable naloxone in our programs is crucial to sustaining the network of programs that actually providing by volume the majority of naloxone to laypeople in the United States.

We have two sources of affordable naloxone in

the United States. There are Direct Relief, which is a nonprofit program that has partnered with Pfizer to provide a million doses of free injectable naloxone over the course of four years. They have so far distributed about 72,000 doses of injectable in 2017 and 65,000 in 2018 through this program. These are largely health centers, rural community health centers, and other public health departments serving low-income communities.

The second is the Opioid Safety and Naloxone Network Purchasing Group. Myself and a woman named Maya Doe-Simpkins, who you've also seen referenced a lot on all these slides in the last two days, operate this group. Formerly we did that with Dan until he passed away in August.

Currently we have 89 programs in 34 states as part of this buyer's club. We limit the buyer's club to nongovernment community-based organizations who are distributing naloxone directly to people who use drugs. We distributed 506,000 doses last year and 845 doses year to date as of last Tuesday. In 2018, we're going to likely hit just under a million this

year.

So collectively between these two sources, 1.5 million doses of generic injectable have been distributed to people who use drugs in the last two years. This data was not included in any of the presentations that you heard yesterday from industry looking at pharmacy and prescription sales.

For community-based programs, we consider the two appropriate products for community-based distribution to be the generic 0.4 milligram injectable naloxone. I'm not going to go through this slide directly, but there are some pros and cons to both forms of naloxone.

My program in San Francisco has been distributing injectable naloxone since 2003, and it is the preferred method of naloxone or the preferred formulation of naloxone for most of our participants. We've introduced other forms with limited success over the years.

The second is the Narcan nasal spray. The reason I'm talking about these two products is because for a long time, we distributed the off-label

IMS version with the atomizer, and it was cumbersome and became too expensive for us. So this product has been helpful.

I'm going to talk just for a moment about best practices. We know from the literature that you see here, there's first responders, referencing summoned first responders like EMS, fire, and police, versus the true first responders, the people who are the witness to the overdose.

So the summoned first responders have to be summoned by someone. The person who summons them is the witness to the overdose, so that person is the person that needs to have naloxone.

We know that overdoses are primarily witnessed by other people who use drugs. Dr. Davidson talked a lot about this yesterday, so I won't spend too much time on this. We know that in large programs like Massachusetts, that distributes to multiple different groups of people and has collected really solid data on those different groups, that while 31 percent of people who are enrolled in the program are not people who use drugs,

87 percent of reversals are conducted by people who use drugs. The data for my program in San Francisco is the same.

We talked a little bit yesterday about the idea of saturation. This is a challenging concept as we don't have any concrete model to determine what saturation looks like, but we do have some guideposts in terms of the literature, in terms of understanding that in order to affect mortality, there's a dose-response effect from Alex's paper from 2013.

There's been some other modeling trying to figure out how much naloxone in a community of persons who use drugs is going to actually impact mortality, but what we do know is that the more, the better and who gets the naloxone matters.

If I distribute 60,000 doses to people who aren't going to witness an overdose, nothing happens. Mortality is not impacted. For example, in San Francisco, we assisted the police department in expanding to carry naloxone. They used it 27 times last year, and our participants used their naloxone 1,266 times.

If you have finite resources in resource-limited communities, your primary distribution should be focused on people who use drugs. Your secondary distribution should focus on other possible bystanders. That could be treatment program staff, shelter staff, family, and other folks who may witness an overdose. Then finally, I do not believe that health resources and public health resources should be going to purchase naloxone for summoned first responders.

Second, training and technical assistance, people who use drugs in harm reduction programs are the originators of this intervention and are the experts in this intervention. We should be at the table. We should be invited to these meetings, and we should be presenting.

My recommendations for the committee and for the federal agencies that may be listening are to approve an OTC form of naloxone that will be available to programs doing community-based distribution without the medical and legal gatekeeping that we currently have to deal with, at a

low cost. When I mean low cost, I mean less than $1, nonnegotiable.

FDA and SAMHSA, clarify language around generic injectable, especially the language that says FDA approved products. SAMHSA and CDC, focus on directing resources and attention to community-based programs that provide low threshold saturation-based distribution directly to people who use drugs.

We would like the acknowledgement of the history and work of harm reduction in community-based programs and honoring the original intention of naloxone distribution as a way to build power, empowerment, among people who use drugs.

Seek our technical assistance and guidance. People who use drugs and other harm reduction experts, researchers, and policymakers are the innovators of this intervention and are the experts. Compensate us for our expertise and ensure that people with lived experience and people who use drugs are involved in decision-making about their own lives.

Finally, to the DOJ, who I don't think are

here, please fund naloxone for law enforcement to ensure that our resources are no longer being diverted from public health to finance law enforcement carrying naloxone.

Overdose education is harm reduction. It was conceived of and first implemented by people who use drugs, allies, and practitioners of harm reduction as part of a radical public health movement based on those principles that you see there.

Finally, just a couple pictures, the woman on the bottom right is Kim Brown. Her son Andy died from an overdose in Davenport, Iowa, and she started a naloxone program out of her own pocket.

That's her taking a boat across the flooded Mississippi to pick up her shipment of naloxone from the post office in order to distribute it on her own, doing outreach to people who use drugs. And that is actually what naloxone access in this country looks like.

That's all. Two seconds left.

DR. BROWN: Ms. Wheeler, can I ask who is funding your community effort?

MS. WHEELER: Sure. We were actually the first health department funded naloxone distribution program in the country. So we're primarily funded by the San Francisco Department of Health, and we recently this year received a little bit of naloxone through the SOR grant administered by the state for the first time.

DR. BROWN: Will speaker number 2 step up to the podium and introduce yourself? Please state your name and any organization you are representing for the record.

DR. HUFFORD: My name is Dr. Michael Hufford. I'm the co-founder and CEO of Harm Reduction Therapeutics. In terms of my disclosures, Harm Reduction Therapeutics is a nonprofit pharmaceutical company that we formed in 2017 after we learned of the FDA's interest in seeing a naloxone product be taken over the counter.

After fundraising for over a year, I personally pitched more than 50 times to a variety of philanthropies and other organizations. We received an unrestricted grant of $3.42 million from Purdue

Pharma to develop our OTC naloxone product. I firmly believe what Mary Lasker said, the famous philanthropist, is true, which is, "Money is frozen energy, and you unfreeze it when you pay people to work." So we were extraordinarily grateful for the support, and we are now running forward as quickly as we can.

Our mission is to prevent opioid overdose deaths by making low price naloxone available to everyone over the counter. We have a nonprofit mission. We're a 501(c)(3). Our team, thankfully, has more than a 20-year history of prescription to OTC switch successes, where it has been shown time and time again that over-the-counter availability increases access.

The good news for someone like myself trying to push this forward, I'm surrounded by colleagues that have deep expertise and experience doing this, which is less of good news to some of the existing companies with naloxone products that are reluctant to see the product be taken over the counter.

I'm going to be driving home this theme of

cost and access and that we need to keep our eye on that prize. I thought it was remarkable yesterday, the verbal contortions you heard from industry trying to tell you that cost doesn't matter, trying to tell you that over-the-counter access somehow won't actually improve access.

Those contortions I thought were worthy of Cirque du Soleil. I'm here to present the alternative scenario that we see time and time again, that over-the-counter availability does increase access. But I think to fully understand the power of that, we need to understand naloxone in the context of the opioid epidemic, so I'm just going to make a few quick points on cost and access to heroin.

A bag of heroin today will set you back about $5, the cost of a pumpkin spice latte. This is where the cost of acquisition continues to fall. So heroin has gotten less and less expensive. The supply chain both for heroin and fentanyl is global in nature and every bit as robust as the coffee beans that you grind up and consume at your local café.

As outlined in Dreamland, I thought very

compellingly, even the retail infrastructure for heroin distribution has seen dramatic innovation over time; so heroin, decreased cost, increasing access. How does that compare to naloxone?

Just to put this in historic perspective, 1971, President Nixon, and cutting-edge technology at the time was a very rudimental scientific calculator, that was when naloxone received FDA approval. It went off patent under Reagan, and the Apple was now your cutting edge, the Apple, original Mac.

Widespread use by paramedics intranasally, lest any of us believe erroneously that intranasal drug delivery is somehow innovative, it is not in general, nor is it with respect to naloxone administration.

Today, we have a variety of different products, and we'll be talking more about those here quickly. I don't need to belabor the point, opioid deaths continue to rise as does the price of naloxone. This is from Meg Tirrell in an excellent investigative article she published looking at those prices over time.

Just to drive home a point, I'm trained as a clinical psychologist in addiction. So I'm going to put that hat on just for a moment and encourage you to fight the anchoring heuristic. So the anchoring heuristic is when someone tells you the price of something is $1,000 and then it's priced at $99, you anchor that estimate of whether $99 is a value based on the fact that it used to be $1,000, right? That's a fundamental way that our brains process information.

So when you see some manufacturers have recently lowered their prices, I would encourage you to think of it in those terms. The fact that something never should have cost $4,500 does not mean that it's now a bargain at a hundred and some dollars. Likewise, the extent to which something has already been price gouged and now is available for $140, the promise to not further price gouge that price should not be the cause of patting anyone on their back.

This was published in The New England Journal of Medicine a couple of years ago talking about that

price increase, and I want to focus just on nasal spray for a moment. Just so everyone's aware, just by gauge of sighs, that's a nickel beside the actual container that holds the naloxone intranasal formulation. I picked 5 cents because at commercial scale, the amount of solution, the cost there is about 4 cents.

The delivery, just to be clear, just so we are all aware, that is an Aptar generic intranasal device. It's very clever. It's used in a variety of different prescription products. But just to be clear, there hasn't been a lot of innovation on that front, either.

When Emergent BioSolutions acquired Adapt Pharma, I think it's worth pointing out that they did so at the cost of $635 million with an additional $100 million in post-acquisition milestones. As a businessman myself doing drug development for the past 20 years, I can assure you that you buy companies because you expect them to increase in value.

Where is that value to be derived from, from

this generic drug being delivered intranasally? Well, I would suggest to you there are two paths. One is by getting it approved co-prescription where it could recognize hundreds of millions of dollars in revenue over the next few years, but I would also point you toward an interview with Bloomberg Press on August 29th shortly after the acquisition where the CEO described schools as a growth opportunity.

So I assure you that one of the very first markets that I intend to steal from Emergent BioSolutions is public schools who price they pay for these products, I assure you absolutely does matter.

I also want to talk about access. You've already heard a lot of this, so I'm not going to dwell on it. Standing orders do not equal adequate access today. Time and time again when you survey pharmacies, many don't stock it. Many pharmacists are unaware of its status through standing orders. We also know that stigma continues to affect access as was touched on repeatedly.

Thought I'd end on this cartoon saying, "I have the invisible hand of the market." On line 2,

"Should I put it through?"

I want to just end with a few final thoughts of things I believe. Since I have the microphone for another 4 minutes, bear with me. I believe despite being the co-founder of a nonprofit pharmaceutical company, I strongly believe in capitalism. Profits drive innovation, and innovation is producing, as we speak, lifesaving treatments that are transforming medicine.

But that capital put at risk to develop those innovations deserves to be returned to investors many-fold. I've been fortunate to raise venture capital, and that's the very promise I make when you're developing innovative therapies. But just as innovators are creating the cures of tomorrow, there's another group, though thankfully a much smaller one, that follows in the wake of these innovators, and uses an imperfect system of incentives to wring profits by exploiting this system. And I'm sorry to say this is the state of the naloxone market today.

I also believe, quite contrary to popular

opinion, that the pharmaceutical industry is fundamentally a noble enterprise. The opportunity to develop new medicines is both an honor and an obligation, but we do so under a social contract where you recoup profits over the lifespan of a patent with the expectations that the price should then fall as the risk is removed.

I believe your work matters. This committee and ones like it can affect policy that in turn can cause lives to be saved or lost. I also, for what it's worth, believe this room should be packed, but the stigma surrounding addiction takes many forms.

Martin Shkreli and his price gouging of Daraprim and his pharma Bro persona made a perfect boogeyman for the media's fleeting attention span around price gouging. Likewise, when Mylan gouged the price of the EpiPen, likewise, it rightly pulled at our heartstrings, imagining children in the midst of unstoppable anaphylaxis not having access to the EpiPen. But make no mistake, it's our collective acceptance of the price gouging of naloxone; it would have received equal scrutiny to the public, if only

we believed collectively these lives had equal weight.

Lastly, I believe that if the free market, composed in part of individuals whose companies are represented in this room, will not do everything in their power to reduce the price and increase access through over-the-counter availability, then I assure you my colleagues and I at Harm Reduction Therapeutics intend to do just that.

Why? I believe that cost and access matter. They always have, they always will, and I would implore you not to believe otherwise. Thank you.

DR. BROWN: Thank you very much.

Will speaker number 3 step to the microphone and introduce yourself? Please state your name and any organization you're representing for the record.

MR. LOTT: This is going to be a dual presentation. Hi. My name is James Lott. I'm a pharmacist and the co-founder and CEO of Fiduscript.

MR. CARRYER: Hello, my name is Straker Carryer. I'm an experienced software developer and technical manager, and I'm the CTO and other

co-founder of Fiduscript PBC, and we're a public benefit corporation focused on technology solutions to help save lives.

MR. LOTT: In the next few moments, we are going to go over our solution to the opioid crisis, Naloxone Exchange. We're going to talk about some of our engagement with our patients and their loved ones, what we learned from them, as well as some of our next steps and how you folks could help us.

We're honored to be supported by esteemed groups such as the Clinton Global Initiative, Google, and Stanford Medicine, and also the nation's top startup accelerator, the University of Chicago, the Polsky Center for Entrepreneurship. And our affiliations, myself, I'm currently a graduate student at the University of Chicago, the Harris School of Public Policy.

MR. CARRYER: And I'm currently employed by Facebook. However, these thoughts are our own and are affiliated with Fiduscript PBC, and we have no other formal disclosures to report.

MR. LOTT: Our intervention to the opioid

crisis is Naloxone Exchange. It's an online marketplace where anyone can purchase the lifesaving antidote, naloxone, receive effective training on how to use it, and have it delivered straight to their door.

With Naloxone Exchange, it's easy to use. It works in three steps. Step 1, you go to our website at naloxoneexchange.com. Select, get naloxone. After that, you can select the version of naloxone that you want, and that's according to your administration approach, or if you're price sensitive, the best price that might work for you. After that, a pharmacy partner processes the order and ships it straight to the user or the entity's doorstep.

What we're providing immediately is easy access and a stigma-free experience, which I would note is extremely important through this crisis for all populations. We're quite aware that there are a lots of pain points to accessing naloxone, and if you're not, I'd like to inform you a little bit.

There have been some studies, quite a few

studies, that have shown stigma is an access point. There are some patients who even if naloxone is available free, they prefer not to go in public and access it because they've had poor experiences or they just can't fathom the courage to do it.

Pharmacy access also continues to be a problem. Before this visit, I walked into a pharmacy to purchase naloxone. The pharmacist didn't know what it was. It took about an hour and a half to get the order. It was not the best experience, and actually, they told me that it wasn't available and you had to get a prescription. This is in the city of Chicago. I don't know what the issue was, but it is an issue.

Community access is another thing. If you are an entity that is informed of the opioid crisis and you want to be responsible and carry naloxone in your facility, how do you get that since it is still a prescription? Then the debacle on price, which you've heard quite a bit on.

We do believe that all of these pain points are intolerable, and we would like to develop a

platform that can address all of these issues to some degree.

Prior to developing Naloxone Exchange, we reached out to over 500 substance users and their loved ones to better understand what they wanted. They also gave us some vital personal stories. One user, or responder rather, said that naloxone is a miracle. "We do not deserve to die for our addiction. If it was made available easily, so many lives would be saved."

This same user, or responder, is from South Carolina. This person remains anonymous. They self-reported that they have used heroin and prescription opioids. And also in their circle, they list themselves, their family, and friends who have also been affected by the crisis as having substance use disorder.

We got other feedback from the survey, which we plan on publishing pretty soon, but one thing that we want to share with you immediately is, through our survey, we found that these consumers want to maintain their privacy. And if given the option,

they want to get naloxone online and get it delivered to their home if they could.

Also, Dr. Leana Wen, who's been a long-term advocate for naloxone distribution, once said, "This is a public health -- when one small intervention can change the trajectory of people's lives." And us as an organization, we could not agree any more.

MR. CARRYER: I want to briefly talk about privacy and security and the technical solution that we're offering. Let me just be very clear. We take our customers' privacy and security very seriously. We're hosted entirely on AWS where we've signed a BAA agreement, and we're entirely HIPAA compliant, and we intend to remain that way the entire time.

Should a customer have any questions about the product despite offering formal training before they order it, we do have medical professionals that will be able to answer any questions they have after placing an order.

Lastly, we've been .pharmacy certified. So naloxoneexchange.pharmacy also goes to the same website, which is an independent third-party kind of

audit in terms of verifying that we are a safe and certifiable pharmacy service.

Additionally, you can see here is Fiduscript's current market position. The light blue represents states that we have regulatory approval to launch in. That is 18 states representing about 40 percent of the U.S. population, and we plan on initially launching towards the end of Q1 2019.

The dark blue states are where we have approval currently pending. We're actively working on getting these additional states onboard. Then obviously, we want to expand to cover the entire U.S. population. It's dependent on state level regulation. We hope to do that by the end of 2019.

You can also see here at the bottom, you heard previously talking about desired customer bases. We don't discriminate against any particular person in the entire United States that wants to get naloxone.

MR. LOTT: Lastly, I would like to close with how you, the audience, and the committee can help us. If you're a physician, please review that map. If

you don't see your state highlighted, write a collaborative agreement with us. If you're an advocate for naloxone distribution, contact us, connect with us, so we can bring naloxone to your state.

If you're a healthcare executive, you have one of the most vital roles in this room. Not only can you expand access, but you can also help consumers reduce the cost.

If you're a government agency, including the FDA, assist us, subsidization, grants, and procuring contracts. This is the way that we found that patients want it, so we would like to scale it. And then if you're an investor, this is a unique social impact opportunity where you can save lives. Thank you.

DR. BROWN: Can I ask you what you expect your price point to be?

MR. LOTT: We are looking forward to working with the manufacturers to get the best rates possible. As a public benefit corporation, we're not about maximizing our returns. We're more so trying

to scale our public benefit, and that's how we measure ourselves as an organization.

DR. BROWN: Do you have any general idea of where injectable naloxone would be, the price point for injectables?

MR. LOTT: Injectable, as an early organization, we're not planning on doing injectable. We're only looking at the -- do you mean injectable as in the Evzio or as in --

DR. BROWN: No, the small vials.

MR. LOTT: Yes. As an organization, we are not offering that at the start. We do plan on doing it later, and we can help entities get that --

DR. BROWN: What about the nasal spray? I'm just trying to get the committee some idea of what your price point would be.

MR. LOTT: We plan on being around the market rate, but we would really like to work with manufacturers to lower the cost.

DR. BROWN: All right.

MR. LOTT: Thank you.

DR. BROWN: Thank you very much.

Will speaker number 3 step to the podium and introduce yourself? Please state your name and any organization you're representing -- 4.

MS. HAAS: Good morning. My name is Erin Haas. I work with the Maryland Department of Health, the assistant director in the Office of Prevention within the behavioral health administration.

Part of my role is to oversee our statewide naloxone distribution program. We have about 100 programs that distribute naloxone locally. Twenty-four of those are our local health departments with whom I work very closely to set up their programs, provide them funding, and direct those resources to getting naloxone in the hands of people who use drugs.

I'm also a national consultant on harm reduction. I've worked with a lot of other states on their overdose prevention programs as well as some tribal nations. I've no financial disclosures or anything like that.

I really appreciate this opportunity for public comment. I just have three simple points to

make, and my goal is just to add a bit of a sense of urgency to the proceedings, hopefully within my modest time limit.

I want to first applaud the FDA. I really understand that this is a heavy lift for a federal agency. It's been a monumental shift to, I think, even have these meetings to bring together committees to focus on overdose prevention and naloxone. Having worked at naloxone policy at the state level, I know what it takes to change those laws, so at the federal level, it's even harder.

I can say that it's without frustration that I view having another meeting about naloxone. When we know that it's so easy to use, so safe, and all it does is restore breathing, it really feels unethical at this point in the opioid epidemic to provide any additional roadblocks to its access to those who are at risk of dying of overdose.

The only thing I can think of right now that's holding us back is stigma. I feel if we really believed that people who use drugs can use naloxone, if we really believe the research that for

20 years they've been saving each other, they've been taking care of each other where the healthcare system has failed them, I think if we really believed that, then we wouldn't have any restrictions to access to naloxone right now.

We've made it available to law enforcement, to friends and family, but the community where there's still a gap is people who use drugs. I think that there just really shouldn't be any more resistance to bringing down those barriers to access, especially in a changing risk environment with fentanyl continuing to permeate the heroin market, different fentanyl adulterants, and different new opioids that are being approved.

My second point is to again emphasize that over-the-counter naloxone would greatly expand access. From my perspective at the state, I think it would benefit our community programs, that they would be able to cut out working with a medical provider to order and distribute the drug.

I've spent a lot of time passing laws to ensure providers that they wouldn't be held liable

for writing this prescription for a lifesaving drug. I've spent a lot of time talking to providers, encouraging them, holding their hand through writing those prescriptions, and putting those laws into action, working with the medical boards. Really, all of that just feels unnecessary.

I think for new programs where the state hasn't made that lift across the country, making it over the counter will encourage them to provide naloxone and make it a lot easier for them to get started and have wide distribution of the drug.

Finally, I think related to the topic that I know is up for debate today, I think co-prescribing naloxone with opioids is a great idea. At this point, it just feels like why not do it. It's another way to expand access. I think it would improve our standards of care for people who use opioids.

Doctors should be having that conversation. If you're prescribed an opioid and you don't understand the risks for overdose, and don't understand that there is actually an antidote to that

overdose, again, it feels unethical at this point in time.

I also believe that that would drive demand at the pharmacy level. We've heard how difficult it is to get naloxone at a pharmacy despite standing orders, and again, despite all the efforts to educate pharmacists, all the CEUs, all the presentations to the Board of Pharmacy, it's still very, very difficult.

I hear over and over again from pharmacists that people just aren't coming in to ask for it, so why stock it, especially when they can order it within 24 hours, which is fine. But I think with that increased demand, we'll see more availability in pharmacies, more ready availability, so that they can provide it to anybody who walks in the door and asks for it, in lieu of it being over the counter.

That's my final point. Thank you very much, again, for the opportunity for public comment, for having this meeting, and I know doing all the hard work that it takes to get to this point in time. Thank you.

DR. BROWN: Thank you.

Would speaker number 5 step to the podium and introduce yourself?

DR. KOCHANOWSKI: Good morning. I'm Barbara Kochanowski, senior vice president of regulatory and scientific affairs at the Consumer Healthcare Product Association. CHPA is the trade association representing the manufacturers of over-the-counter medicines and dietary supplements. CHPA is one of the oldest trade associations in America and the only one representing OTC medicines.

CHPA has been a long supporter of access to appropriate medicines without a prescription, and that's what I'm here to talk about. I'll tell you how the power of access through prescription to OTC switch benefits consumers and the healthcare system.

Prescription to OTC switch has a 40-year track record of providing value to Americans through access, affordability, trust, empowerment, and at-hand benefits. Today I'll talk about these values, share some specific examples of the benefits of switch, and key principles behind prescription to

OTC switch.

Access to appropriate medicines without a prescription empowers consumers to take greater over their health and provides tremendous public health benefits. Fueled in part by innovation and prescription to OTC switch, the U.S. market for OTC medicines is strong, providing Americans with accessible, affordable, and trusted healthcare options available 24/7 in a wide range of retail outlets, including pharmacies, supermarkets, and mass merchandisers.

Looking broadly at the importance of access and affordability, CHPA worked with Booz and Company to estimate the value of OTC medicines to the U.S. healthcare system. The 2012 study determined value for seven of the largest treatment categories based on the cost of alternatives, including nontreatment if medicines were not available. It looked at behavior based on both actual experience with prescription to OTC switches and using a nationally representative survey of 3200 Americans.

Among the study's key findings, OTC medicines

saved the entire U.S. healthcare system, employer-sponsored healthcare plans, government programs, self-insured, and the uninsured $102 billion annually. For every dollar spent on OTC medicines, the healthcare system saves 6 [dollars] to $7.

The availability of OTC medicines in the seven treatment categories provides relief for millions of Americans in the U.S., 60 million of whom would not seek treatment if OTCs were not available. And the study found that OTC medicine offers additionally potentially 23 billion in potential worker productivity benefits by keeping the American workforce at work and not at home or in doctors' offices.

This original study has recently been updated, and while we're still analyzing the data, we expect to announce in the first quarter of next year that OTC medicines are even more important to the U.S. healthcare system than what we saw in 2012.

Looking at naloxone OTC access at an affordable cost definitely empowers consumers to be

prepared to act. We have active interested healthcare consumers who want to take control of their healthcare needs. They must have trust in the safety, quality, and effectiveness of their medicines.

For instance, in qualitative research we released in 2013 by Nielsen and IMS on drivers of trust, we found most Americans surveyed prefer to use OTC medicines instead of a prescription when the OTC is available. Three of those five surveyed visit a healthcare professional one to two times a year, and yet the average U.S. household reports four to five instances of cold and flu, three to four instances of heartburn each year.

The point, for a range of common illnesses or conditions, Americans rely on OTC medicines without having to see a healthcare professional. But that doesn't apply solely to patients. Healthcare professionals also report high trust in OTC medicines. For instance, 98 percent of primary care physicians report that they trust OTC medicines and recommend them to their patients.

Looking at naloxone, we've heard first responders and community-based organizations have had success administering naloxone. If naloxone becomes available OTC, consumers will need to trust that this very effective medicine with little risk can be used effectively by them to treat overdose.

Let's look at three specific prescription to OTC switch examples underscoring the power of access. First, the late 1990s brought us prescription nicotine replacement therapies. More than one study found a 150 to 200 percent increase in their use in the first year after switching to OTC status. That enhanced access has resulted in tens of thousands of people quitting smoking every year. That's longer, healthier lives. That's a $2 billion public health benefit every year.

The past ten years have seen consumers receive the benefit of OTC access to frequent heartburn and allergy medicines. In the case of allergy medicines, since 2009, 5 medicines once available only via prescription, including intranasal steroids, are now available OTC.

A study by Nielsen and CHPA showed a very significant shift to OTC allergy products and a slight decrease in healthcare provider visits, indicating the important role access to OTC treatment provides without overwhelming healthcare providers with more visits for more sufferers.

Finally, a recent paper by Chang and Brass showed the benefit of OTC proton pump inhibitors, first introduced in 2003, in reducing doctor office visits for upper GI conditions.

The switch of a prescription medicine to OTC status is a science-based, data-driven process involving extensive interaction between the sponsor and FDA; as you heard yesterday from Ms. Cohen, thorough research to develop labeling, testing to make sure the consumers understand when the product is right for them and how to properly use it.

This research also informs education and the type of education that may be helpful in the OTC environment. Consideration of a switch also involves an analysis of risk-benefit. This is a model being used more and more. It's an international framework

for issue review, and in 2011, Drs. Chang and Brass and colleagues proposed it for use in switch.

While there's yet to be a determination from FDA about whether naloxone should be switched, we can look at some of the historical criteria and see how naloxone stacks up.

OTC status will certainly improve access to naloxone. Naloxone can reverse otherwise fatal opioid overdoses. There's a clear understanding of the expected benefit and often little to no time for physician or other healthcare professional to intervene and evaluate the condition. There's no special toxicity risk, a wide margin of safety, and no risk of overdose.

We await the development of a consumer-friendly label and demonstration of appropriate use of an OTC product. It's very rare for a potential OTC medicine to have such lifesaving possibilities.

In conclusion, access provides tremendous power for consumers. CHPA supports science-based, data-driven decisions on switch applications for direct consumer use. Evidence supports individual

and public health benefits of OTC medicines, including through prescription to OTC switch. I trust FDA will include consideration of the benefit of access as they evaluate naloxone for OTC status. Thank you.

DR. BROWN: Thank you.

Would speaker number 6 step up to the podium and introduce yourself?

MS. McLEMORE: Good morning. My name is Megan McLemore, and I'm an attorney and senior health researcher at Human Rights Watch. I have no financial interest to disclose.

Human Rights Watch is the largest independent, nongovernmental human rights monitoring organization based in the United States. We have researchers in more than 90 countries. We investigate human rights conditions, do policy and legal analysis, and advocate with governmental entities for change.

For more than a decade, I have focused much of my work on increasing access to health services for stigmatized, marginalized, and criminalized

populations, including people who use drugs.

We support efforts to increase co-prescribing naloxone with opioid medications as one of the many responses that are required in the midst of a public health emergency that is seeing hundreds of Americans lose their lives every day. But my remarks today will focus on the issue of over-the-counter naloxone, as we believe this is necessary and overdue as part of an all-hands deck approach that will reach the majority -- the majority -- of people dying of opioid-related overdose in the United States.

I would like to share some firsthand experiences from the ground that might help to understand why this is so important.

I spent this last week in Iowa, where I joined two community-based organizations in their harm reduction activities, Quad Cities Harm Reduction and the Iowa Harm Reduction Coalition.

In the three short days I spent with them, they attended one funeral of a friend who had overdosed after coming out of jail. The receptionist at the methadone clinic told us her brother had

recently died of overdose, and when we did outreach at the Davenport bus station, someone had overdosed in the bathroom a half an hour before we arrived. The fire department vehicle had just left.

Such is the situation on the ground in America's heartland, and the rate of overdose in Iowa is actually relatively low.

Kim Brown, whom Eliza mentioned in her presentation, started Quad Cities Harm Reduction a few years ago after her son Andy died of overdose after leaving the county jail. In their little office, they have a white board up with the latest data. In 2018 through Thanksgiving, they have distributed 1,201 naloxone kits and 240 reversals had been reported.

This reporting is informal and surely underestimates the number of reversals, as not everyone lets them know. That is at least 240 lives saved. And I don't need to remind you that these are more than numbers. These are people's mothers, fathers, brothers, sons, and daughters whose lives are saved by volunteers who are giving out naloxone

kits at the shelters, at the food banks, at motels, at trailer parks, at the methadone clinic, and at the bus stations.

These are all injectable kits because Kim says, quote, "We can't afford the nasal spray, and these work just fine."

How could moving naloxone over the counter help community-based organizations? The requirement for a standing order was a barrier. Kim said it took seven months to find a provider to do a standing order for them, and that is in a city. For smaller towns and rural areas, it might prove impossible.

Also, people who use drugs are not likely to use pharmacies when interaction with the pharmacist is required. Lindsay, a 23-year-old volunteer with QC Harm Reduction, told me that, quote, "When I was using, the last thing on my mind was health insurance or dealing with any of that. I wasn't about to go into a pharmacy and have a session with somebody in a white coat who might look down on me."

Lindsay might not have the money to buy a naloxone kit for herself even if it were over the

counter, but over-the-counter status would make it easier for community-based organizations to buy naloxone in bulk and then distribute greater amounts of the product for free. Mail order initiatives that are underway would also be able to scale up much more easily.

Prescription status is a legal barrier as well. In Florida, where I'm from, community-based organizations are not expressly permitted to distribute it under the naloxone laws, and none of the 67 county public health departments in Florida distribute naloxone. With no public health support and no express legal permission statewide for either Naloxone or syringe exchange, community-based distribution is extremely limited.

In Jacksonville, for example, no community organization distributes naloxone despite alarmingly high overdose rates in that city. In their minds, the prescription status raises liability issues, the law is unclear, and they do not distribute naloxone as a result.

In contrast, in Miami, under a pilot program

permitting syringe exchange, the one in the state of Florida, the syringe exchange has reversed more than a thousand overdoses in a year and a half of naloxone distribution. In order for a community to be saturated such as in Hamilton County, Ohio, every barrier must be addressed and reduced or eliminated. That is the only way to achieve significant results in mortality rates such as we heard about yesterday.

I call your attention to the public comment submitted by the National Health Law Project in your docket papers. NHeLP has addressed the misunderstanding that the FDA must wait for a manufacturer to apply to transition their product to over-the-counter status.

This is incorrect. The FDA has the authority right now to initiate a transition to over-the-counter status for numerous formulations of naloxone. Indeed, the commissioner has the obligation to do so when the product at issue has proven safe for over-the-counter distribution and the prescription is no longer serving the public health.

Naloxone is a safe generic medication that

has decades' long track record of use by laypeople, and in fact, many formulations are now expressly designed for use by nonmedical personnel. We applaud the efforts of the FDA to prepare every step for a manufacturer to come forward, including doing the label research for them, but the fact is that none have done so to date.

We support the recommendation by the National Health Law Project, the Harm Reduction Coalition, Dr. Peter Davidson, and others who spoke yesterday and today that at least some formulations of naloxone be approved immediately by the FDA for over-the-counter status.

Cost is certainly an issue, but one barrier should not be used to justify continuation of another. Some formulations could remain under prescription status for insurance purposes, and we believe that the public health emergency more than justifies government action to subsidize bulk purchases.

But most people who are dying are outside of the medical and insurance model. The fact is that

people like Lindsay in Iowa don't have insurance, they cannot afford naloxone now, and only community-based distribution is saving their lives. As a matter of public health and human rights, the FDA must use every means available to it to scale up those operations.

Human Rights Watch has submitted comments that are part of the docket, and if you need further information, please do not hesitate to contact me. Thank you very much.

DR. BROWN: Thank you.

Could speaker 7 step up to the podium and introduce yourself?

DR. PLUMB: Hello. My name is Jennifer Plumb. I'm a pediatrician, an ER doc, a mom, also a sister who lost her brother to a heroin overdose in 1996. I wanted to talk to you a little bit today about my experience in Utah and taking lessons that I've learned, trying to figure out how to effectively get naloxone out in my state with the hopes that it can help inform you on what we really need.

To give you an idea, Utah is a little bit of

an unexpected spot to be thinking about this realm from. Here's an idea of what our injury deaths look like. Injury death equals preventable death. Injury doesn't happen; death doesn't happen. And in the state of Utah, we lose more people to drug poisonings or overdoses than we do to firearms and motor vehicle crashes put together.

Our opioid deaths in that state, this very conservative state, which actually has a lower usage rate of alcohol, tobacco, many of the illicit substances and doesn't have the highest prescribing but decently high prescribing, has opioid deaths, at least as of 2016, two-thirds of which were attributed to prescription opioids and one-third of which attributed to heroin and other illicit substances. We bury one Utahan every single day in this state.

This led to, by 2014, Utah being fourth highest in the nation for overdose deaths. Again, kind of an unexpected place certainly for most Utahans, but I think for a lot of the nation, you don't think of Utah that way. Kentucky, West Virginia, New Mexico were higher than us at that

point.

2014 was a pivotal year when we realized this, and we said we've got to step in. We've got to start doing something. Naloxone access was one of the largest steps that we took in doing that. By 2015, we'd fallen to 7th in the nation. By 2016, we'd fallen to 19th in the nation.

Now, sadly, our rates weren't changing. We were still in the 22 to 23 per 100,000 range. Other states were leap frogging over us, so at least it felt like we'd held the dam. But we learned a lot of really important lessons in that time, and I think those are lessons I wanted to share with you today.

Lest it sounds a little bit negative and gloom and doom, and I show you as it goes across county by county by county, some of our counties have death rates up into the 50 to 70 per 100,000 in the center of the state.

We have actually finally started to see a bit of a turning of the tide in Utah. In 2017, as is reported by CDC data, we are one of the less than ten states that did experience a decrease in our death

rate, down about 19 percent in 2017. What that actually looks like as reported by our local Salt Lake City Tribune is that we've seen decreases in our heroin-related deaths, our prescription opioid-related deaths, but a bit of an increase in our bulk substances.

2017 meant that there were nearly 90 fewer people buried, 90 fewer families that had to go through what my family went through, 90 fewer devastations that happened. That is still one death every day, and that's too many. But I feel like we're perhaps on to something, and those are not lessons that I necessarily knew off the bat.

We wanted in 2014, like I mentioned, to impact change, and that was when we first got naloxone access laws. You're probably surprised; not many of you. Utah is fairly behind the curve in a lot of things. But 2014 was our first naloxone access laws, and they were important because they allowed for people to be prescribed or dispensed naloxone, so the very mainstream way that we think about, doc or pharmacy, if you were someone at risk

of overdose or at risk of witnessing an overdose. All right; makes sense.

We also put into our law that there was no physician-patient relationship required, which I think is very important when we look at ways that we need to get access out and not have communities experiencing what many of the other public speakers are talking about, difficulties getting someone to prescribe it.

Our initial law did require -- the only legal requirement was that 911 would be called if you used your layperson naloxone kit, and then finally it clarified that this was a voluntary action to use it.

We felt really good about these laws. I felt really good about these laws, and I suppose on some level, I was thinking of it like a flu shot. Get it in the clinics, get it in the pharmacies, get it in the health departments, get it in the docs' offices. Guess what? Everybody is going to get naloxone.

I was wrong, and I was thinking at it, I suppose, from that doc, that MD, that mainstream perspective because there were about two docs, maybe

three, in the entire state that would write those prescriptions. And thankfully, because we had no physician-patient relationship required, I wrote a lot of scripts, literally across a huge state, north to south, east to west. But that's not a solution. Right?

So we went back in 2016 and created a clause in our law that authorized overdose outreach providers. These are people who can furnish naloxone without civil or criminal liability. And as you can imagine, we put everybody who would need to be on a list on the list: law enforcement, fire departments, EMS, folks that work in recovery settings, folks that work in health departments, folks that work with those experiencing homelessness, all the way down to, probably the smartest thing I will have accomplished in my lifetime, individuals.

Any individual in the state of Utah is allowed to furnish naloxone, and that's exactly the model that has worked for us because this mainstream setting idea is not where a lot of people who are at risk of witnessing or experiencing an overdose are

willing to go.

It's folks that work in outreach settings. It's folks that work in needle exchange. It's moms. I know one mom who 4 of her 8 kids are heroin addicts. She has saved dozens of lives by equipping other moms and other folks around her because they're not comfortable talking to their doc or their pharmacist, but they're comfortable talking to Lana, an individual within her community.

We did also get a standing-order bill and law through in 2016, which I think has been important for that behind-the-counter model as well as for other programs. But again, it's not where the majority of naloxone access is.

Where we are getting wins or where we are having lives saved is by getting kits directly into the hands of people who use drugs, the lessons learned from Dan Bigg and from Eliza Wheeler and from Sharon Stancliff in New York.

Actually, I thought I could do this much differently, and I was wrong. It wasn't a pharmacy model. It wasn't a go-by-the-mainstream model.

People don't want to go to the pharmacy, and they don't want to go to the health department where they get their benefits. And they don't want to talk to their doc because sometimes they're concerned their doc will cut off their prescriptions.

We've got to put it directly into people's hands by providing local points of access from people who know, by strategically targeting, and by getting into the communities of people that need it by trusted entities.

These are oftentimes atypical strategies. It isn't go just to the health department, go just to the pharmacy. It's the Lanas. It's getting kids in libraries. It's EMS setting leave on scene kits. And we do ensure training and competence as well, but we really believe that these atypical strategies are what have made a difference for us. Again, it's not like the flu shot. I really wish it would have been as simple as that. It is not like the flu shot for us.

To give you an idea, community versus pharmacy access, in 2017 with our standing order in

Utah, 4,275 doses of naloxone went out through 165 pharmacies. They had 99 reversals reported. In 2015 to 2017, Utah naloxone community-based distribution strategies put out 34,400 doses with 2,056 reversals reported. This year in 2018, we are on slate to have provided 44,000 doses out across our state, and our reversals are now up into the 2600 range, as it shows here.

Our total time, 74,000 doses have gone out with 2628 reversals. These are parents and spouses and friends and outreach workers. These are not EMS or doctors. We have trained and worked with 64, now 65, law enforcement agencies in that same period of time, and in about a 1 to 10 ratio, they've had 268 reversals reported to the 2600.

We've launched programs with EMS agencies where they leave naloxone kits on scene after an overdose where the family has seen it work, the friends have seen it work, and they are then provided with a kit.

In one of my favorite strategies, all of our 18 Salt Lake County libraries given our outreach

prevention law, our librarians are furnishers of naloxone. Guess what? Librarians are the most trusted entity. I used to think it was firefighters. It's not; it's librarians. But you have to have ways for people to get naloxone from trusted folks, syringe exchange services as well.

Finally, what we do need? Well, I think honestly for me and the community-based setting, which is what we need to focus on, please clarify that a syringe and needle are FDA approved medical devices. They have been longer probably than I have been alive. Continue to support that 0.4 milligram intramuscular dosing. Approve a cheap, less than $1 over-the-counter form. Directly fund community-based organizations.

Don't let these new good ideas like co-prescribing and going big in the pharmacy take away the really good lived experience and effective community programming. Low-based, saturation-based distribution is really where the overwhelming wins are.

I support law enforcement and health

departments and pharmacies and co-prescribing and all of this, but please don't let these new good ideas squash what has really been thousands and thousands of lives saved. Thank you.

DR. BROWN: Thank you very much.

Would speaker number 8 step to the podium and identify yourself?

DR. BRATBERG: Good morning and thanks for the opportunity to talk. I'm Jeff Bratberg. I'm a clinical professor of pharmacy from the University of Rhode Island College of Pharmacy, and I'm a co-investigator or consultant on grants from the AHRQ, NIDA, the NIGMS, and the URI Foundation. These grants focus on expanding access to naloxone, addiction pharmacotherapy, hepatitis C treatments, and analyses of databases to enhance that work.

I'm also an unpaid advisor to two websites there, Prescribe to Prevent, where we've trained over 60,000 health professionals in naloxone education, and Prevent-Protect, which provides tools for organizations conducting overdose prevention and naloxone advocacy, outreach, and communication

campaigns.

I want everyone to pause a little bit and think about why we're here. We're here because of death, unprecedented death. Four hundred people died of drug overdoses in this country while we debate, and they're going to die the next two days, and the next two days after that. So think about that.

I'm here to talk about solutions. So in Rhode Island, we've been working together across the state, across agencies, across disciplines to implement policy solutions, both supply and demand solutions. In the interest of time, I'm going to focus on three of our solutions; namely, documentation of naloxone in our prescription drug monitoring program, mandated insurance coverage of naloxone, and prescriber naloxone co-prescribing.

We saw a financial barrier to pharmacy access on naloxone, and so one of the laws we passed was mandated insurance coverage, both public and private payers. And we're the only state in the country that mandates insurance coverage for third parties. So anyone who has insurance in Rhode Island and goes to

a Rhode Island pharmacy can get naloxone for them if they're in a position to help someone from overdose, which is everyone in Rhode Island.

We also had a tracking barrier. We passed these policies; how do we know whether people are picking up naloxone? So we put it in the PMP, and we had a distribution barrier. Over five years ago, we were the first state to have a statewide collaborative practice agreement with pharmacies and a prescriber in Rhode Island, and we extended that to a standing order in 2014, and then just recently this summer, we mandated naloxone co-prescribing through regulation and statute.

Now, the desired outcome that many of my colleagues in presentations have outlined is to saturate the community with naloxone, understanding that community access is the number one access.

Here's our law. There are lots of words here like most laws, but the key phrase there is on the bottom under C, which is "intended for use on patients other than the insured." So that's the key thing here.

I think it was mentioned about how we define fraud. Fraud is defined as processing insurance under a name that does not appear on the prescription. So Jeff Bratberg goes to the pharmacy, and Jeff's Bratberg's insurance covers it. That's okay. You can do it for naloxone if you have a third-party access law.

Mandatory naloxone and PMP reporting, we've heard a lot of data on naloxone from these expensive comprehensive but not time sensitive databases where PMPs in most states are real-time comprehensive cost-effective solutions, and there are requirements for prescribers in opioid treatment programs who are treating the highest risk folks here, must check PMP.

Still when the law was passed, the third bullet there is that "the rules and regulations from the department removed prescriber information." So pharmacists and prescribers are unable to see naloxone in it, but the data I'll present are collected in aggregate and analyzed at the department of health level.

In July, we finished a year-long process to

do a regulation on the behest of what was done in Virginia in terms of co-prescribing but expanded it significantly. So we looked at CDC guidelines, aggregate greater than or equal to 50 MMEs of opioids, opioids plus benzos in the past 30 days or co-prescribed together, and anyone with opioid use disorder or a history of opioid overdose.

The bottom box really outlines the accountability, which is if co-prescribing is not appropriate for the patient, if it fits into one or more of those categories, they must document the reason in the patient's medical record. When the regulation was passed, all prescribers were notified in July of this year.

Now, in May, we introduced a bill that was passed at the end of our session in Rhode Island in June 30th, and the law is the most wide-ranging law for co-prescribing in the country. So I divided this to compare that regulation and the law and to see a lot of discussion has occurred on high-risk populations.

I paralleled this to a website from the

American Medical Association opioid task force question. PMP shows my patient's on high opioid dose. You've got 50 MME; further delineated in the statute, high dose extended-release and long-acting opioids, so more broad.

History of substance use disorder, in the regulation, substance use disorder or overdose history, but importantly, the law addresses some of the data that you've heard presented here: known history of intravenous drug use; documented history of alcohol or substance use disorder.

So patients who have cocaine use disorder, methamphetamine use disorder who inject drugs of any sort or misuse of prescription opioids, whether injecting or not, they should all get naloxone. The other bullet extends the overdose history to include hospitalized for opioid overdose, another solution, we've implemented in Rhode Island in providing naloxone at emergency departments.

We extended it further. Documented history of mental health disorder, respiratory ailments, and not just benzodiazepines, but also with other

respiratory depressants like alcohol, vaguely defined as other drugs.

Here's the data. I think it worked. Importantly, I want to start with April. We had 165 -- there's the numbers at the bottom in terms of the numbers of naloxone dispensed. This is all formulations here. 165 percent increase was seen between our March and April numbers. That was due to three prescribers at one clinic in one of our 39 cities and towns in Rhode Island. That might have been correlated to the Surgeon General's announcement earlier that month. We're not sure, but you see it fell down to normal levels there.

After the policy passed, there was a 387 percent increase from June to July that was sustained over the last 4 months. Yesterday, I got our November numbers, which were 970. So more naloxone has been picked up from pharmacies in Rhode Island in the last 5 months than in the previous 24 months due to co-prescribing.

We see a gender difference. There was really no difference until co-prescribing happened. Here

you can see in orange, females picked up more naloxone from pharmacies in the last 4 months.

Again, we've had the longest standing pharmacy access to naloxone in the country, we feel, and when we look at standing order versus co-prescribed. Again, the numbers are on the bottom there. The orange line clearly shows a massive increase in those co-prescribed.

Importantly, we see sustained standing-order naloxone from the prescribers who signed those standing orders. It remains the same. Actually between April and May, we saw a 57 percent increase in standing-order naloxone, so that's still trucking along there.

Who is prescribing this? It was an increasing number of prescribers from November '17 through June '18, but again, a massive diversity of prescribers that were writing these prescriptions.

Who's paying for this? Remember, we mandate insurance coverage of naloxone, so the PMP breaks it down into five categories. I didn't have worker's compensation on here. But we look at Medicare,

Medicaid, and commercial insurance. You see sustained levels of each of those categories. Interestingly, Medicaid coverage is important. We have 96 percent of Rhode Islanders are insured. We see sustained Medicaid payment with Medicare showing a spike and then decreasing a bit throughout this summer and fall.

We have seen unintended consequences as stated. Pharmacists and pharmacy students in both informal surveys and in anecdotal conversations with me have said that prescribers -- one of the other solutions we have is starting in a year, we're mandating E-prescribing that other states have done for all prescriptions. We're already prescribing. About 92 percent of all prescriptions are E-prescribed.

So naloxone is being E-prescribed along with opioids to pharmacies. Pharmacists are filling it. Patients are unaware their prescribers have sent that prescription, creating perhaps an unintended conversation between the pharmacist and the patient. We've tried to train pharmacists. We think that

they're the best trained in the country because my colleagues and I helped train them, but I know that we have barriers there, too.

There are insurance co-pay barriers. My co-pay for insurance is $25. I can pay that. Other people cannot. And I want to recollect Dr. Walley's data that we think that there's probably a 10-dollar price point in terms of co-pay. Even among people who interested in naloxone, if it's more than $10, it's probably not going to do it there.

Limited formulation stocking, this goes to the generic vials of intramuscular, which again are the formulations saving the most people primarily through community groups. We provide that. Our law mandates generic naloxone. That needs to be stocked.

I'm sure you all have questions about please, Jeff, spend an hour and break down all of those different categories in the naloxone dispensary. I can't do that just yet, but we're working on it. And there may be stigma or discrimination, the pharmacist who doesn't want to dispense naloxone or doesn't have an emphatic conversation with a patient who may be

resistant to get it, the patient's not going to leave with it.

I must bring in my community colleague here. Michelle McKenzie presented this data sponsored by the CDC, interviewing people who inject drugs, a hundred of them. Luckily, 85 of them knew naloxone, 65 carried it, 40 had used it.

When we look at this pie chart, the majority of naloxone getting to this high-risk population comes from the community, comes from syringe exchange, comes from drug treatment. We have an innovative partnership with pharmacies in our opioid treatment programs to process naloxone through insurance and deliver it to them.

We also have a mobile pharmacy system that allows -- for example, I last got my doses of naloxone from a conference room at the University of Rhode Island Memorial Union because the pharmacist had a laptop, a labeling machine, and a Square card reader to take my co-pay, labeled it, and handed it to me. That is something we should explore further.

What are the benefits? Lots of discussion

about does this does this reduce death? All the epidemiologists should hear in their heads, correlation is not causation. So I'll start with a graph looking at our mortality. This is from the Department of Health website.

Looking at the last 12 months, again, preliminary data is clearly linked there. Even though September data is still probably preliminary, we did see a 43 percent reduction in total deaths and a reduction in both fentanyl and non-fentanyl deaths.

We'd like to see where this goes. This is part of a general downward trend in overdose deaths in Rhode Island. We were one of the states that saw a decrease in 2017 of about 3.5 percent. We did see decreases between June and July in terms of overdoses in other years, so I don't know if this correlates with the policy change or the increase in naloxone.

Some other suggestions or potential benefits, pharmacies are harm reduction providers. They provide syringes. In some of our unpublished work, we've seen 70,000 syringes dispensed from pharmacies in high-risk areas in Massachusetts. So pharmacies

are syringe service programs if destigmatized pharmacists are working there.

Maybe this is increasing provider conversations about whether they need naloxone, whether they need opioid and benzo prescriptions. We've seen a downward trend in new opioid prescriptions, in high-dose opioid prescriptions above 90 MMEs. We've seen a decrease in opioid-benzo co-prescribing. Actually, we saw a 15 percent decrease between quarter 2 and quarter 3. This is all on preventoverdoseri.org, our public reporting website.

Potential benefits, again, insurance coverage, we don't know how many people were prescribed naloxone and how many people picked it up. That's an important ratio to determine but difficult to identify in the PMP data.

I think that while we mentioned and was cited several studies concerned with pharmacists' knowledge of standing order and with stocking naloxone, I can assure you that there's probably a very high coverage of naloxone in pharmacies in Rhode Island because

they're dispensing naloxone every day or every week instead of once a month. So they're keeping it stocked because it's being co-prescribed.

What can we do? I've talked about what Rhode Island has done compared to other states. Pharmacists do well, as most health professionals, when we're paid to practice at the top of our license. So recognizing pharmacists as providers is really important things that I know FDA can't do, but other federal agencies can do.

We can declare an actual public health emergency through the Stafford Act and deploy federal resources, makes naloxone generic through emergency means, add it to the strategic national stockpile, and deploy it because people are dying, hundreds of them every day. It's time that we get naloxone out in every single way possible.

Rescheduling to OTC, having an insurance-based mechanism to cover OTC, to cover prescription naloxone; it's got to get out there in every single way. Having layperson access to IM vials; we could require naloxone with syringe

purchases. Why don't we make syringes over the counter? We know that they save lives when we increase the quantity and actions of syringe service programs.

I have 30 seconds for questions. Thank you for the time.

DR. BROWN: Thank you very much.

Will speaker number 9 step to the podium and identify yourself?

MR. SMITH: Good morning. My name is Grant Smith, and I'm here representing the Drug Policy Alliance, the nation's leading organization working to reduce harms both from drug prohibition laws and illicit drug use. The Drug Policy Alliance appreciates the opportunity to contribute our perspective during this meeting, and I have no financial interest to disclose.

We were here in 2012 and 2015 when FDA also held public meetings examining the value of expanding naloxone access in community settings. We called then for FDA to prioritize support for community-based naloxone distribution by harm

reduction programs and bring an over-the-counter naloxone product to market.

We strongly believe that these same priorities apply today. While we support making naloxone available in as many settings as possible and have worked to help implement standing order and pharmacy-based access laws in a number of states, the continued stigmatization and criminalization of people who use drugs illicitly is likely to limit the effectiveness of these approaches of getting naloxone to people at highest risk of overdose.

Seeing a doctor or pharmacist can be a major barrier for people who use illicit drugs who report feeling stigmatized in healthcare settings. While guidelines recommending co-prescription for high-risk patients could help reduce overdose deaths, it's not clear how much this approach would mitigate overdose among people who use drugs illicitly.

The emergence of potent fentanyl and fentanyl analogs is a leading cause of overdose death across the country, underscores the urgent need for affordable and reliable access to naloxone in

community settings, and we urge the FDA to prioritize strategies that maximize the ability of heavily stigmatized and criminalized populations impacted by fentanyl and other illicit used opioids to have affordable and reliable access to naloxone products.

We see a critical strategy for accomplishing this is maximizing the loss in distribution to the community through harm reduction programs. Community-based harm reduction programs currently serve populations vulnerable to fentanyl and other contaminants in the illegal drug supply, providing access to naloxone and other essential overdose prevention resources without judgment.

These distribution efforts are crucial to reversing the alarming rise in fentanyl-related overdose deaths as well as continuing to reduce preventable overdose deaths from prescription opioids and heroin. These efforts are also critical in light of the proliferation of drug-induced homicide laws and law enforcement hysteria regarding fentanyl that are undoubtedly deterring people who witness an overdose from calling 911.

We heard yesterday from Dr. Davidson that naloxone distribution programs distributed more than 500,000 naloxone doses in 2017 alone, and this year are projecting to distribute up to 1 million doses in this alone.

The cost of naloxone is a huge issue that has hampered the ability of harm reduction programs that typically operate on shoestring budgets to distribute naloxone. Two concrete steps FDA can do now and that was discussed yesterday could help lower costs for these programs are approving intramuscular injectable naloxone for community distribution and extending to five years the shelf life of naloxone.

We also urge the FDA to prioritize making at least one formulation of naloxone available over the counter. FDA has the authority to do this through rulemaking, and a speaker earlier from Human Rights Watch went into detail on this. Having a low cost over-the-counter option could help eliminate many barriers to this lifesaving drug that having to obtain a prescription or consult with a pharmacist can perpetuate.

OTC would not take away a doctor's role in counseling patients about overdose risk, and a doctor can still prescribe an OTC product to their patient. Having an OTC product on the store shelves could also help remove stigma in society of talking about overdose risk, a factor identified in this meeting as an ongoing issue.

We applaud efforts by FDA to support industry development of an OTC product. We urge FDA to support any effort to bring a low-cost OTC product to market.

Finally, we urge FDA to give more opportunities for people who use drugs and harm reduction providers who are working on the front lines of this crisis to contribute wisdom and experience to agency meetings and process.

Peer-to-peer naloxone reversal was pioneered by people like Dan Bigg who used drugs long before the practice became mainstream. People who use drugs deserve an opportunity to have a greater role in meetings like this one, and FDA and other stakeholders have much to gain by listening to them.

Thank you.

DR. BROWN: Thank you.

Could speaker 10 step to the podium and identify yourself?

DR. MAYBARDUK: Thank you and good morning. My name is Peter Maybarduk. I'm here for Public Citizen. We're a consumer advocacy group based in Washington, D.C. We have a 45-year history of representing the public interest before the federal agencies, Congress, and the courts.

I direct our Access to Medicine program. We're focused on issues of price and patents and competition in the United States and around the world. I have no conflicts of interest to declare. Public Citizen is supported by membership, dues, and foundations. We take no money from corporations or governments. We have approaching half a million members and supporters now.

We've heard quite a bit over the past couple of days of the challenges of cost that we are facing as a country in order to appropriately scale up our response to the opioid addiction crises. Depending

on the estimate, it seems that there are tens or hundreds of billions of dollars needed under current circumstances, but a spread of potentially hundreds of billions of dollars in the differences between using the patent-based products or potentially generic products.

Given that we face such an entrenched and complicated problem in many ways, we advise the government to do certainly every simple thing that it can, and we actually believe there is a relatively simple unexplored solution to the problem of cost where the U.S. government could essentially snap its fingers and open up the market to generic competition to deal with this public health crisis.

I'd like to take back the clock to 2001 during the anthrax scare. At that time, Bush appointee, Secretary of Health and Human Services Tommy Thompson was in negotiations regarding the price of the anthrax response treatment Cipro. A mechanism of law came to that office's attention, and this is documented in the New York Times article and a Yale Law Journal article elsewhere that we can send

you.

It was noticed that the U.S. government actually has the authority to authorize generic competition any time. Secretary Thompson presented this possibility to the manufacturer of Cipro, Bayer. Bayer cut its price in half within a week at the prospect of potentially losing the monopoly rights that it had valued so highly.

Now, if the U.S. government was willing to take that action for anthrax, which ultimately resulted in 5 deaths, what will we do for one of the worst health crises in history, certainly in our nation's history, where probably that many people have passed away since we sat down this morning.

Our ask is essentially is that the federal government procure naloxone treatments and supply them to local health and law enforcement programs, to authorize such programs to procure generic versions of patented naloxone treatments.

Pursuant to 28 U.S.C. Section 1498, the government should authorize use of any and all patents necessary to allow for the production of

generic naloxone treatments and delivery devices to respond to the opioid addiction epidemic. This will facilitate competition and make treatment more affordable, and accessible.

We've made this request in writing. It's in the comments that you have with you. It's also in the letter that we filed with the administration together in partnership with the City of Baltimore Health Department earlier this year.

A little bit on the problem faced by our partners in Baltimore due to the high prices of Narcan, most especially. Everyday residents have used naloxone in Baltimore to save more than 1800 lives since 2015. That total does not include the lives saved by first responders who reversed more than 10,000 overdoses over the same time period.

Baltimore city has approximately $1 million per year to spend on naloxone, which even at the steeply discounted rate of $75 per Narcan kit, purchases about 13,000 kits for the city.

Now, to have enough kits for every Baltimore resident with opioid use disorder, let alone kits for

their loved ones or community members, that number would need to be doubled under current budget estimates. To get to the point where Baltimore could actually have naloxone appropriately on hand for everyone, the city would have to spend $49 million, which is twice the city's entire health budget.

Now, I think it bears mentioning that we're not talking about a product that is inherently expensive. We're not paying for manufacturing costs or even for technology. Naloxone was FDA approved in 1971, and the delivery systems are not technically very complex. What we're really paying for is monopoly. We're paying for patents and exclusive control of the devices.

Now, it's a basic but sometimes forgotten principle of patents and the grant of patents by government that they are there to serve the public interest, and that the government always reserves the right to make use of patented technologies as it sees fit. This goes back to the very first patent statute in 1474 in Venice and has been used by many governments since. We don't give away exclusive

rights to essential technologies without reserving our fundamental right to protect the public interest.

A little bit on how this could work. One model for the type of -- once you make the authorization of the patents for what can be done, one possible model is the Vaccine for Children's program. Under the VFC program, the Centers for Disease Control purchases vaccines at a discount, distributes them to state health departments and certain local and territorial health agencies, which then provide them at no charge to physicians' offices and clinics that are registered as Vaccine for Children program providers.

Putting in place a similar program for naloxone purchasing and distribution would allow the government to purchase naloxone indicated for community use at lower costs and distribute it to local health departments, police departments, fire departments, first responders, and so on.

In the alternative, the federal government could authorize states and territories that receive federal funding to essentially act as federal

contractors under the statute and purchase their own generic naloxone. The statute that I'm talking about is a relatively simple and short one. This is something that the U.S. government can do at any time. There isn't even a negotiation or request for permission.

The entirety of the statute is about conditions and the royalty payments that will be made back to the patent holder as compensation for their investments in research and development. There's an academic literature about how to appropriately set those rates so that we are investing in R&D appropriately without giving away windfall profits.

This is a statute that the U.S. government has used routinely in other sectors such as defense, and while it was presented in 2001, not recently used, but as a commonly used vehicle for pharmaceuticals, a commonly used vehicle in the United States and around the world to ensure competition and deal with the problem of monopoly rents.

Narcan is protected by 7 patents that expire

in March 2035. while Evzio is protected by 25 patents, the latest of which expires in July of 2034. So unless we act, this is a problem that is going to be with us for a very long time. And it seems to us that the choice is essentially one between treatment rationing, which we have today, obviously in excess and costing a great many lives; coming up with tens or hundreds of billions of dollars; or taking a relatively simple step to authorize competition so that more producers can enter the market and we can bring prices massively down for the naloxone delivery systems, saving the federal government and many of the programs in this room, a tremendous amount of resources.

Obviously, there would be a short lag time while different producers figure out what sort of product they want to introduce and go through the FDA approval process, but we're talking about a very large market, so the incentives are there.

The only thing that is standing in the way is that we have accepted monopoly power by a few companies, price gouging access to some of the most

important products of our time. It's not the technology or the science that we are paying for at this point.

The statute is a very diffuse authority. It can be exercised by FDA for programs under its jurisdiction and other entities in the federal government.

This is the first opportunity, I think the only opportunity, we've had to discuss this idea with U.S. government, certainly to discuss it in a public forum. We believe that what your committees say, what your recommendations will be, matter quite a bit, and we'd urge you not to overlook this relatively simple response to an otherwise very complex problem that could save a great many lives. Thank you.

DR. BROWN: Could you repeat the specific section of the U.S. code?

MR. MAYBARDUK: Of course, and it should be in your materials. It's 28 U.S.C. 1498.

DR. BROWN: So that would be 28 U.S.C. 1498?

MR. MAYBARDUK: That's correct. We can

provide with a law review article and other materials that document the history and particularities of this statute.

DR. BROWN: It would be possible to be exercised by who?

MR. MAYBARDUK: The authority is diffuse. It can be used by essentially, I think, any official of the federal government. The question is what programs come under the purview of that official.

FDA could exercise this authority but can only directly authorize generic competition or use of the patent essentially for programs that come under its jurisdiction. But the federal government as a whole certainly could create a new program to deal with the opioid addiction crisis and authorize the use of the patents through that program, and just purchase generic products on behalf of everyone that needs it nationwide.

In other words, the federal government has this solution at its fingertips, (snaps) like that. It just has to decide to exercise the authority.

DR. BROWN: Thank you very much.

MR. MAYBARDUK: Thank you.

DR. BROWN: Could speaker number 11 step to the podium and identify yourself?

MR. TRIPODI: Good morning. My name is Mark Tripodi. I serve as chief development officer for Venebio Technologies, a Richmond-based life sciences research firm. I've spent 27 years in the health analytics space with various firms, small and large, mostly in the Medicaid analytics arena, run PBMs, population health, health analytics, and other businesses. I served as Xerox's chief innovative officer in government healthcare for several years.

My focus at Venebio is in the area of predictive analytics, specifically predictive analytics to identify elevated risk of overdose in patients prescribed opioid treatment.

Venebio is a firm mostly made up of doctorate level epidemiologists, biostatisticians, clinicians, and other researchers. It's a private firm servicing commercial and government clients in a variety of research funding agencies, including NIDA. Venebio provides services in epidemiology, bioinformatics,

biomarker, and drug safety research, and health economics.

For all of its ten years, Venebio has specialized in understanding the causes and treatment of addiction with a focus on opioid safety, and the firm's principals have maintained that same focus for well over 30 years. Venebio's opioid risk research and publications are well regarded. Some are, in fact, referenced in the CDC's current opioid prescribing guidelines.

Venebio has also worked with makers of naloxone delivery systems, with manufacturers of medication-assisted therapies for substance use disorder. And we, frankly, recognize the remarkable lifesaving value of naloxone. We acknowledge that universal co-prescription would indeed make this country a much safer place for opioid-treated patients.

However, we also recognize that in an environment where resources are limited, it may be that universal co-prescription of naloxone is determined to be impractical or cost prohibitive, and

we also recognize that a patient's risk of overdose exists on a spectrum. And while there is no zero-risk opioid use, there are tools that can effectively identify which patients are at elevated risk so that we can focus efforts to ensure that those patients at least have access to naloxone.

Based on its extensive research, Venebio created an algorithm-based tool able to predict the likelihood of overdose for opioid-treated patients. Venebio Opioid Advisor, or VOA, bases a risk prediction on a patient's readily available drug and medical data either taken from healthcare claims, extracted from the EMR systems, or manually entered by clinicians.

VOA targets 16 specific risk factors for overdose, constructs a patient risk profile, and predicts each patient's likelihood of experiencing a life-threatening opioid overdose in the subsequent six months. VOA also provides personalized clinical decision support to stakeholders and clinicians to guide them in reducing patient risk.

Importantly and unlike other tools, VOA

applies equally well to patients with substance abuse problems as it does for nondrug abusing patients that might have elevated risk for other clinical risk factors.

The patent pending algorithm is relatively lightweight, easily implemented, and per a 513(g) RFI was determined not to be a device. The tool is being used in hospital and retail pharmacy settings to inform opioid prescribing and dispensing, and it's used by health plans and Medicaid programs as a triage tool to surface patients at elevated risk for purposes of targeted naloxone distribution.

The research behind VOA is substantially funded by NIH, specifically by NIDA. It includes an initial discovery study of 2 million opioid-treated patients in the national VA system followed by a study of 18 million opioid-treated patients from a national commercial database.

Resulting from that research, Venebio published four peer-reviewed papers which document VOA's scientific underpinnings and demonstrate that the algorithm predicts the average patient's risk of

opioid overdose with 90 percent accuracy.

As shown here, VOA stratifies patients into 7 different risk classes, each class corresponding to an average risk of overdose from a low in risk class 1 of just 2 percent to patients in risk class 7 who would have an average risk of overdose of 83 percent.

The dark blue bars show the algorithm's predicted risk of overdose in each class, and the light blue bars show the actual incidence of overdose observed in each group in the study. In each class, the variance is between 0 and just a few percentage points, thus the 90 percent predictive accuracy.

Healthcare algorithms with predictive accuracy in the 70s or 80s are generally considered excellent. Predictive accuracy in the 90s is exceptional, and that not only speaks to the quality of the algorithm but also to the fact that opioid overdose, as it turns out, is a highly predictable event.

All of this is to say that existing, validated, proven tools can assess with a high degree

of accuracy the average prescription opioid patient of overdose. Tools like VOA are built on the notion that digital data are available and ready to be used for purposes such as patient safety.

If we look at a sample Medicaid program, in this case with about 200,000 total patients, roughly 55,000 had filled one or more opioid prescriptions in the prior six months. If we break down users by risk, not surprisingly, about half of those patients end up in that lowest risk class, risk class 1, with an average risk of overdose of just 2 percent.

At the other end of the spectrum in the highest three risk classes, where collectively the patients would have a 30 percent or greater likelihood of overdose, that's only about 11,000 patients or 20 percent of opioid users in this program. If we expand that group to include patients that have a 15 percent or greater risk of overdose, we're still at less than a third of the opioid-treated patients in this health plan.

So you can see very quickly we can stratify patients by risk to determine who is most likely to

require rescue so we can focus resources to ensure that the highest risk patients are covered with access to naloxone.

In the absence of more reliable methods for identifying elevated overdose risk, healthcare practitioners will intuitively rely on a limited set of criteria in assessing patient risk for overdose. Abuse and addiction will remain a primarily focus, and while that population is certainly at elevated risk for overdose and should have access to naloxone, they represent less than half of the highest risk patients.

We also tend to focus on opioid dose or morphine milligram equivalent, and while it's also an important factor, MME alone is not necessarily a good indicator of overdose risk. As shown in the graph to the left, relying on SUD and MME markers alone would fail to identify about 40 percent of the patients in this program who had a 30 percent or greater likelihood of overdose.

A more comprehensive risk assessment must incorporate a larger number of weighted risk factors,

including medical code sets and an algorithm that goes far beyond possible top-of-the-head calculations. The graph on the right shows a distribution of the same high-risk patients but by the different types of risk factors contributing to the VOA risk score.

We're still capturing high-risk SUD patients, we're still capturing high utilizers, but importantly, we're also capturing harder to find patients who may be perfectly compliant with their opioid regimen but are still at high risk of overdose due to less obvious risk factors.

VOA is in use in hospitals, in health systems, in Medicaid and commercial payers, and in retail pharmacies. The tool has proven to be an effective and efficient method for evaluating and managing overdose risk.

In this example, a nationwide network of community pharmacies implemented the algorithm to identify high-risk opioid patients in 500 pilot locations. The highest risk patients in those pharmacies at baseline had an average naloxone

dispensing rate of just 4 percent.

After about 3,000 interventions, we're seeing a naloxone dispensing rate now of over 30 percent in that same group, almost an eight-fold increase in on-hand naloxone for those high-risk patients. That increase was achieved in just the first three months of the program. That work was co-funded by a NIDA grant, by the Pharmacy Network, and by Venebio.

We encourage the committee to consider making digital risk assessment tools like VOA a core component to the federal government's strategy in promoting opioid safety and specifically in assessing appropriateness for naloxone dispensing. We believe this more targeted approach will reduce costs; will more accurately identify high-risk patients, including the hard to find high-risk patients; and will focus meaningful risk mitigation on the patients most in need of assistance.

Thank you, and I'm happy to answer any questions.

DR. MEISEL: Steve Meisel with Fairview. Just a clarifying question, this is available today?

And you say you can integrate this with electronic health records. Could you elaborate on that, please?

MR. TRIPODI: Yes. The tool is available today. The algorithm has been licensed by entities and embedded in their analytics engines. Pharmacy Network, for example, in EMR can embed the algorithm. We can also provide the algorithm on a web services basis to entities that wish to use it.

DR. BROWN: Dr. Ciccarone?

DR. CICCARONE: Dan Ciccarone, UCSF. Mr. Tripodi, in your pilot data, you have 2700 or so interventions in that pilot study. What did you mean by intervention?

MR. TRIPODI: VOA was used in the pharmacy setting to identify high-risk patients. The intervention occurred when the pharmacist conducted an MTM-type consultation with the patient to promote the use of naloxone, and in some cases, to coordinate therapy with the prescribing physician.

DR. CICCARONE: How long was the pharmacist-led intervention?

MR. TRIPODI: The duration of the

intervention averaged about 10 to 12 minutes.

DR. BROWN: Dr. Staffa, you have any --

DR. STAFFA: Yes, Judy Staffa from FDA. Are the details of the methods around the validation work available or published?

MR. TRIPODI: The validation work is published in four separate publications that are available. We're happy to share those. They're publicly available, yes.

DR. STAFFA: Thank you.

MR. TRIPODI: You're welcome.

DR. BROWN: Any other questions?

(No response.)

MR. TRIPODI: Thank you very much.

DR. BROWN: Thank you.

Could speaker number 12 approach the podium and identify themselves?

DR. GREEN: Hello. My name is Traci Green. I'm an epidemiologist, and I'm an associate professor of emergency medicine and community health sciences at Boston University, as well as professor of emergency medicine and epidemiology at Brown.

Today I am going to talk with you about some of the work we've been doing through AHRQ-funded and NIDA-funded research work. I am a special government employee of CDC and of FDA, and the views expressed today here by me are my own and do not represent those of the agencies.

First, I wanted to share with you this diagram that really emerged directly from our work at the AHRQ-funded MOON study, some of which you have seen previously. But this really is an important component to what we unearthed, and that is that the pharmacy is much more than the entity on the corner in your community.

Moving from left to right, we've really been focusing on the first two components, direct to consumer through the prescriber approach and perhaps co-prescription contributes to that idea. It's a very traditional approach.

The second, where the pharmacy provides naloxone directly to the consumer through a co-dispensing model, is one that has emerged in the last couple years since about 2014, spearheaded in

Rhode Island.

The third and the fourth, though, are ones that have emerged almost exclusively from the challenges put forth by the opioid crisis driven by fentanyl. And by this, I mean the idea that the pharmacy can be a massive distributor of naloxone to high-risk institutions or at high-risk times, those kind of partnerships that we've been able to catalog and to promote the expansion of through regulations, or through by storytelling even, and connecting dots, partnerships, and collaborations where the pharmacy is critical to that.

The last one also reflects the idea of a mobile pharmacy and innovations. I've observed them in Kentucky. Dr. Wermeling actually spoke to you about his mobile van from University of Kentucky, and until you run out of gas, it's a great idea.

Also in Massachusetts and in Rhode Island, we've been pioneering these ideas, whether it's a rally for recovery and a pharmacy like Walgreens showed up early on and created their own makeshift pharmacy in the middle of a park; or a pharmacist

like Dr. Bratberg had suggested that goes to his hospital.

These are really important because they address the time and space challenge that fentanyl poses to us and the nature and innovation that all the community, health departments, community activists, and organizations can use with the tools that you provide us, prescriptions, dispensing mechanisms, reimbursement models.

These are important because we need an opportunity to have rapid deployment of naloxone. You can imagine something like this model in the hands of CDC when we have a carfentanil outbreak in a certain part of the country and can mean naloxone in the streets and in the hands of people who need it just as our community organizations are partnered and doing so as well.

I want to reflect to you that these multiple paths to naloxone are a real focus of our work. You can discover these on our volunteer run prescribetoprevent.org site as well as the prevent-protect.org site, which is AHRQ funded.

The important components of our study were really recognizing that we need different models to address the nuances of naloxone need in our communities. After 16 focus groups with over 65 people and interviews with 85 patients who taught us that we need passive and active offers of naloxone, the patients said that some of them don't know about naloxone, and they needed awareness.

Some of them were afraid to know, and they needed help to see their risk in a compassionate and partnered conversation. Some of them knew all too well that they and the people that were around them and that they loved were at risk, and they needed help to ask for naloxone.

So each of these tools were meant to help us understand and help the patients ask for naloxone under a standing-order model.

The pharmacists also needed help, and underneath that black box, you can see on prevent-protect.org. as well as on prescribetoprevent.org, the full guide. It's an academic detailing guide, a very simple teaching tool

for the pharmacist to use with a patient, but also the pharmacist to work with their technician and staff to talk about access to naloxone, and to set a bar for how to create consistency and an environment that is conducive to non-stigmatizing, low discrimination, and improved naloxone receipt.

Developing a trust and a harm reduction environment in the pharmacy was something we learned from the community because we asked them in a partnered approach to help us develop these tools.

In particular, for instance, the second image that shows the sticker, this is the sticker that's placed on 10 packs of syringes that are sold in a non-prescription form at pharmacies all over the country because we know that non-prescription syringe sales complement well the activities of state health departments and community organizations getting naloxone and syringes out in the community.

Much of your discussion has been focused -- for instance, your questions 3 to 5 are directed on the patient and risk factors, and the prior speaker just noted to this, the indications and

diagnoses, the importance of identifying patients.

I would urge you in our work, and as you've been continuing to hear, that stigma is so profound around addiction, and by consequence, around naloxone, that the importance of focusing on the dose, the drug, the agent, or the combination and less on the patient is something that your labeling and your words can help direct. By doing so, you erode the stigma. Being stigma aware is a really critical component of what you can do today.

I'd like to take a second just to talk about some of these additional distribution hubs. We discovered in Massachusetts and Rhode Island that a number of the drug treatment programs were providing naloxone to their patients and their clients.

In Massachusetts, this was a natural history evolution, but in Rhode Island, following an emergency regulation that required all detox and residential sites to provide overdose education and naloxone distribution to patients, created a mechanism where everyone going into treatment had access to naloxone.

In truth, this really brings Dr. Katzman's work from the OTP program that she presented yesterday to scale, and we've been doing this for years. You can see on the left that any pharmacy involvement in naloxone provision in these drug treatment programs was actually pretty high already. This was in 2016. The idea of creating a collaboration with a pharmacy in their neighborhood was something that naturally emerged in the blue in Massachusetts treatment centers.

In Rhode Island, at the orange lines, you can see they were required. Ninety-six percent of the treatment programs had an active -- they were complying with the law, thankfully, but they had the means by which naloxone could be accessed and then sustainably provided to their clients and caregivers as well.

I wanted to also reflect that Rhode Island is a great example of when you have insured mandated coverage, private and public. You have low-cost access to community-based naloxone. You have a comprehensive combined approach that maximizes

naloxone distribution, and this leads to mortality reductions.

We've seen it last year, and we continue to see it this year. It's very exciting. But as you can see, whether it's through a hospital ED, through the pharmacy that partners with the drug treatment program, or provides direct to consumer, or as I mentioned, the mobile option, or community organization that is really out there doing the work, amazing good Samaritan work, we have a more comprehensive and broad access to this lifesaving medication.

Now, while there are many intended and unintended good consequences, as Dr. Hertz mentioned yesterday, there are many potential bad consequences, too. I am extremely disappointed to share that in both states that I work, we have two examples of good Samaritans, healthcare providers, who have obtained naloxone and unfortunately also this fall, attempted to obtain life insurance.

These were different people in different healthcare institutions, a federally qualified health

center, and my own Boston Medical Center. These were not the same life insurance company. There are multiple of them. If you want to know what stigma looks like, that's it. If you want to know what discrimination looks like, that's it.

We need parity. We need leadership. We need to shame these institutions because it's unacceptable, and it's inconsistent with the Surgeon General, with your task today, and with the science. Thank you.

DR. BROWN: Thank you.

Would speaker number 13 step to the podium and identify yourself?

MR. BRASON: I'm Fred Brason from Project Lazarus based out of North Carolina. I have no disclosures to declare, and I'd like to thank the FDA for the opportunity for me to share but also to thank the FDA for your approach to not only reduce harm but also to prevent and for the hearing over these past two days.

Project Lazarus is a community-based initiative mobilizing communities around substance

use, specifically opioids, heroin, and fentanyl. In dealing with that, we developed a model years ago in order for communities to be able to replicate their efforts. Part of the spokes on the wheel of our model is harm reduction, but everything we do is harm reduction.

I want to just make one comment about harm reduction. When we talk about the infrastructure of communities, it isn't some other entity that's out there. It is part of the infrastructure in the communities and should be supported and funded just like any other component and sector within that given community.

As we studied in communities and worked in our own communities in Wilkes County, North Carolina, we realized to reach the individual, we had to change the village, which means we had to empower every single community sector in order to do that with the right best practice, with the right messaging, whatever it was that was necessary for the population that they served.

Our harm reduction component that we

initiated was and is naloxone. Now, we have syringe exchange in our community and other things, but I had to learn about harm reduction because I was not familiar with it. I had to learn about naloxone. And I first heard about it in 2006 when we realized in our community how many people were dying from overdose from prescription medications. When I learned about it, my first question was, "Who has it? Where is it? If it can reverse an overdose, let's have it."

I found out EMS had it and the emergency department, but the folks in our community never made it that far. They were at home. They were on their couch. They were at a friend's place. They were in the same room with other individuals in a living room dying from an overdose, and the others did not even realize it.

When I realized that -- I'm a logical thinker -- I said, "Well, okay. If it's legal, can be prescribed, why isn't it available to those individuals who are at risk?" And I made inquiries, and we did some studies within our community to find

out what's the face of the person? What happened to them? Who were they? Who are they? So that we could investigate and learn the trail of what led to that eventual overdose.

We did have patients who misused their medication. We did have patients who took more of their medication than they were supposed to or mixed something else with it. We do and did have family and friends who shared medication to self-medicate. Wasn't to get high; wasn't to divert. It's just that there was medication in the home and they had an ailment that that possibly could fix. Unfortunately, it didn't.

We had accidental ingestion because of the amount of meds that are in the home. We have recreational users where the prescription opioids and now heroin and others become part of the party mix, not somebody with substance user disorder but somebody who is just out with friends. Then, of course, we do have individuals with substance use disorder in and out of treatment and recovery.

Those were all individuals in our community

that we learned were dying. So we looked at, okay, how can we reach all of those individuals within our community, how can we ensure their safety, and how can we get naloxone into their hands? Well, when I asked the question where is naloxone and found out only two places had it, I made the logical conclusion and called the president of our North Carolina Medical Board, Dr. Janelle Rhyne, and said, "Why isn't this not routinely available to somebody who may be at risk? Because we have patients who simply are dying because of a comorbid condition or misusing their medication."

Thankfully, she said, "Yes, let's take a look at this." And they gave us a public hearing in 2007, and five of us went over to Raleigh to sit down at the medical board and present our case to five policy directors, medical directors on their board for doing that. They gave us 30 minutes.

Well, we're a little passionate. We took 45, and after 45 minutes, he stopped us. The policy director admitted at that time, he says, "You know, we discussed this program before you came, and we

were pretty much against this program. But you have shown us, through what you've been doing in Wilkes County and the studies that you've done, that we ourselves as practitioners have patients in our own practices that are at risk from an overdose right now."

So therefore, they were the first medical board in the country, in 2007 and published in 2008, for a position statement that simply said -- and here's part of it -- "The Board has reviewed and is encouraged by the efforts of Project Lazarus, a pilot program in Wilkes County that is attempting to reduce the number of drug overdoses by making the drug naloxone and an educational program on its use available to those persons at risk of suffering a drug overdose.

"The prevention of drug overdoses is consistent with the Board's statutory mission to protect the people of North Carolina. The Board therefore encourages its licensees to cooperate with programs like Project Lazarus in their efforts to make naloxone available to persons at risk of

suffering opioid overdose."

The practitioners did not say we're going to stop prescribing, no; we're going to make it safer, and we're going to do more education, and we're going to provide naloxone, and then we were able to do that. And we provided them the risk factors, some of which you saw in some of the presentations yesterday, of all the different factors where somebody could be at risk: opioid treatment; recent incarceration; previous history; comorbid conditions of sleep apnea, asthma, emphysema, and other concurrent issues.

As we provided that to individuals, we provided the education to the practitioners of looking at pain, culture, genetic factors, substance use, mental health, environmental factors, that if you're prescribing 120 tablets into a home every single month and there could be other individuals, toddlers or individuals with substance use disorder within that home, naloxone should be co-prescribed, and it should be looked at across the board.

I have concerns sometimes about co-prescription when we look at just an MME as a

factor and realize, well, because of the conditions we have now, where you're on 90 MMEs and the recommendation or guideline is 50, so therefore, I'm going to titrate you down, might not take care of all the pain that's necessary -- the same factor is looking at naloxone, can you just say, well, if it's 50 MME, maybe I'll only take you to 40 so I don't have to go into that route and have that overdose conversation.

That's where my mind goes in just looking at all the barriers that might come up, because when I see a barrier, I prefer to go under, over, around, or through in order to make that change to make it better for the individuals.

We did it in the military. They instituted co-prescribing naloxone back in 2009. Their overdose deaths were 15 per 400. In one year, it went to 1 out of 400. Yet, there was not one rescue. It was the education and awareness surrounding that medication of the soldier, the family, the spouse, whoever it was that brought about change in behavior surrounding that. But naloxone was still available

should there have been an adverse event.

When we first started with the community dispensing, the first call I got was the spouse of a chronic pain patient thanking us that their practitioner had provided the education, given them information, given them the naloxone, and they understood the ramifications of adverse events and so forth.

The first rescue was a brother who saved a sister because that brother had received naloxone through the methadone treatment program, because it gets into the environment where naloxone needs to be, and that's the community; community education, provider education, so co-prescription is across the board for many different factors, all of the risk factors, not just the MME.

Hospital emergencies, if somebody is there and warrants it, they should walk out with that. Addiction treatment, when we talk about co-prescription, it should also be co-prescribed for somebody in methadone, buprenorphine, and naltrexone, also.

In corrections, harm reduction, of course, we could give Eliza's programs across the country 2 million and they still would not be enough to saturate the communities, but it should be done. Law enforcement and EMS, that's on the back end. I'd rather have it on the front end; co-prescribed, opioid treatment programs, community-based, and we can do that by saturating through all the different entities and modalities and the devices that we currently have. Thank you.

DR. BROWN: Thank you, Mr. Wells [sic].

Could speaker number 14 step to the microphone and identify yourself.

DR. TWILLMAN: Good morning. My name is Bob Twillman. I'm the executive director of the Academy of Integrative Pain Management. I have no potential conflicts of interest.

For two or three years, AIPM has had an official position on the issue of naloxone co-prescribing. In short, our position boils down to this: Every patient prescribed an opioid analgesic should have a risk assessment based on an available

empirically derived assessment instrument; a complete understandable explanation of his or her risk; the opportunity to discuss that risk assessment with a competent clinician; and a prescription for naloxone, which the patient may choose to fill or not to fill.

Assessment of the patient's overdose risk when using an opioid analgesic should be routine and should be carried out using an empirically-derived assessment instrument such as the RIOSORD or VOA.

It's our belief that this assessment should be carried out for every patient prescribed an opioid analgesic, for acute pain as well as for chronic pain, to minimize the possibility that a high-risk patient will be overlooked because of an incomplete assessment conducted due to the short-term nature of a prescription to treat acute pain.

The only patient who has no risk of opioid overdose is the patient who's not using an opioid. Any patient who uses a prescribed opioid has an elevated risk of overdose, and you've seen data indicating that most patients who overdose do so while prescribed doses below 50 MMED.

Policies that encourage risk-based prescribing thus require that the prescriber determine philosophically what constitutes an acceptable risk that does not require a naloxone prescription. We find such a requirement to be challenging on both clinical and ethical grounds. Clinically, risk is dynamic and can change for unforeseeable reasons, almost always in a direction of increased risk.

Such a policy also fails to recognize the limited extent to which a prescriber can anticipate the likelihood that the patient's opioid analgesics will be accessed and used by some unintended party.

Additionally, asking the prescriber rather than the patient to determine what level of risk is acceptable is ethically challenging. Such a policy requires the prescriber to make a paternalistic decision about what constitutes an acceptable level of risk and denies the patient's autonomous right to make that decision for himself or herself.

Any time a patient's given an prescription for any medication, that patient ultimately exercises

his or her autonomy right in deciding whether to fill that prescription. There may be a variety of factors influencing such a decision, but in the case such as this where a foreseeable adverse outcome is death, considerable efforts should be made to ensure the patient is making a truly informed decision. The patient has no decision to make if no risk information is provided and has no decision to make if a naloxone prescription is not offered.

In conclusion, we note that the mere fact of offering the patient a naloxone prescription prompts a discussion about risk, and that can only be a good thing. The patient should be given the opportunity to make an informed decision about his or her need for this important risk mitigation tool. Thank you.

DR. BROWN: Thank you.

Could speaker number 15 step to the mic and identify yourself?

DR. WAGNER: Good morning. Thank you for the time to speak today and for your attention to this important topic of increasing naloxone access for people at risk of dying of opioid overdose.

My name is Karla Wagner. I'm an associate professor of public health at the University of Nevada Reno. I'm here speaking on behalf of myself based on my experience doing research in this field, not on behalf of my institution. I have no financial conflicts of interest, though I do hold several grants from NIH and the Laura and John Arnold Foundation related to research in this area.

I've been doing research on community-based naloxone distribution in the U.S. since about 2006. This morning, I don't have any slides or really any data. What I'd like to do for the next couple of minutes is call your attention to the rural west and some of the issues that we face there.

Since 2014, I've lived and worked in Reno, Nevada. Just to give you a little bit of perspective, 87 percent of Nevada is rural. Reno is 7 hours by car from Las Vegas. If you were to drive seven hours north from here, you'd end up somewhere in New Hampshire after passing through 5 other states. When you drive seven hours north of Las Vegas, you end up in Reno, and then you still have

several hours to reach the border.

Transport times, as you can imagine, to hospitals can be several hours in Nevada. Many of our frontier counties are served by EMS agencies staffed by few, if any, paramedic level responders. Many of those agencies consist mostly of volunteers.

Fifty percent of Nevada is federally designated as a healthcare shortage area. One implication of that shortage is that a large share of the population doesn't have regular or easy access to a healthcare provider. When I moved to Nevada, it took me almost a month to find a primary care doctor.

My research and that of others have shown that less than half of overdoses come to the attention of uniformed first responders via a 911 call. In rural communities, it can take a long time for those uniformed first responders to arrive, if they're called at all.

Even though in Nevada we have regulations that allow for pharmacists to furnish naloxone without a prescription, significant barriers remain, not the least of which is that the sale of naloxone

is at the discretion of the pharmacist. This means that a pharmacist can refuse to sell naloxone without a prescription if they don't want to.

I understand that your charge today is mainly related to questions about co-prescription, but I'd like to ask you to consider that a low-cost, over-the-counter solution could supplement existing efforts and dramatically lower barriers for people who use illicit opioids, their friends, and family members. Those folks face numerous barriers to accessing naloxone via a co-prescription model, including lack of insurance, cost, stigma, lack of interactions with medical providers, and geography.

Focusing solely on a co-prescription strategy ignores this population, and it does a disservice for rural communities where access to healthcare providers is limited. Stigma, long distances, and lack of access to providers are huge barriers to having ready access to the medicine when it is needed, especially if access requires interaction with a medical professional.

As you heard yesterday and this morning, we

have decades of collective experience and thousands of accounts of success from community-based naloxone programs. But in some states, even finding a provider to sign a standing order to empower a distribution program is difficult; never mind getting individual prescriptions for people through individual one-on-one interactions with healthcare providers.

Removing barriers is critical. We need as many solutions as possible to allow states like Nevada to craft solutions that work for us. Co-prescription might be one of those solutions, but supporting easy, affordable over-the-counter access is another solution that should be seriously considered. Thank you.

DR. BROWN: Can I ask a question? And other members of the panel may want to ask you some questions, also.

Do you have any idea -- have you looked at, or investigated, or do you have any knowledge of what a reasonable price point would be for an OTC product that would make it available for folks that are

actually going to buy it?

DR. WAGNER: I don't have any data that would allow me to speak to that with any confidence. I would defer to my colleagues who've talked about a dollar price or a $5 price. I don't have any good data to inform that, though.

DR. BROWN: Any other questions of this speaker?

(No response.)

DR. BROWN: Thank you very much.

Could speaker number 16 step to the mic and identify yourself?

MS. BELL: Hello. My name is Alice Bell. I'm the overdose prevention project coordinator for Prevention Point Pittsburgh. I don't have any financial relationships to disclose.

Prevention Point began distributing naloxone at our syringe exchange site in 2005 with medical prescribers who volunteered to write individual prescriptions for people who were injecting heroin and other opioids, who came to get safer injection supplies.

In the first two years after we started naloxone distribution through prescription, we saw a drop in local heroin overdose deaths, while at the same time experiencing the rise in deaths from pharmaceutical opioids that was witnessed across the country.

We began working with physicians prescribing naloxone through the syringe exchange program and a few other medical providers to develop messaging and navigate logistical issues to co-prescribe naloxone in their medical practices. We also worked to educate local pharmacists about take-home naloxone.

We saw the value of this practice as, one, getting naloxone in the hands of people who use opioids but did not inject and, two, to reduce stigma. If it became routine to prescribe naloxone to anyone who used opioids, the hope was people would not need to identify or be identified as, quote, "substance abusers" to get naloxone.

While we had some limited success, regular prescribing seemed to hinge on a high level of commitment by individual prescribers and pharmacists.

The complexity and irregularity of insurance coverage, pharmacist knowledge, and individual fear of being seen as a substance abuser made these efforts extremely labor intensive with a generally low rate of people actually naloxone.

In 2015, Pennsylvania Act 139 allowed naloxone prescription to anyone who might witness an overdose, followed by a statewide standing order for pharmacies. However, the standing order does not cover the generic injectable formulation of naloxone, nor does it provide for community distribution.

Availability has increased in Pennsylvania but unevenly. Rural areas without syringe access programs continue to have great difficulty getting naloxone in the hands of people who need it. A major obstacle seems to be the need to have a doctor's help with purchasing, writing a separate standing order, and/or overseeing the dispensing process in some way.

Making naloxone available over the counter would be a tremendous help to people who are struggling and watching their loved ones die in rural parts of the state and country.

Prevention Point has provided naloxone to more than 4,000 individuals just in our local area and documented close to 3,000 rescues, 635 in 2017 alone. Ninety-eight percent of those reversals were accomplished by people who use opioids themselves. We distributed over 7,000 doses of naloxone since January of 2017, only possible due to our ability to purchase cheap injectable naloxone.

While our efforts have been augmented in the past two years by distribution of nasal naloxone through the county jail, hospitals, and other settings provided by state funding, the injectable formulation works fine and is literally and figuratively a lifesaver. Its availability is vital to programs like ours, which are sustainably providing naloxone to the most critical population.

While reports across the state and country are of continually rising deaths, Allegheny County may be turning the corner. In 2017, deaths dropped each quarter throughout the year. While the total number of deaths for the year was a record, each quarter dropped. Early medical examiner reports

anticipate a drop in overall deaths for 2018. We're cautiously optimistic in this.

While we applaud all efforts to make naloxone available, community-based distribution should be the highest priority for scarce resources.

I also just wanted to note that in Allegheny County, as in many other places, we've seen a dramatic increase in fentanyl in the heroin supply. In 2013, 3 percent of deaths in the county involved fentanyl. In 2017, over 80 percent involved fentanyl.

We provide 2.4 milligram per milliliter doses of injectable naloxone in a kit along with two intramuscular syringes and an instruction card. And while the amount of fentanyl in the heroin supply has dramatically increased, we've continued to find that in 93 to 95 percent of the cases where naloxone is used, one or two doses of that type of naloxone has been sufficient. We haven't seen a dramatic increase in the number of doses of naloxone needed. That's just a point that I wanted to make as well. Thank you.

Clarifying Questions

DR. BROWN: Thank you very much.

Are there any questions by any members of the panel for any of the speakers that we've heard today? We've gotten some wonderful information that will help us in our deliberations, and I want to make certain that everybody has an opportunity to clarify the information we have heard.

DR. BROWN: Not seeing any -- Dr. Ciccarone?

DR. CICCARONE: Dan Ciccarone, UCSF. Thank you so much to the community members and researchers, and activists. You all are wonderful in advancing this agenda. Thank you.

Does any one of you -- I could be looking at Eliza or someone else, maybe Peter or someone else -- want to give us a number of doses that we need? We heard from economic analysts yesterday. It's a huge dose.

I think in terms of targeted programming, the work you all are doing, what is a reasonable number? What do we need, not necessarily for saturation, but what do we need for the work you all do, whether it's

over-the-counter or low-cost generic, what do you all need?

DR. DAVIDSON: Peter Davidson, responding after a very quick consult with my colleagues.

(Laughter.)

DR. DAVIDSON: I think one of the ways to answer that question is to talk about what the busiest programs in the country are already doing. Eliza's DOPE project, covering the San Francisco Bay Area, gives out 60,000 doses a year for a population of 800,000 people.

My colleagues Ricky Bluthenthal and Alex Kral did a study about two years ago in that city. One of the things they were studying -- they were doing a big cohort study with injecting drug users in that city, and one of the things they asked all the participants was have you been trained to use naloxone, and if so, do you have it on you right now? And in that study about two year, about 25 participants of the study actually produced the naloxone they'd received from Eliza.

So by the estimates of the number of drug

users in that city, about 1 in 4 drugs users in that city actually was equipped with naloxone on the day that they participated in that study.

The death rate in San Francisco dropped from a high of around about 18 per 100,000 people in 2008 down to about 13.6 per 100,000 in the most recently available year, and that's during a period where fentanyl was entering the community.

So I would say that 60,000 doses per year for a community of 800,000 is basically the bottom of what we want to be doing to actually completely flood a community with naloxone. That's some ball park numbers for you to start playing with.

Does that answer your question?

DR. CICCARONE: Thank you.

DR. BROWN: Dr. Besco? And these questions need to be clarifying questions based on the presentations.

DR. BESCO: Thank you very much, and again, thank you all for those great presentations and your commitment to this work.

I do have a clarifying question in that fact

that many of the recommendations presented involve action outside of FDA's authority. So how would any legislative recommendations made today by the panel be socialized with other agencies? And perhaps that's a question for our FDA friends.

DR. HERTZ: This is Sharon Hertz. That's a good question. I think the best that I can offer is if the committee ultimately has a strong sense of particular actions that aren't necessarily those for our agency; we are actively working with other agencies to address many aspects of the current problems with prescription opioid abuse, naloxone distribution, development of more effective MATs, all of that.

We don't work in isolation. If we need to share the discussion, we have a number of different venues where we can try and do that. I'm on an interagency pain research coordinating committee with a large number of other federal agencies, as well as there are members of patient advocacy groups and academics as one example of the kinds of things that we can try and use to spread the word.

Judy's on a committee. We're on number of different -- we have the opportunity through many different venues to try and share the messaging and also just simply calling them. We have contacts.

So I would encourage the discussion to really reflect what you think -- I feel like I'm getting to the charge now -- but really reflect what you think are the best approaches, even if those aren't the ones for us to work on directly because we will share the messaging to the extent that we can, but we have those opportunities.

DR. BESCO: Thanks.

DR. BROWN: Dr. Goudra?

DR. GOUDRA: Dr. Goudra from Penn Anesthesia. A couple of questions; as an anesthesiologist, the only time we use naloxone is if we suspect a patient has too much of morphine or whatever, and we use in small quantities, typically 100 mics and maybe up to 400 mics. Even then, we are very, very careful in terms of possible potential side effects, including pulmonary edema and things like that.

In my 27 years, I probably have given maybe

10 times. So as a result, I don't have any experience in using it or any direct knowledge of anybody using it, and that the committee [indiscernible].

My question is, since a lot of you guys have been doing that work, a couple of things, one, you all talk about decreased hospitalization. My guess is if somebody gets naloxone, they're probably required to go to the hospital for a problem like re-opioidization; maybe they can go back into an overdose again, number one. And second, there could be issues with acute withdrawal symptoms and excitation, delirium, and things like that.

Has anybody had any experience with these issues?

DR. HERTZ: Dr. Goudra, I'm going to step in here. We're going to have to close the open public hearing section of the meeting now, just based on the limitations of what the rules allow us to do in terms of engagement.

So rather than asking broader questions of the speakers from the OPH, I think hopefully we have

a committee here who has both personal knowledge and background, and based on the speakers who gave the presentations yesterday, hopefully we've given you a lot, if not enough, if not everything, to work on the questions.

I will say that if you have a particular interest in the dose and that question, we covered the dose for what we would encourage development in products back in 2016. So the interest that we have now is about access and availability, and some of the other questions, which are still important, we have tackled in other settings.

DR. BROWN: Thank you, Dr. Hertz.

The open public hearing portion of this meeting has now concluded, and we'll no longer take comments from the audience. The committee will now turn its attention to address the task at hand, the careful consideration of the data before the committee as well as the public comments.

At this point, we're going to take a break, and we will reconvene in 15 minutes. Panel members, please remember that there should be no discussion of

the meeting topic during the break amongst yourselves or with any member of the audience. We will resume at 11:10.

(Whereupon, at 10:55 a.m., a recess was taken.)

Dr. Sharon Hertz will now provide us with a charge to the committee.

Charge to the Committee - Sharon Hertz

DR. HERTZ: Hi. This is Sharon Hertz. I think that we've had a really interesting day and a third, and I just feel like we're going to have a really good conversation based on the bits that have arisen so far, and I'm really looking forward to that.

I think what I'd like to emphasize in this charge is what I said before: This conversation is much broader than just whether or not we should co-prescribe. This conversation is about where resources may be best applied to increase availability of naloxone in the community where it's needed. What we tried to do with the structure of this meeting was to make sure that the committees had

a good sense of what that is.

I suspect the ultimate answer will not be simple, and it will be multifactorial, and that's okay. But we'd like to hear what you think might have the biggest bang for the buck; what might be the most effective; and what role, if any, you think we should be having as part of that solution.

The questions will be read prior to each one. I'm not going to go over them now. If you have questions about the wording, we'll try and clarify, and we'll go from there. Thank you.

Questions to the Committee and Discussion

DR. BROWN: We will now proceed with the questions to the committee and panel discussions. I would like to remind public observers that while this meeting is open for public observation, public attendees may not participate except at the specific request of the panel.

I'm going to read through the first question. Naloxone is currently available through individual prescriptions for patients from their healthcare providers and without individual prescriptions

through community-based programs offering overdose education and naloxone distribution and by direct access from pharmacies under programs such as statewide naloxone standing orders or collaborative practice agreements.

Discuss the comparative and collective effectiveness of these programs with regard to prevention of overdose death and their ability to get naloxone where it is most needed in the communities to save lives.

Is that clear to everyone? Questions or discussion? Dr. Ciccarone?

DR. CICCARONE: Thank you to the researchers, community representatives, and all the folks who spoke this morning, for your concern, your expertise, and your work in the community. This committee has learned a lot from you, particularly also from the folks who spoke yesterday.

My own experience is as a street-based public health researcher looking at the heroin use and consequences over the last 20 years, I was involved, since the late 90s, in some of the early rollout

community-based naloxone distribution. My two publications came out in 2003 and 2005. Karen Seale now at the VA led this work. We showed the feasibility of peer-based distribution of naloxone. The work has continued in a tremendous way the evidence base has built.

The clarion call is clear, that opioid to heroin to fentanyl triple wave epidemic is a crisis. The fentanyl opioid deaths rose 45 percent just in the last year. There was no peaking of that curve. We need urgent action on expanding naloxone access, and we need it now. Community-based naloxone delivery has a good evidence base. It's showing that it's dose dependent, therefore, we must increase access by all measures. We need a saturation model.

The current issue is pricing and availability. Given the scale of the crisis, we need to quickly move forward with over-the-counter availability and generics.

The co-prescribing will help in the ways that the still high opioid pill, overdose death rate will come down, but particularly through the conversations

that will happen with patients and providers, and also by increasing overall pharmacy access. And I'll leave it at that.

DR. BROWN: Ms. Numann?

MS. NUMANN: Thank you for your time.

I believe the collective effectiveness of these programs appears to be quite successful, but it does feel that generic is the only way that's going to help serve them the most.

I had a quick question for FDA in regards their invitation to the companies for that. By chance, did they state why they declined? Did they give any reason? Did they just decline the invitation, or did they give any indication as to why they're not here?

Secondly, curiosity, did any insurance representatives, were they invited at all? Thank you.

DR. HERTZ: I don't know that we specifically invited generic companies. We invited commercial sponsors that we knew were involved in the area. We did not specifically invite insurers.

MS. NUMANN: Thank you.

DR. MAHONEY: I actually think you might have been referring to the question yesterday about OTC rather than generic, and I just want to emphasize that we have had a robust response from sponsors in the IND phase.

As you know, the IND phase is confidential, so it's not surprising to me that not all of those companies are here to talk today. But once the public information regarding FDA's unprecedented step in designing and conducting a label comprehension study, once that information became public, we had a big uptick in interest from companies who do want to develop OTC naloxone products. They recognize that FDA's really bending over backwards, trying to make this possible.

MS. NUMANN: Thank you. Yes, that did answer my question. Thank you.

DR. BROWN: Dr. Zacharoff?

DR. ZACHAROFF: Hi. Kevin Zacharoff. I have a number of things I jotted down with respect to this issue, but first as a question for the FDA, we heard

a lot of presentations talking about the fact that the least expensive way to effect delivery of naloxone was kits that contained syringes and injectable forms of naloxone.

My question is, is it within the scope of reality that the FDA make a decision to approve, without a number of studies, injectable naloxone to be distributed and disseminated freely, or is that something that would require typical safety and efficacy studies in order to happen?

DR. HERTZ: I feel like there is a couple pieces in there, so I just want to clarify.

DR. ZACHAROFF: Okay.

DR. HERTZ: Naloxone is approved for injection.

DR. ZACHAROFF: Right. I'm talking about in a community level setting.

DR. HERTZ: So are you asking what would it take for a kit to be made available? Are you asking about it being generic or OTC? I'm not completely sure.

DR. ZACHAROFF: If somebody's making a kit,

if I decide I'm going to put together a kit with two syringes with needles, enough injectable naloxone to be packaged along with that for injection, whether intravenous or intramuscular, is that an off-label use of naloxone, to be administered by a non-healthcare professional?

DR. HERTZ: I would say that it's not technically off label because it's being used for what's written in the indication.

DR. ZACHAROFF: Okay.

DR. HERTZ: The product is something else, but the use of the injectable is not off label.

DR. ZACHAROFF: Okay.

I just want to make it clear so if and when we get to a discussion, because I heard a lot in the public comments this morning about the fact that it's the least expensive, most effective way. I want to make sure it's within the scope of reality as things exist today, from a labeling perspective, that it's really possible that if we arrive at a decision that that's the way to go, that that doesn't create a whole series of steps that would need to happen in

order for that to take place.

DR. THROCKMORTON: This is Doug Throckmorton. Dr. Zacharoff, we've heard this concern. We've heard a lot of -- it's on the list of things that we're going to need to take back and look at. I think this isn't the place for us to say what's on label and off label; details matter.

Making naloxone widely available is a goal we're all sharing; so how to do that, where this piece fits in, one of the things we need to do.

DR. ZACHAROFF: Thank you.

Other points that I took away with respect to question 1 is we did hear some encouraging data in Rhode Island about outcome measurement in the presentation this morning, but I did hear a lot of talk about reversals.

It's not entirely clear to me as to whether or not those reversals end up really saving lives at the end of the day, whether or not those reversals resulted in situations where people did end up seeking medical attention and the naloxone administration was truly utilized as a bridge to a

higher level of care or not.

I did find that troubling with respect to the collective effectiveness because it's hard for me to know whether or not a reversal ended up saving lives, especially with the data we saw come out from CDC just last month.

Additionally, we heard a lot in the public hearing this morning about substance abuser level risk reduction. I didn't necessarily hear a lot with respect to patient level risk reduction like we heard about co-prescribing of benzodiazepines and things like that yesterday. And that leads me to believe that a lot of what we heard in our open public forum this morning was really directed towards PWUD, people who use drugs, not an acronym I use, but I know it now, and I'll use it again.

People who use drugs don't necessarily have a lot to do with, in my mind's eye, people who are prescribed opioids for therapeutic reasons. I think Dr. Goudra definitely brought up an issue with respect to effectiveness about negative outcomes, withdrawal, pulmonary edema, seizures, things that

could happen to truly physiologically addicted patients because I have certainly in my 34 years in anesthesia witnessed that when naloxone has been administered to people who have high level of opioids in their system. It makes me wonder, again, about the fact that maybe not necessarily these people who had reversals are ending up seeking medical attention.

Then just lastly, as a physician who's licensed currently in the state of Arizona, last year, the governor of Arizona made any naloxone administration a state reportable incident, and that includes hospital administrators, emergency first responders, physicians, and nurses. Just about anyone who can administer a naloxone dose in the state of Arizona is mandated to make it state reportable under the penalty of the laws in the state, no different than a child abuse situation. Everybody's a designated reporter.

That to me is an example of a situation in which the state decision might not necessarily be in line with what the broader goals are. Because if I

were actively practicing in the state of Arizona, I'm not sure as a clinician I would know what to do if somebody came back to me and said I need a second prescription, a third prescription, a fifth prescription, because as a mandated reporter, I would need to be able to account for what's happened to the naloxones that I've already prescribed.

We didn't hear anything in the course of this day and a half so far about what people might do in a prescribe situation when people repeatedly came back for refills and what would be documented in the medical record every single time those refills were provided if we were under the assumption that a prescription was necessary.

Obviously, with respect to this question, a lot of things were going through my mind.

DR. HERTZ: This is Sharon Hertz. I think you raise a lot of really interesting points, but I want to say that there is a reason why we did not start the presentations with does the use of naloxone in the community work; does it achieve a goal? Because I take it personally as an assumption that

that's already known. There are data that support that. The assumption is that people are already aware.

I see this AC as starting a step further along the way, that the only way you can help someone with opioid use disorder who overdoses get into treatment is by helping them live long enough to get there; that patients who mistakenly take something that they shouldn't combine with their opioid needs an opportunity to survive that to be educated how to avoid that in the future.

Also, going into opioid withdrawal, that was a big part of the 2016 discussion. And we all know that in the ER, with somebody who is well trained, who's going to be oxygenating the patient, careful titration is the standard of care, but for somebody on the sidewalk with a layperson, there's not really an opportunity.

We're trying to teach people to know about naloxone and give it, and to ask them to titrate the dose in that setting was also something that was discussed, and at that time agreed upon that first,

get them up even if they're in withdrawal. It's still better than the alternative.

I don't want to dismiss any of that as important, but we progressed to this meeting past that to ask what specifically our committees think and our invited guests think about how to get what we think is an effective approach to saving lives out into the community in the greatest way possible.

I don't know what's going on in Arizona. That is a little disturbing, but state items aside, local authorities aside, I'd like to ask us to focus on the opportunities we have here to hear your thoughts on the different approaches and how to facilitate the wider, bigger safety improvement.

DR. ZACHAROFF: Thank you.

DR. BROWN: Dr. Lloyd, could you introduce yourself?

DR. LLOYD: Josh Lloyd, deputy director in FDA.

DR. BROWN: And just to reiterate exactly what Dr. Hertz said, specifically, we're here to address how we can assist the agency in understanding

how to increase access.

Dr. Hernandez-Diaz.

DR. HERNANDEZ-DIAZ: Thank you. I would like to thank the presenters yesterday and the participants today for the very important information that we are absorbing here.

I agree with them that this is an emergency and we need to move quickly, and I think we have enough data to understand that saturation mode is important and that the benefits are clear. We hear about some potential adverse effects from naloxone, from the opioid withdrawal.

I think two things that we hear today also is that there are some complications with insurance and legal issues that I think need to be solved. And I know it's not up to FDA, but maybe passing that to the appropriate agencies would be important because these are the adverse effects that we are discussing that are beyond the pharmacology that we are expressing.

Then another potential adverse effect to consider I think is the education component of the

access that might be missed depending on which strategy is recommended. But regarding the effectiveness, I think it was clear from the discussion that we need to get naloxone where the overdoses are happening, and that that means putting it in the hands of individuals that are likely to witness the overdose, and that includes users, and family members, and others.

I think to get there, we have to consider at least two populations, and we heard that this morning in the presentations. One is the individuals that misuse or abuse opioids. I think the crisis is there, the explosion is there, and most of the overdoses, not all, are happening there. So I think if we have to prioritize high risk versus cost, we have to start there as step number 1.

I think we just want to get them as much naloxone as possible. I understood from the discussion these days that either over-the-counter or online access to get to universal access in that population and particularly collaborating on learning from the community-based programs that have been

saving lives already, and they are the best thing to teach us how to do it, will be important.

Then there is this other population being prescribed opioids for pain management, and that's probably where we need to start because of the cost right now with a targeted approach and maybe selective co-prescribing to higher risk groups that are easy to identify and being aware of not creating the stigma that we discussed today.

We mentioned risk factors like high dose, co-prescription of benzodiazepines, and that's another thing that is not part of the discussion, but why are we prescribing benzodiazepines is another topic; substance abuse, mental health, and so forth.

So I think in that approach, we might have to start with a targeted approach, and I think that would help also saturate -- by prescribing to those patients and reaching the households so that the naloxone is there, it will indirectly help the saturation and the availability of naloxone and probably also reduce the stigma because it's given in a prescription way and indirectly increasing access.

I think that's what is in my mind for the discussion.

DR. BROWN: Dr. Hertz, is it within the purview of FDA to create a model community program or suggest how a community based program -- we've seen and heard about a lot of models, and my question is along the lines of there are some places that are very successful, and some places don't have a clue, that if we gave them 2 million amps of Narcan, they would not know how to distribute it.

Is it within the purview of FDA to push that along?

DR. HERTZ: Not specifically. Whether or not you think what we can do would facilitate that within the realm of things that the agency does, OTC generic, co-prescription, that sort of thing, you can consider that. There are other agencies that are involved more with that kind of outreach. SAMHSA comes to mind, and I think I heard some other collaborations as well as some of the state and local authorities.

DR. BROWN: Dr. Dasgupta?

DR. DASGUPTA: The SAMHSA toolkit on naloxone already has a lot of the best practice guidelines in it, and that was made in consultation with many of the community groups we heard from this morning.

The experience with the syringe exchange programs and having national standards has had both good and bad effects. I think part of what we heard from Dr. Oliva's presentation was that what has worked in the VA system is the ability to have each facility tailor the program to their individual needs. The amount of collaboration they have to foster the heterogeneity is part of what has made the VA program a success.

I think while national standards and practices are helpful, I think maintaining that flexibility at local levels is going to be critical.

DR. BROWN: Dr. Meisel?

DR. MEISEL: Steve Meisel. Once again, I want to reiterate how excellent this last day and a half has been in terms of quality and depth of the speakers and thought provoking.

One of the things that strikes me is that one

of the most effective things that could come out of this is to take this last day and a half and replicate it everywhere around the country with audiences like state health commissioners, county health commissioners, insurance companies, professional practice groups, HHS, you name it, legislators and governors and whatever. Let's take this on the road. That in and of itself would have a major impact. I mean that very seriously. It is that powerful.

One of the themes that strikes me about everything that we've heard yesterday and again this morning is the word "innovation" comes to mind. We saw lots of innovative programs from New Mexico or the VA or Rhode Island or elsewhere, Utah, that are all a little different.

One of the things that I think we need to encourage is more and more innovation and more and more freethinking in this space because I don't think anybody has got the right answer. They've got some answers that help to some extent, but nobody has gotten this down to zero. Nobody has gotten this

down to a 90 percent reduction of anything. It requires a lot more work, but the innovation that happens on a local level, I think is very important.

I see this as really a two-part problem. One is it's a public health problem, and public health problems have to be solved in a public health manner. The notion that by co-prescribing or those kinds of tactics are going to help with people who are taking fentanyl on the street, that's not going to happen, and that's 60, 70 percent of the deaths that we're seeing out there. That has to be approached by a public health problem.

The saturation programs that we heard about are one tactic to get there, but I think there is other ways of getting there, many of which haven't been thought of yet, and that's where I get back to the innovation. But I think the idea of co-prescribing and all that is probably not all that helpful.

We heard about co-prescribing for patients who are admitted with overdoses. Well, you're not going to be co-prescribing them because you're not

going to be prescribing a narcotic. That's primary prescribing of the naloxone. That's a little different. That's a different type of model.

I think the lessons that I took away from this is innovation and saturation are the key and how can we get there with that. That co-prescribing piece of it, will it help a little bit, maybe, but that's not going to be the same as the public health model.

Two other points, one is we can start thinking about naloxone as we have for decades thought about ipecac. Every parent with small kids has got ipecac in the home because you never know what they're going to swallow. Well, what if we put naloxone in everybody's home like we think about ipecac? How do we get to that framework?

The over-the-counter stuff helps with that maybe, the saturation stuff, but all of the educational pieces with that. It starts in the pediatrician's office. Perhaps even it starts in the obstetrician's office, in that space. To think about that in a public health framework and really raise

that level of awareness so that people are demanding to have naloxone in the home like they would have ipecac in the home, I think would be helpful.

Then the last point I'd make in this space before ceding the floor is that there's been a lot of suggestion that if we just had some generics, the prices would go down. I don't buy that. I think our experiences with generics over the last number of years, whether it's the hospital space or the ambulatory space, is that the prices are going up dramatically. Unless there's a buck to be made, people aren't going to make this stuff, and so we have fewer and fewer generic manufacturers and the prices go up.

We see that over-the-counter forms of ibuprofen and naproxen, whatever, are more expensive than the prescription versions of that because of the marketing and what have you. So I would just caution us not to be lulled into an assumption that if something's available generically, it's going to lower the price.

Now, if it was available over the counter and

there was generic, and it was subsidized by somebody, Congress, somebody, that might be a different story where you have a maximum price point. But just the idea that you have it over the counter and have it generic doesn't by itself guarantee a price point.

DR. BROWN: Dr. Brand?

DR. BRAND: Thank you, Mr. Chair.

I won't reiterate it, but some of the stuff I was going to say Dr. Hernandez-Diaz already commented on, and Dr. Meisel, too, just that we do have two distinct populations that need two distinct strategies.

One of the unintended consequences we have to be sure we don't do is in any way impede the wonderful work done in the community with the community distribution centers. So whatever decision is made by the FDA today, if anything, we need to help expand those programs nationwide as quickly as possible. While we've been here for 2 days, over 300 people have died, so this is an emergency.

One of the big things -- and you touched on it a little bit, Dr. Meisel -- I hope I'm saying that

right --

DR. MEISEL: I've been called so many things. That's okay.

DR. BRAND: -- and I'm not sure it's been emphasized enough, is education as a public message, not through the doctor's office or through the pediatrician's office, but on television, on the radio, everything else, education to the patients, education to the prescribers. In every publication that we need naloxone co-prescribed, we need naloxone in these community programs.

That's the only way to destigmatize it, is to start talking about it, how to recognize the signs of overdose. Just like we're seeing on television right now about how to recognize the signs of stroke, we need to see those messages constantly on television to destigmatize overdose. We need people to understand accidental overdoses are going to occur. There's no stigma attached to it. It's a disease for some people just like diabetes.

I think we need to focus on two separate distinct ways to get naloxone. I do disagree. I do

think that it should be co-prescribed with high-risk patients in particular.

But at the same time, and to answer the question one of the other gentlemen, anesthesiologists -- I'm sorry, I forgot your name -- as far as over the counter, the kits that we have right now, just keep in mind -- and this is down the road -- we teach people how to use insulin and Lovenox in the community all the time, EpiPens.

People can very quickly be trained how to do an intramuscular or subcutaneous injection. I just want to make sure we're not limiting their ability to do that with whatever decision we come up with.

DR. BROWN: Dr. Krebs?

DR. KREBS: Thank you. I'll echo what everyone has said about how outstanding the presentations were, and I'll say that I came here with, I think, a reasonable understanding of the evidence and limitations of the evidence related to co-prescribing and how this might work in terms of practice, primary care, pharmacy, physician, and collaborative models.

That's where I was familiar, so that's probably my bias coming. I understand the potential of those kinds of approaches better than I understood the potential of other kinds of approaches.

Since this question is really about comparative effectiveness, what I'd like to emphasize is that it seems clear that the community distribution model is highly effective in getting the naloxone to the people who will use it to reverse overdose and save lives. It seems like that is very clear.

We don't have any similar information about prescribed naloxone to patients receiving opioids. In fact, the evidence we have really actually suggests that if there is a benefit, it's not the naloxone itself that is the benefit. It's the discussion about the physiology of opioid poisoning causing sedation and respiratory depression, and that we're not having that conversation.

That's the conversation that is needed. That's where the value probably is. Even in Dr. Coffin's study, I think the best thing we have

showing that there's some potential benefit, again, it did not seem to be from the naloxone itself.

So we don't need to give the drug to get the benefit there. If what we're talking about is a labeling change, there are things other than recommending co-prescribing of naloxone that could get that information that seems to be the active ingredient out to the patient.

Of course, in reality, we talk about two populations here, pain patients and people who use drugs who may or may not be patients. That's one way to look at our two groups of populations, and it can be sometimes helpful. But I think actually a better way to look at it -- because sometimes we don't know when you see a person if they belong to one or both of those groups.

No fancy statistical modeling can do it. If you dig right in, the positive predictive value of those models is never very good. You just don't always know, especially, when people who use drugs have a really strong incentive to not let their physician know sometimes.

I think really what we're doing with this two types of at-risk persons, we have people who know they are at risk or their loved ones are at risk of an overdose. Those people are the customers for naloxone, and so they're the ones who are the most likely to use it, the most likely to benefit from it, and we just need to make it much easier for them to get it.

The other type of at-risk person are the people who do not know they are at risk, and these are the patients whom we are prescribing to perhaps higher intensity regimens than we should; perhaps a low value regimen, more risk than benefit to the regimen. What they need is information because getting naloxone may not itself be what changes their risk.

Then a related issue I think, too, again when advocating for it, yes, let's do everything, to me, I think we need to always think about unintended consequences of our actions. I think although we have some hypothetical benefits of co-prescribing, mostly that it would promote education, or decrease

stigma, or make pharmacists stock the drugs more frequently, we also really have some hypothetical harms. Recommending co-prescribing for the many, many millions of people who are receiving high-risk opioid regimens would drive up drug costs in unpredictable ways.

The debate we had yesterday about this really convinced me that I have no idea what the heck would happen, but it could be really bad, and that could adversely affect the community programs that we think are the most effective.

Also, let's always remember there's an opportunity cost. I work for the government, and I know we can't do everything at once. So if we focus a lot of energy on something that has a hypothetical benefit maybe for some people, to what extent are we missing out on the opportunity for some other activity to really push forth something that could be much more high value?

Ultimately, when we're talking about people who know they're at risk and people who do not, those highest risk patients for whom I'm prescribing

opioids, they know more than I do about their risk. If the drug is available at a low threshold for them, they can go get that or their family member who's concerned about them can get it. They don't need me to do a predictive model to say, oh, I think you might be at high risk so here's this prescription.

The truth is that when I prescribe something, people often fill it whether or not they want it, so I'm not respecting their agency on that level. Thanks.

DR. BROWN: Dr. Gerhard?

DR. GERHARD: Tobias Gerhard, Rutgers. I also want to start with thanking the presenters yesterday and today both for the information they provided, but also in the majority of the cases really for the tireless work they've done for many years, often decades, and that really should be appreciated.

I want to start by saying I think the discussion and the answers to many of the questions we're discussing really depends on the framework we're taking to look at this. Are we thinking about

this as business as usual within the regulatory framework that we've used for many of the other questions that we've addressed in similar advisory committees, or do we think about it in the context of a public health emergency that kills tens of thousands of people every year?

I think that changes the answers and our ability to think out of the box dramatically. I would very much recommend that we take the latter approach and really do not treat this as business as usual and think about unorthodox approaches that might actually work.

I think as not somebody that's in the field specifically, it's very clear that saturation of the community with naloxone really is the goal. Everybody that should have access needs to have access at minimal cost with minimal barriers. In some form that is clearly the goal.

I think the narrow question of the committee today, the issue of co-prescribing, when we remove other considerations, so without other interventions, I think is a very inefficient tool to get to

saturation. It would be very expensive. It would target, depending on the targeting mechanisms of which high-risk populations would be selected, groups that aren't at the highest risk. It certainly would miss the particularly high-risk groups of drug users, vast majority of which would not have insurance and so on.

So I think that by itself it's an inefficient tool, and that doesn't mean that there isn't a role for it as well.

I think reducing barriers for naloxone availability, and use is what it is all about, those barriers are slightly different or the context is slightly different depending on what population we're talking about. Are we talking about drug users or are we talking about people that have a prescription for an opioid for chronic pain or for acute pain?

Nonetheless, I think reducing the barriers to availability, the solutions are actually similar and would support ideally both populations. Number one, I think is clearly the price. So it's really an issue of how do we make this available at -- and I

don't know what the number is, but I think a dollar a dose or something like this should be the goal. That is a number that I think is not feasible if we stay within the traditional framework, but it is a number that's feasible to achieve when we step out of that framework and think about real government buying power, invalidating patents -- I'm not a specialist in these subsidies -- some way to make through commitment of regulatory authority from the federal government plus funding in some form, make naloxone available at a dollar a dose to whoever wants it.

We can talk about what dosage form this would be or so on. That's a significant commitment, but again, we're talking about the response to public health emergency that we would take for many other types of public health emergencies.

The second barrier I think is the issue of access and stigma, where standing orders clearly help but still have problems. I think there the move to somehow get this to OTC availability would help because it would cut down on problems in some states where maybe standing orders aren't in place or more

difficult to implement and would take that level of access away.

I think the move to OTC without any intervention on the price, I probably wouldn't do so much. It wouldn't help to have a 200-dollar naloxone product OTC in a pharmacy. It would not reach the right populations. But together with this price intervention, I think it could be incredibly powerful.

I think basically what we need is a concerted effort by multiple government agencies that certainly extends the purview of what's under the authority of FDA. But again, if we think about it as the response to a public health emergency, I think this becomes very much justified, and I think it's the only way that we get to something that really works.

One last brief comment, obviously, even with all that effort, this would not be a cure-all by any means. I think to think about education, availability, and support of addiction treatment ideally would be part of this discussion. Other areas of stigma like what we heard, the effect on the

availability of life insurance and things like that, would be part of that discussion. But I think the intervention on the price and lowering any regulatory barriers on access together would be the solution that I think is needed as a response to the problem we're facing.

DR. BROWN: It's close to lunchtime now, and rather than get started on another question, I'm going to break for lunch. We'll reconvene again in this room in one hour, about 1:00.

Please take any personal belongings you may want with you at this time. Committee members, please remember that there should be no discussion of the meeting during lunch amongst yourselves, with the press, or with any member of the audience. Thank you.

(Whereupon, at 11:58 a.m., a lunch recess was taken.)

A F T E R N O O N S E S S I O N

(1:37 p.m.)

DR. BROWN: We're going to reconvene and continue with our discussion of question 1. Again, I'm going to ask that we focus our attention on the specifics of the question, which in this case relates to the comparative and collective effectiveness of the various programs that we have heard about in the last two days.

The next person would be Ms. Robotti.

MS. ROBOTTI: Thank you. Sue Robotti. Follow-up question to Dr. Hertz. It's a follow-up to Dr. Zacharoff's question, and then I have a comment afterwards about on and off label.

Does the needle packaged with the generic naloxone impede approval of a drug going OTC?

DR. HERTZ: I don't understand the question.

MS. ROBOTTI: Sure. If naloxone was to move to be an OTC product -- you did a really good review of what makes it such a unique drug. It's a drug that people will have and generally can't use on themselves, somebody else uses it; all of that. And

it has a needle if it's the generic syringe one.

The fact that it has a syringe, are there other OTC products that have a syringe?

DR. MAHONEY: Yes. This is Karen Mahoney from the nonprescription division. Regular and NPH insulin are OTC.

MS. ROBOTTI: Of course. Thank you. Great.

I'm still back on question 1 or discussion point 1, and I just want to say the community-based programs are clearly the priority. But what happens in the many areas of the country that don't have these programs in place? Even needle exchange programs are still very controversial in many places.

I have intelligent and poorly informed friends who think that naloxone encourages drug use and mutter about naloxone parties, which I believe are mythical because they make no sense. There's a lot of public information that has to be straightened out.

I live in one of the most famously liberal areas of the world, the upper west side of Manhattan, but if somebody parked a truck on the upper west side

and was giving away naloxone, there would be an outcry, "Not on my street, not in my neighborhood. It will attract drug dealers. It will attract bad people."

So expansion of this program, I a hundred percent support it, and I think it's the way to go. I think it's going to be very difficult, and I don't know how the government supports it and can make that happen, but I hope you can.

Separately, the discussion at the doctor's office or at the pharmacist counter of using naloxone when somebody is first prescribed an opioid, I think is a crucial discussion. I think that it will make people stop and think. If I'm at risk of overdose, do I have alternatives to using this drug? Maybe I really should try some alternative pain relief methods before I go on the opioid.

Just having the discussion, while most people will continue to get the opioid, just having the discussion not only helps destigmatize it, but also it makes it personal, the risk of overdose. It makes people realize that it's not just other people who

might overdose, that you yourself could overdose by mistake. It's a big destigmatizer. Those are my points. Thank you.

DR. BROWN: Dr. Besco?

DR. BESCO: Thank you. Kelly Besco, OhioHealth. I just want to add a little bit more to what Dr. Brand was saying about OTC status and just cautioning against moving toward OTC status without some sort of provision that it be obtained by individuals from behind the pharmacy counter.

I feel like, as we heard yesterday, that pairing access with education produces successful outcomes, and I think omitting that educational component would be a missed opportunity to ensure that naloxone is used appropriately by individuals.

That being said, I do believe that we need to remove access barriers and provide a greater government funding stream or procurement program for national distribution programs. Coming back to I think during one of the public presentations, thinking about the CDC pediatric vaccination distribution program, is there something innovative

that we could put together for a national naloxone distribution program?

Those are just my comments, especially on the OTC status.

DR. BROWN: Dr. Garcia-Bunuel?

DR. GARCIA-BUNUEL: Thank you. Martin Garcia-Bunuel. I'll try to cut to the chase; a lot of great comments and thoughts.

One, once again, I think to the agency, thank you for this opportunity for all of us. What I'm struck by, the data suggests a public health crisis. I'm not sure. I think we tried to dig into the data, but right now what I can walk away with is that we do have the public health crisis in terms of overdose and death from overdose.

Having said that, the community-based programs just stand out remarkably in terms of how we address the crisis. Coming from the established healthcare system, I want to caution us because the established healthcare system at its best won't touch this. Co-prescribing is an excellent tool, and I think we should engage around it as a tool, once

again, to engage patients.

In the opening remarks, I'm still struck by one of the graphs that show how many opioids we prescribe in the healthcare system. So I would be remiss not to make sure we keep that on the table in terms of trying to come up with naloxone as a cure-all or co-prescribing as a cure-all for a problem that we created.

I was here a few years ago where we were discussing all kinds of permutations on how to discuss risk of opioid prescribing with patients, and how we should engage the continuing medical education industry to support this effort in conjunction with the pharmaceutical industry. This was just several years ago, but we were still on a launchpad to prescribe, as we are, millions and millions and millions of doses of these medications that are killing people.

Having said that, I want to make sure that we do discuss this from both sides as a healthcare system and have a good discussion and recommendation about co-prescribing, but definitely already want to

mostly emphasize how do we leverage community partners to help us.

Organized healthcare because of fragmentary payer systems, potential less reliability of payer systems and coverage for individuals in the community throughout our country, will not be something we can rely on to solve the problem.

As a primary care physician, I also caution us to try to solve public health problems through the primary care office. There's a tremendous shortage of primary care physicians throughout the country. It will only get worse.

We have medication-assisted therapy that we also want primary care to get involved with. We have coronary artery disease, type 2 diabetes, hypertension. I could go on. And these are all expectations, as we move forward, that the primary care office will be the touchpoint for all of these illnesses and how do we keep preventing morbidity and mortality through organized medicine? Impossible. But to then put another layer on this by saying that we will solve it by co-prescribing, we just have to

be careful and cautious.

My last comment would be, I would ask us also to strategically think, as we make recommendations today, how can we actually see the community-based organization as the future of addressing problems such as this.

In the here and now, we need to actually make some recommendations I think that address the crisis right now. I can't imagine how we couldn't. I can't imagine looking at this data for a couple more years and expecting it to change if we don't do something differently.

I'd also like to think that the community organizations that have shown us what they can do when coming from the patient perspective and the family perspective and the community perspective, they can actually offload the organized healthcare system. They can offload the primary care physician, the urgent care physician, the subspecialty offices. They can actually help us address healthcare issues that we will never be able to do as an organized healthcare system.

My struggle with the co-prescribing is, look at me; currently, I work in the VA healthcare system. So I am an incredible supporter of organized healthcare systems that share data, that collaborate care, and look at human beings through their lives from a population health model, but that's still a limited approach.

I thank everybody, and especially thank those who have shared the information about what they've done out in their communities because it's impressive and inspiring. Thank you.

DR. BROWN: Dr. Goudra?

DR. GOUDRA: Basavana Goudra from Penn Medicine. Going back to the question again, one of the points for discussion, or at least part of the discussion here, is comparative and collective effectiveness of these programs with regard to prevention of all those deaths. I asked at least two speakers yesterday, and one of my colleagues asked this question as well.

I'm not convinced whether anybody came up with definite data, robust data, suggesting that

these measures have contributed to reduction of death. The closest I came was in the state -- I forget which state -- that they moved from number 1 and then number 4 and then 14 and 17. That might very well that others have gone up, not necessarily this data has gone down.

I still wonder where is proper data to suggest that naloxone was specifically contributing to the reduction of death at the exclusion of many other measures that have initiated or implemented over a period of time.

It looks like FDA has made up its mind that naloxone is effective with regard to prevention of all those deaths.

DR. MAHONEY: Mr. Chairman, if I may. This is Karen Mahoney, nonprescription. I just want to make one clarification. In the United States, there is not a behind-the-counter status. Drugs are either over the counter or prescription. I just want to make that clarification.

DR. BROWN: Thank you. Dr. Faul?

DR. FAUL: Hello. As we think about the two

different types of users, illicit and prescription-based users, I wanted to clarify the CDC graph that keeps getting presented.

A lot of people think that the line represents people. It really does not. It represents the substance found in the dead person's body. So it's easy to look at that graph and say, well, this is the proportion of prescription drug deaths, and it's just a misinterpretation of it.

It's a mirror of the death certificate where there's an underlying cause of death, is the main reason why the person died. In this case, it would be a drug overdose. But there's ten different multiple causes of death that get scanned; if there's heroin, there's fentanyl. Opioids, you cannot distinguish between illicit and prescription opioids in a body. There's no way, but that falls under the prescription opioids because that's where it makes the most sense.

The point of bringing this up is that there may actually be more illicit type opioid, heroin deaths than actually projected on that graph because

it's a combination, it's a polysubstance problem. So I just wanted to clarify. Thanks.

DR. BROWN: Dr. McCann?

DR. McCANN: Hi. Mary Ellen McCann. I have a couple of points. One, I'm still struck by the ipecac model, and I looked it up this morning. Families before the year 2001 were recommended by their pediatricians to buy ipecac to prevent poisoning in their children. I don't know how many families got it, but I would presume a majority of households went out and bought some ipecac.

It's over the counter. The price presently is about $8 a bottle. And I actually think if this were an over-the-counter product of naloxone, that a price point between $5 and $10 per household would not be unreasonable. Now, that's dealing with the not high-risk community, the low-risk community.

The other point that I'd like to make, I would like to say that I think co-prescribing is a very inefficient, super expensive way to saturate the low-risk population with naloxone. In our households, I probably could find three or four

bottles of some sort of narcotic that we've accumulated over 30 years, such to the degree that when I broke my arm a couple of years ago, I didn't bother to get any pain pills. I knew I could find some at my house.

The question is, the at-risk population is not necessarily those that are getting prescribed new narcotics, the low-risk population is probably all American households or most of them. So then it comes down to the question of the expiration dates, are they parallel? Because I'm sure my narcotics at home are technically expired. I'm also pretty sure that they're probably still effective.

Are we going to advocate that people get naloxone for the house somehow every three years, or do we have any data whether it really does expire every two years?

DR. BROWN: Dr. Bateman?

DR. HERTZ: Did you want an answer?

DR. McCANN: I did.

DR. BROWN: Sorry.

DR. HERTZ: This is Sharon Hertz. So those

very old opioids that you're taking --

DR. McCANN: Rarely.

(Laughter.)

DR. HERTZ: On the very rare occasion of a broken bone -- sorry about that; it sounded terrible -- yes, there's probably still some opioid in them, but there's also degradants. So it's not a quality product anymore, and there are certain standards for how a product behaves on stability that support an expiry.

The expiries are databased. What people may be surprised to hear is companies -- I always hear this from family members. "Oh, those pharmaceutical companies want a really short expiry so you have to keep buying drug," but the reality is, I think in general, it's much easier to have a longer expiry in terms of manufacturing and storage than to have a very short one.

The two years is based on data. So at two years and a month or two and a half years, there's still naloxone in there, but the question is, how much is left and what are the conditions under which

it's been stored? Do you want it on hand? Has it been in a glove box during the summer?

So there are a lot of circumstances in which the potency of the actual drug substance can be affected, so the expiry is there. So it's not that the drug turns off at the day the expiry is over, but you start to lose the reliability of having a quality product. That's the part I'll answer.

DR. BROWN: Dr. Bateman?

DR. BATEMAN: Thank you. I agree with the comments that were made, that really the most important thing that we can do as a society is to scale up the community-based distribution programs. This gets the medication to the patients or the people who are at the highest risk and the people around them who are at the highest risk.

But to achieve the kind of saturation that we've seen in the model programs, the Hamilton County programs, some of the Bay Area work that's ongoing, is going to require an enormous amount of medication. Dr. Davidson suggested that for the community of San Francisco, which has 800,000 residents, it would

require 60,000 doses. If we translate that to what would be required across the entire country, that's something in the order of 20 to 25 million doses of this medication.

I think it's going to be hard to achieve that kind of penetrance of the medication through traditional models, whether it's even converting Narcan to a generic or making it available over the counter.

Someone raised the point earlier that what we need is a national naloxone distribution program. And if the federal government can pay for half of the vaccines that are administered in the U.S. -- I think the CDC does that and other government entities together do that -- this is something, given the scope of the opioid crisis, that our government should pursue.

DR. BROWN: I'm going to stop our discussion of this right now unless somebody's on fire. I'm going to try my best to say what we have said over the last 45 minutes to an hour.

The overwhelming majority of deaths occur in

those using illicit opioids or prescription opioids without therapeutic purpose. In order to provide the maximum effect, these subjects, as well as patients prescribed opioids for therapeutic purpose, must be considered.

Co-prescribing of naloxone with opioids could provide some benefit but would be expensive with no model suggesting the extent of effectiveness that could be expected. Education at the time of prescribing may be as effective as the drug itself. Community-based programs have been very effective but lack the resources to expand their effort.

For the agency to provide the maximum efficacy, assisting these community groups would seem to be the best use of scarce resources. This should include using the available capacity of the agency to produce over-the-counter naloxone rapidly. This may also mean a change in the distribution of naloxone through the federal government.

Can we move to question 2? I'm going to read the question. Discuss potential burdens and barriers associated with co-prescribing naloxone currently

with opioid prescriptions for all or some patients and with targeted prescribing for individuals considered at high risk for overdose.

Discuss how these burdens or barriers may affect implementation of co-prescription or targeted prescribing and what steps could be taken to mitigate these impacts.

Is that question clear to everyone? So we're going to be discussing the issues of burdens or barriers to co-prescribing of naloxone with opioids.

Ms. Numann?

MS. NUMANN: Sabrina Numann, patient representative. Thank you. In regards to burdens and barriers, this is in regards from a patient standpoint, not a patient that Dr. Krebs described. Even as an informed patient, stigma and language is very important.

A discussion from my physician and/or my pharmacist advising naloxone, due to possible risks and interactions with opioids and comorbidities, it will catch my attention much more effectively than advising that I'm being prescribed naloxone for

opioid overdose.

Language does matter, thus the education and/or media campaigns -- Dr. Brand touched on that very well -- geared towards reaching all the patients, it's vital for the average opioid-prescribed patient who is not abusing in any form or accidental ingestion from maybe small children.

However, people who use drugs, opioid use disorder, I understand they're more receptive to the overdose word, but I think that this is a barrier that requires industry, physician discussion, and maybe FDA label discussion of interest for sure.

I understand that this is crisis mode, but for mass distribution and making sure that every household receives this for reasons such as I've described, I believe the language itself needs to be thought thoroughly to remove the stigma and make sure that patients like myself understand what they're really saying, rather than implying that I'm misusing my opioids or that I'm suicidal, which may turn me around from that. Thank you very much.

DR. BROWN: Dr. Zacharoff?

DR. ZACHAROFF: Thank you. Kevin Zacharoff. With respect to discussion point number 2 and co-prescribing, I'd like to share with you that one of the pieces of knowledge that I have really assimilated into my mindset by serving on this committee is the idea that my old definition of a risk-benefit analysis is not what it used to be with respect to this medication.

I try to communicate that to almost everybody I meet and at talks that I give. Dr. Argoff mentioned warfarin yesterday, and he probably got that from me because I use the Coumadin analogy all the time. But that's a situation where the risk of prescribing something directly affects the patient, and the healthcare provider, like most other medications, needs to just weigh that risk with respect to the patient.

Something I've learned is that with respect to opioid prescribing and risk, it now has to expand beyond just the bubble of the patient and the prescriber. It needs to include the household, it

needs to include the community, and it needs to include society. When it intersects society, I think is where we see the intersection of maybe these two distinct risk populations.

For me, with respect to co-prescribing and mitigating risk, one of the things that I think is really important and it could be a challenge and it could be a barrier, is to bring up the issue of how does a healthcare provider capture the information necessary to formulate an appropriate risk-benefit analysis. It could be difficult, and it could be a different paradigm.

When I talk to primary care providers, who I consider to be the most important group in this discussion, I talk about how important it is to ask if there's someone else in the household with a history of substance abuse. Are there people who possibly may come into the household who have a history of substance abuse, and so on and so forth.

With the simple act of co-prescribing naloxone concurrently for all patients, I don't know that I would feel that that would be a barrier that

could actually be overcome. Certainly in reading a lot of the comments that were posted on the docket for public commentary, we heard a lot about the second population, which is substance abusers, but we heard a lot from pain patients about the burden of being saddled with that.

We had a lot of discussion yesterday using the word "offering naloxone" to patients and that the act of offering naloxone to patients actually promoted a certain mindset. It promoted a certain level of discussion, and that it's possible that just the act of offering the medication naloxone to patients where there might be increased risk is the most important ingredient.

As opposed to co-prescribing, I would really urge the idea that the offering part be what really happens and the documentation of that offering. Taking into account of what I call the new math for the risk-benefit analysis is the way it gets decided. I've been telling people for years that every time an opioid is prescribed or refilled, there needs to be re-justification of the fact that the medication is

the appropriate thing to use.

Continuing current treatment plan just doesn't cut it anymore, and if we do consider risk to be something that is dynamic, as we heard mentioned this morning, then that idea of offering it when appropriate seems to make a lot of sense to me.

I worry about the over-the-counter model because I think that might circumvent the communication and the discussion part of this. I think most patients who seek medical attention for a pain-related complaint, we all know, those of us who are clinicians, patients have tried over-the-counter solutions before they ever come through the office door. I worry about the fact that over-the-counter distribution could short circuit the communication process and short circuit all the benefits of that. So I wouldn't be a fan of that, and I don't consider offering to be the same thing as co-prescribing.

Then just lastly, while I think targeted prescribing for individuals who are high risk for overdose is important, I would change that wording to "targeting situations where there may be high risk of

overdose." That would take into account that new math and not just imply that the only person at risk is the patient because they have COPD or they have obstructive sleep apnea, because I'm not hearing a lot of discussion about that. I'm hearing about people getting into Mary Ellen's medicine cabinet because they know she stores three different kinds of opioids --

DR. McCANN: Now they do.

(Laughter.)

DR. ZACHAROFF: -- and getting their hands on them.

I think targeted prescribing with the mindset that you're really targeting whether the situation, where the person lives and the context of where they live, sets up a stage for a high-risk situation is much more deep than just using a simple tool to determine opioid-induced respiratory depression because that only applies to the patient. It doesn't apply to other members of the household, other members of the community, and other members of society.

Just lastly, a major barrier in this situation, in my mind, with this whole thing, is the fact that the person who's going to be receiving the education is not likely to be the person who's going to be using the naloxone. While I could teach a person to give an injection, the likelihood of that person actually giving the injection, if I determine them to be high risk, is extremely low.

I really struggle with the idea of how am I going to reach everybody else on the planet how to give an injection, and that leads me to think about innovative things, which maybe we'll talk about when we get to Item 3, like AED models for naloxone, where everybody knows there's a naloxone available in the area if I witness somebody having what I think is a respiratory arrest, but we'll get to that.

Those are my thoughts with respect to the burdens and barriers associated with this and my definition of what I consider to be targeted prescribing. Thank you.

DR. BROWN: Dr. Meisel?

DR. MEISEL: Steve Meisel. First of all,

well said, Dr. Zacharoff, excellent points. I have a hard time teasing apart questions 2, 4, and 5 on here because I think they interrelate. But let me point out a couple of additional barriers to this beyond what Dr. Zacharoff described.

First of all, if this becomes we're going to pick a target population, well, we don't really know what that target population is. That calculus is changing as research goes on. Dr. Oliva yesterday had a model that may be helpful here, but that's not going to be the same model that's going to apply to everybody.

So how do we apply a risk-benefit model? What do we define as high risk, moderate risk, low risk? That needs to be defined. If you put it into labeling we're going to co-prescribe for high risk and try to define what that is, that's a moving target and will be for some time.

What's going to happen here is a doc makes the decision that it's not a high-risk situation and doesn't co-prescribe, but then something happens, and then there's a lawsuit. And now somebody is going to

say, well, look at all the recommendations, and you co-prescribed it in a higher risk situation. Maybe it's in the package insert, maybe it's elsewhere, and maybe it's in a REMS, and, "You didn't do it, Doctor. Why not?"

That sets up a lot of failure and then a lot of over-prescribing and defensive medicine that comes along with that. And it's no longer high risk; it's darn near everybody. We have to, I think, account for that because this isn't really clear if A and B, then do C. This is a moving target.

Then what happens out of that is it becomes a rote exercise. It becomes part of an order set or an order panel or something. Every time you prescribe something, a naloxone dose comes along with it, that sort of thing. And what you lose is exactly what's going to be effective, and that's the conversation.

I think we heard many times yesterday and through some of the discussion today that the key here, particularly when dealing with patients as opposed to the public health piece, is the conversation. If it becomes rote, because now it's

required, we're going to do it for this population and we're going to build it into order sets, we lose the opportunity for that conversation. I think we have to be aware of that.

I go back to the notion that we want to be careful not to stifle innovation. I think Mary Ellen mentioned it before. It's so inefficient a model to saturate the community by this particular methodology, and I think we need to keep that in mind.

One other point is, Kevin, you mentioned the fact that people who you're going to be prescribing a narcotic to are not the persons to use the drug because if they get into trouble, they're not going to give it to themselves. It's got to be somebody else.

We also have a population of people who live alone. Well, now what? Somebody lives alone. Maybe they are high risk. Maybe we all agree they're high risk. Well, what do you do? Co-prescribing in that situation is not going to make a hill of beans of difference because they're living alone and there's

nobody there to give it to them.

So again, we have to think about more innovative models in those kinds of settings beyond this co-prescribing thing. I think the co-prescribing is a tactic that will get us to a very, very tiny advance in reducing narcotic overdose deaths.

DR. BROWN: Dr. Hernandez-Diaz?

DR. HERNANDEZ-DIAZ: I think when we mention -- one thing that comes to mind is cost, and I'm not sure how cost will move up or down with an increasing demand. It might go down. But leaving cost aside for a second, we discussed that to saturate the populations that most need to have naloxone available, we may need 25 to 30 million doses per year.

I was wondering if increasing the demand through the co-prescription might, at least short term, deplete the resources and maybe actually be negative to saturate the demand where it is most needed through this and is probably not the most efficient way to get it to the market. I don't know

if that's a concern, at least short term, for the production of enough doses to saturate the market as we want it to.

DR. BROWN: Dr. Amirshahi?

DR. AMIRSHAHI: I actually was going to bring up that point. One of the things that we've talked about today that's been a common theme is really saturating and flooding the market, which I think is a great idea to improve access.

However, one of the things I think that we really need to consider is the fact that we may not be able to do so. If you look at prescription drug shortage trends in the past decade or so, you'll find that naloxone has been impacted by multiple, multiple long-term shortages during the course of the past two decades.

That being said, when we're thinking about implementing these strategies, we have to think about how we are going to have capacity to saturate the market. We know that there's not a lot of redundancy in a lot of pharmaceutical productions, and we know that generic injectable drugs are disproportionately

impacted by drug shortages.

I think a lot of these ideas that we've thrown around today and the past couple of days have really been great for improving naloxone access. We have to think about how we're going do that with regard to manufacturing capacity, and that's something that we're going to have to engage industry in as well as the FDA.

DR. BROWN: Dr. Dasgupta?

DR. DASGUPTA: In 2018, we can't have a conversation about drugs in America without addressing race, and what we have seen in the slides that Eliza presented, the faces there, and the data that have been presented in the community programs is that the community programs are serving a large minority community.

We also know, as been well established, that minorities in the healthcare system, when they have the same pain conditions, are less likely to get opioid treatment. So what we need is parity in naloxone as well.

Right now, we have two products that are

being considered for co-prescribing, which have specific label language that enables community use. The liquid injectable used in the community programs does not because it's an evolving labeling thing.

If we don't have parity in the labels between these formulations, we are perpetuating a form of institutionalized racism. I think an action that can be taken immediately, and I think FDA has the authority to initiate it, is to update the injectable label to include, specifically and explicitly, that community-based distribution is allowed.

DR. BROWN: I'm sorry. What was the -- community distribution is?

DR. DASGUPTA: Is an allowed use of that medication, the same as the wording in the two branded labels.

DR. BROWN: Dr. Bateman?

DR. BATEMAN: I guess I want to speak out or speak against the notion of universal co-prescribing, in addition to the economic consequences that we've talked about and some of the supply issues and the way that practice may redirect supply away from the

community-based programs that really need the medication most. I'm also a little bit concerned about the alarm fatigue that might along with that type of a recommendation.

I remember as an intern writing medications, and every other medication you'd write into the EMR, there'd be a popup that warned about a drug-drug interaction, or about an adverse effect of a drug.

Just clicking through those, I think if every time you're prescribed an opioid, there was a recommendation that popped up to co-prescribe naloxone, and you're writing a prescription for low-dose oxycodone for a short supply to a patient who had some type of an injury, very quickly you would start to ignore that recommendation and perhaps not think about prescribing naloxone when you had a patient who really was at risk, who was on high doses and co-prescribed benzodiazepines.

I think if we're going to think about co-prescribing, it really should be targeted to those who are going to benefit from it the most.

DR. BROWN: Dr. Ballou?

DR. BALLOU: Yes. I just wanted to echo some of the comments that have already been made, certainly with Ms. Numann in talking about how language matters with patients, as well as Dr. Besco and Dr. Meisel about OTC status.

I think the hope is that -- I'm speaking as a pharmacist -- when you all co-prescribe, the hope is that it then is co-dispensed; as our debate yesterday, whether it's 10 percent of prescriptions that eventually get dispensed, or 70, or somewhere in between.

Just thinking about recent drugs that have come to the market such as the Shingrix, the new shingle vaccine, for example, became a huge shortage because it was marketed out to the public drastically.

Now the pharmacies can't get it and can't give it, cannot provide the second dose for those who got a first or even a first for those who have none; just thinking about things like that and if then the naloxone products are no longer available, and the level of trust that a patient has in their pharmacist

to provide them with the drugs that they need, particularly with something that is lifesaving, and that not being available for patients, if we do flood the market in this way, in this co-prescribing model.

Additionally, a second point -- and not to be bashing any particular industry, if you will -- we are in a period now of time where insurance often dictates healthcare instead of the healthcare providers. I worry about co-pays being a barrier. We've talked about cost a lot; prior authorizations being a barrier as well for our patients. And those are things that I think FDA can regulate to help prevent those issues of -- again, increasing access through these means of going through the healthcare system that we've discussed are important as well.

I just wanted to raise those two points related to shortages that has been already mentioned, as well as insurance and cost access issues as well.

DR. BROWN: Dr. Macher?

DR. MACHER: I just want to briefly echo some of the comments made by Drs. Hernandez-Diaz and Amirshahi [indiscernible].

First, I think at least in the short run, any solution that provides naloxone to all patients is a theoretical ideal. Instead, we need to look at feasible alternatives, at least in the short run. There's simply not going to be the supply there that you'll need in order to do a blanket coverage.

The discussion of that, if this is a public crisis, is going to require that you put the right amount to those patient populations that are at the most high-risk. And it seems, as far as I've seen, evidence-based policymaking has some data out there with which we know what high-risk populations are, whether they're concurrently prescribed opioids, whether they're engagement pain management, if they have a history of substance abuse disorders, if they have mental health disorder, if they have some other medical issues. So there's a lot of data out there with which FDA can make these hard and fast choices.

Finally, any change to that is going to take some time. The industry has indicated, yes, they're going to double capacity, triple capacity, but that takes time. Narcan has indicated it's doubling

capacity in 2019 and up to 10 million or 20 million devices in 2020. Generics, facilitated by the FDA, will take time. Any procurement of large purchases by the government will take time. Any effort by FDA to promote OTC will take time.

Right now in the short run, I think the best solution and the only solution is targeted prescribing for individuals that are high risk. Then hopefully, through the competitive forces if we believe in markets, which I certainly do, the market will work its way, and more generics will find themselves -- more individual companies will put forth an effort to increase the supply into this industry.

If we don't, I think, realize the short run implications of non-targeting, we run a dangerous precedent.

To Dr. Hernandez-Diaz, I would agree completely with what she said about the drugs going to the wrong individuals, and therefore not allowing what I think is a great approach, community-based approaches, to do their heroic jobs.

DR. BROWN: I think one of the most important burdens that we've heard about is capacity, and I cannot imagine a model where the current capacity would take care of the saturation model that we have heard is successful in saving the number of Americans that we have.

The saturation model that we have now is that we're being saturated with fentanyl and white and black tar heroin from Mexico, and we have not demonstrated any capacity whatsoever to reduce that. We must figure out another way to rapidly increase the capacity to produce naloxone. I simply do not believe that industry has that -- although that is the American model, that they have the wherewithal to do that. There must be some other way to do this.

Someone mentioned the childhood vaccine model this morning, and I think that that has to be invoked on an emergency basis to get us enough product to attenuate the number of deaths that we're having.

Ms. Robotti?

MS. ROBOTTI: Hi. Suzanne Robotti. On the concept of getting naloxone into every medicine

cabinet, we've been told several times that there are no bad side effects to naloxone and that it can be used safely by anybody at any time. But when I go into websites and look to see what are the side effects of naloxone, there are side effects, and some can be significant.

I get concerned if we put it in every cabinet like ipecac, you can't overdose on that because it makes you puke, but this you could. What happens if a child in a home finds it and uses it? What if an anxious bystander gives 3 doses when 1 would have been fine? All I heard earlier was that's not going to happen or it wouldn't cause any problems, but somehow I feel it would.

Also, to remember the vast majority of people using opioids never overdose, never come near it. So co-prescribing would create a huge amount of wasted naloxone and increase costs. I push for require the offer of naloxone in an opt-in kind of program, but definitely no co-prescribing requirement.

DR. BROWN: Dr. Krebs?

DR. KREBS: Just going back to barriers, I

previously said it seemed like from what we heard that the hypothetical benefits of co-prescribing are mostly about the education that is received. So I think the relevant barriers there are really the time of the prescriber.

As was mentioned, primary care has a lot to do, and there aren't enough of us. I don't think there are enough pharmacists to automatically take over for all those challenges, either. Ultimately, primary care prescribes probably more than 90 percent of the opioids, so would be responsible for 90 percent of these co-prescriptions.

We currently have a situation where many policymakers think the main answer to any problem with opioid safety is make another requirement for the prescriber. So if I prescribe opioids, I'm required to check the PMP, get a urine drug screen, get consent, or have my patients sign an agreement. I have multiple documentation requirements.

The average primary care visit is 18 minutes, so when is that happening? Did I assess the pain? How did I do that also in that time? Now what we've

heard about how long it takes to do the naloxone education, everyone has said 8 to 10 minutes, so where's that coming from?

Also, aren't I supposed to be assessing whether my patient has depression, drug use, is feeling suicidal, has intimate partner violence, might be at risk of cardiovascular disease, is overweight? When are these things happening?

We're going to have this targeting occurring in primary care. We have a resource issue there, too. I agree, universal is not practical, but if we're targeting, are we relying on primary care to do a risk assessment, whether it's a computerized risk assessment, or a psychosocial history, or any of those things, again, it's yet another thing, yet another barrier.

Like I said before, people who know they're at risk, probably those are the people who could most benefit from naloxone. So let's let self-selection be what targets the naloxone.

DR. BROWN: Dr. Besco?

DR. BESCO: Kelly Besco. Just revisiting the

theme of drug shortages, even if we could increase the capacity of our manufacturers to make enough naloxone to saturate our entire country, it will go on shortage eventually.

Just one thought I have is we have a chemical cache of antibiotics, vaccines, antidotes, other antiviral medications. If this is a big enough crisis and we need to keep naloxone in the pipeline, should we consider a national cache of naloxone for instances where we do have an overwhelming depletion of supply? Just one thought.

DR. BROWN: Dr. Gerhard?

DR. GERHARD: First, a brief comment about the co-prescribing in general. I think as I said before, I believe it's an extremely inefficient way to get naloxone in the community. It probably targets exactly opposite to the way you'd want to target it. It would be distributed to people with the best insurance that probably would be at lowest risk for actual witnessing an overdose or experiencing an overdose.

So I think it's an extremely inefficient way

that at the same time really would just generate a windfall to industry because prices wouldn't be affected in any meaningful way, maybe over a really longer time frames, but certainly not in the immediate future.

Again, I believe we need a different level of response to a public health crisis. That means not relying on market forces and slow change in adaptation strategies to slowly increase production capacity. It would mean some kind of coordinated government intervention to secure access. And obviously, it can't be done immediately but on a shorter time frame to assure the needed supply in naloxone.

If there were something like an anthrax outbreak, nobody would suggest that we should let market forces address this issue and find a cure or find capacity to produce vaccines in time. It just wouldn't occur to everybody. So I think here we need to recognize what we're facing and what the appropriate response is. I don't think the normal channels are appropriate for that response.

DR. BROWN: Dr. Pisarik?

DR. PISARIK: Paul Pisarik. I have a question for the FDA. Somebody else mentioned this, is that we have two issues here. We have an issue of illegal substances being overdosed on and legal substances being overdosed on.

My question is, there's obviously a crisis in the illegal substances being overdosed on. What about the legal substances? Is there a temporal trend that's showing us that that's also increasing a lot or a little bit?

DR. STAFFA: This is Judy Staffa, and I think some of Dr. Faul's comments address this. I think from the latest data from CDC, we are still slightly increasing with regard to prescription opioid deaths, but the challenging part is that people who die from overdoses often don't die from one substance. There's often multiple substances involved in deaths.

So I'm not sure that we can cleanly separate it out that easily. I think we have to look at it overall in terms of opioids in general because oftentimes, both may be onboard.

DR. PISARIK: Then another comment, if we co-prescribe with narcotics, unless the cost of the naloxone is reasonable, it's going to be really expensive, number one. Number two, we have no idea what the efficacy is of co-prescribing naloxone with prescribed opioids.

What is the cost effectiveness per life saved if we do this? I don't know if we have any data on that at all.

DR. STAFFA: This is Judy Staffa again. I think when we went to the literature and found what was there, we've tried to invite a lot of our guest speakers to be talking about all the different ways to get naloxone out there and what's known. So what you've seen and what was in our background packet is what we know. And I agree with you; we haven't seen a lot of data to say how effective it is. It doesn't mean it isn't effective. We just haven't seen data.

DR. PISARIK: I'm just concerned about the cost. One of the downstream side effects of co-prescribing naloxone along with opioids, however it's done, is that healthcare costs are going to go

up. And then employers can't afford insurance; employees can't afford it. So the downstream side is that more people might be hurt overall if naloxone is co-prescribed with narcotics than would be helped by having lives saved by naloxone being co-prescribed.

DR. BROWN: Dr. Hernandez-Diaz, and this is going to be our last comment for this section.

DR. HERNANDEZ-DIAZ: Very briefly just to highlight that when we say prescription opioid overdoses, I think that the data included opioids that are given by prescription. That doesn't mean that they were used by the person that was given the prescription for the pain, but could happen in the context of a party and young people having opioids, and one of them dying of an overdose. That would be counted as prescription opioid, but it wasn't in the context of a prescription for the pain.

DR. BROWN: Number 2 is discuss how these burdens and barriers associated with co-prescribing and how these burdens may affect the implementation of co-prescription, and this is what I think I've heard.

The major burden to co-prescribing is cost. That includes cost to the patient certainly but also the healthcare system and secondary costs. Secondary burdens are also failure to address the larger public health issue of increasing illicit opioid deaths and the stigma of revealing a need for naloxone to a healthcare provider.

If we try to target a high-risk population, that is a problem because we don't know what is high risk. We have not identified what a high-risk population is and what it is not. We may need to develop a separate situational targeting model. Offering naloxone rather than co-prescribing naloxone may be more important.

Shortages are a problem. We will need to expand capacity dramatically to meet the needs of any expansion in the distribution of naloxone.

How can the FDA affect capacity? What happens when we need influenza vaccine? This will likely not be something that industry will be able to keep up with and will require the intervention of the federal government, FDA, and other aspects of HHS.

Any other comments?

DR. DASGUPTA: And the parity between the branded and the generic -- I'm sorry.

DR. BROWN: I'm sorry?

DR. DASGUPTA: This is Dr. Dasgupta. The parity between the branded and the generic in terms of community use.

DR. BROWN: I will include that.

DR. DASGUPTA: Thank you.

DR. BROWN: Let's go on to discussion question number 3, which I'll read through. Because of the significant costs for patients and the healthcare system associated with increasing naloxone availability, prioritization of strategies will likely be needed.

Discuss in terms of available data on effectiveness and cost. Which, if any, of the following approaches may be beneficial for public health? A, relying on alternative approaches for increasing naloxone availability such as community-based distribution programs or statewide standing orders; or B, limiting co-prescribing or

targeted prescribing to certain populations that may potentially benefit the most from having naloxone available such as those at highest risk for overdose or death due to overdose. If so, identify these populations along with the evidence supporting this benefit.

Anybody? Dr. Ciccarone?

DR. CICCARONE: Dan Ciccarone, UCSF. Not to repeat all of what I said earlier, the fentanyl epidemic is the gamechanger here. It's increasingly illicit. It's increasingly street-based. It's increasingly an overdose problem among non-patients. Therefore, community-based programs are the current best solution, the most evidence-based, and the most cost-effective solution. We need a saturation model, we need generics, we need over the counter for that.

If we decide to move forward with co-prescribing, the best evidence is for high-risk populations. That would include people with known substance use disorders. I would suggest that the best single population to target would be folks who have been brought into clinic, emergency room,

hospital situations who have had an overdose.

Anyone with a history of an opioid-like overdose should be co-prescribed, and that would include someone who is a patient on chronic pain who has overdosed on their meds. People with comorbidities, that would include other illnesses that put them at risk for CMS or respiratory problems, and also, comorbid prescriptions including benzodiazepines. That way, we can be more cost effective with the co-prescribing because this is the population that's at the highest risk within the clinic.

DR. BROWN: Dr. Zacharoff?

DR. ZACHAROFF: Kevin Zacharoff. I briefly mentioned this before, and this is in line with thinking outside the box, innovative kinds of solutions with the idea of controlling cost. Maybe there's an AED model, which can be utilized. Maybe having a naloxone that's available to be administered, available to a thousand people is wiser than giving a thousand naloxones to a thousand people.

When AEDs first became popular, they were pretty darn expensive, and they were very difficult to get. Living in a community at that time where we had our own little police force, we had to as a community chip in to buy AEDs so all the law enforcement officials in our community could have one if they needed one. So just a thought; maybe that's an outside-the-box kind of thing that kind of tempers it.

There's no question that what Dr. Dasgupta mentioned, I couldn't agree more. The least expensive way to deliver the medication that we saw presented to us multiple times definitely seems like something we really need to consider.

Then maybe lastly, maybe there's some kind of situation where we could have people who don't have third-party insurance or government-supplied insurance to get vouchers.

Dr. Green isn't with us anymore. I've done a lot of work with her over the years, and she's done a lot of work with the homeless patient population. And homeless patients are not likely to be able to go

into a pharmacy and buy anything off the shelf, over the counter, et cetera, et cetera. But maybe giving them a voucher where they could go in, no questions asked, and get a naloxone is something that could be done.

Those are just some ideas that I've been thinking about over the course of these two days that are maybe a little bit of a way to temper the cost because certainly if there's 134 million prescriptions written or 200 million prescriptions for an opioid written every year in this country, there's no way we're going to supply those kinds of naloxones to people. Thank you.

DR. BROWN: Dr. Bateman?

DR. BATEMAN: I think while I agree that the greatest gains are to be obtained in the population that's using fentanyl, that's using heroin, that's using opioids illicitly, there is a robust body of epidemiologic literature identifying risk factors for overdose amongst those that are dispensed prescription opioids, so higher than 50 milligrams of morphine equivalent, co-prescribed benzodiazepines,

having psychiatric disorders, having history of overdose.

These are patients who are interacting with physicians who are able to identify those risk factors, so recommending co-prescribing in those circumstances, really targeted co-prescribing for patients that have quite a high absolute risk of overdose, makes a whole lot of sense to me, and I think would be cost effective.

DR. BROWN: Steve? Dr. Meisel?

DR. MEISEL: Steve Meisel. It just occurred to me as Dr. Bateman was speaking, the system that we heard -- I can't remember their name -- that presented this online modeling of risk factors, that may or may not be a perfect model. But if one could build that into the electronic health record and as you're prescribing, you're told that this is a high-risk patient, that might ease some of that decision-making and make it more standardized.

That might be something to consider, whether it's from that vendor, or independently, or whatever, that's something that could overcome a barrier for

identification that's front and center.

Another caution I would have about the AED approach, I was thinking about that as well, I think we ought to be thinking real hard about doing something like that. There's an AED over here at the front desk in this building. Took a while to find it, but there is one here. But the likelihood of somebody OD'ing on narcotics here in the Great Room is pretty slim. They're more likely to overdose in their apartment, or under the bridge, or someplace like that where access to an AED is pretty limited.

The location, at least for the illicit overdoses, is unlikely to be in places where AEDs are located, and the accidental overdoses, they're probably also not going to happen at the airport. They're probably still going to be at home and places like that where AEDs aren't. But I think it's a model that we ought to be thinking about pursuing to see what can come of that, but I worry that it may be one of those false hopes.

DR. BROWN: Oh my, who else would like to speak? Dr. Garcia-Bunuel?

DR. GARCIA-BUNUEL: I know Dr. Hertz warned us about not coming up with simple solutions, and I completely agree. These are very, very complex situations. But having said that, I'm still caught by Dr. Dasgupta's comment about does the FDA have the ability to clarify labeling language for generics that could help us. Though maybe simple in its construct and clearly not the end-all, but is that something as an committee and obviously the partnership with the agency that we could support in order to then help and leverage that?

Once again, seeing examples of how other organizations, other communities could potentially benefit from that, there might be a multiplier there, understanding that there could be either lack of supply, depending on how industry responds to that, if that would be something that would be potentially be a gamechanger. But I'd still like to put that on the table as a simple solution for our very complex problem.

DR. BROWN: Dr. Ciccarone?

DR. CICCARONE: Dan Ciccarone, UCSF. I just

want to agree with this notion on parity of labeling to allow the much lower cost injectable to have the same label as the fancier intranasal products.

I also want to remind us, we've heard several times the Surgeon General Jerome Adams telling us that naloxone is one of our top ways of addressing the overdose crisis in America. He suggests greater access, much greater access, which would include family, friends, neighbors, his language, of folks who are using opioids and illicit opioids.

In order to get that, it's an over-the-counter product. In order for the family members -- family members are not going to go to the doctor and say, "You know, my nephew has" -- those conversations aren't happening. Maybe they would talk to the pharmacist and get it; ideally, over the counter.

Community-based programs, if the over-the-counter product is cheap enough, will be able to access it at a better price point. Australia and Canada have both moved to over-the-counter naloxone. If they can do it, we can do it.

The FDA commissioner can initiate the over-the-counter switch for naloxone. They have the authority to exempt drugs from the Rx requirements for the protection of public health. We're in a public health crisis, and we can move forward on this.

DR. BROWN: Dr. Shoben?

DR. SHOBEN: I'm just re-reading the question here, and I'm struck by the discussion in terms of available data on effectiveness and cost. We don't really have great data in order to compare these different approaches.

As a statistician, I really wish you could have better data, and I don't think that necessarily precludes making decisions, but we don't really have the data on how effective are some of these community-based programs. We have a lot of anecdotes and some suggestions that they really work. I'm not trying to argue that they don't work. I just don't think that we necessarily know is this community-based program more effective than co-prescribing would be.

I think we can speculate, and there are certainly very smart people who have speculated, but we don't really have the data in order to answer the question in terms of available data on effectiveness and cost.

DR. BROWN: Dr. Krebs?

DR. KREBS: Just a comment on that, the real outcome we really want to hear about is mortality, but there is this interim outcome, which is naloxone being administered. What I heard is that when you prescribe it to patients, it doesn't get administered. It just sits there in somebody's medicine cabinet. That seemed to be the case, whereas these community organizations are clearly getting the drug administered. It's not the perfect outcome, but it is an outcome.

DR. BROWN: If we are thinking about how we could do an expansion of naloxone in a cost-effective way, I think that Dr. Ciccarone is moving in the direction that I would move in suggesting that the commissioner of the FDA likely at this point has the capacity to move OTC naloxone ahead much more rapidly

than it has been moved ahead in the past.

We've been talking about moving to OTC naloxone for about at least 2011. I think it's time to do that. And what I fear is that moving OTC ahead will be done in the same way that every other drug is considered within the FDA, and this is an emergency. So I'm not certain that that's really something that needs to happen right now.

The second thing I would say is that the United States, I believe through the FDA, carries a strategic drug pharmacopeia, which allows for emergencies. I'm not certain of all the drugs that are in there. I believe morphine is in there, maybe Cipro, but if naloxone is not in there, it should be.

If it was and if the federal government was purchasing naloxone at scale, then the cost could be lowered, or they could use the U.S. code that was suggested this morning, 28 Code 1498, to take the patent and negotiate a lower cost. Those drugs could be distributed at a lower cost to the community programs.

Yes, ma'am?

DR. MAHONEY: This is Karen Mahoney, nonprescription. I'd just like to address the idea that the FDA process for a nonprescription form of naloxone would go along at the same pace as the development progress for other types of drugs. So that's not the case. That's not what's happening now. We're doing everything we can.

Because we have performed the label comprehension study, the development program for a nonprescription form of naloxone would be much shorter, and also, when an application is submitted, it will be considered very quickly. I just want to clarify that point.

Separately, I just want to clarify one thing that's a bit unrelated, but there's been talk of an ipecac model. The idea would probably still be the same, but I just want to clarify that the American Academy of Pediatrics and poison control centers recommend against stocking ipecac in your medicine cabinets and against using it immediately in the case of a poisoning. I just didn't want that to get out there that ipecac is recommended all the time.

DR. BROWN: Thank you. I know you're doing everything that you possibly can to move this forward in the usual way. I think that what we're saying is that this is a highly unusual time in the history of the United States and that we may have to move beyond the routine management of this. But I'm not in any way suggesting that individuals within the agency are not doing everything they can to solve this problem.

DR. MAHONEY: I'm in complete agreement that we want to move as quickly as we can, and I just want to clarify that nothing is off the table in terms of trying to use whatever authorities we have.

DR. BROWN: Thank you. Dr. Dasgupta.

DR. DASGUPTA: I'll keep it brief. I think having an impact assessment is going to be critical before we make any large-scale policy recommendation that would introduce a very large new player into a small market that's dependent on controlled substances as a precursor to make naloxone.

What had happened during the shortages that were alluded to with naloxone over the last decade, when there were other shortages, the big

institutional purchasers like health systems, VA, and other places, were able to find their suppliers to get more naloxone. But it was the community programs that had the least clout, were the smallest buyers, and were the ones who were squeezed the most. And people died during those shortages because the smaller programs could not have access to naloxone.

If we make any sort of recommendation that causes a perturbation to the market, I think there needs to be a formal impact assessment that includes all of the community-based programs to understand what could happen to their supply, and that needs to be an ongoing process throughout any rollout to continue bringing them into the table. Because if we do anything to impact their availability of naloxone, then we are doing more harm than good.

DR. BROWN: Point well taken.

Thus far, we have spoken to a lot of different ways for getting naloxone into the environs. Folks have spoken about identifying high-risk populations as a possibility that would reduce the amount of naloxone that was required, but

we've heard also evidence that identifying the population is very difficult.

We've heard about using the AED model to distribute naloxone geographically rather than distributing it to individuals. We've heard about the use of voucher programs for patients or subjects that don't have any fixed address, and then we mentioned bulk buying of supplies of IV naloxone cheaply from major distributors by the federal government, either using the U.S. code to expand capacity or not.

We also talked about moving the agency to increase the likelihood that OTC naloxone would have an availability in the shortest possible time, keeping in mind that if we change the market, that we have to be concerned about who is getting the naloxone that they need. We need to examine what the possibilities are prior to the time that we make major moves.

Is this a reasonable time to take a break? Why don't we take a break for about 15 minutes and come back and begin to talk about question number 4.

We'll meet back here at about 20 till.

(Whereupon, at 2:22 p.m., a recess was taken.)

DR. BROWN: We can re-gather and begin our discussion of question number 4. I'm going to read the question. Discuss any potential unintended consequences that should be considered if naloxone is co-prescribed to all or some patients prescribed opioids and what steps can be taken to mitigate them.

Is that a reasonable question that everyone can understand and respond to?

DR. HERTZ: Hi. This is Sharon. I just want to say I don't want to quell discussion, but I think we definitely covered some of this, so there can be reference back as well.

DR. BROWN: Dr. Besco?

DR. BESCO: Kelly Besco. One thing I don't think we've touched on in terms of consequences is what the impact of community access to naloxone means from an inpatient acute care setting.

I'm from Ohio where, quite frankly, we no longer have an epidemic, but we have an opioid

plague. I'm well aware of stories that happen in our hospitals where patients bring in their illicit substances and unfortunately overdose in the hospital and need to be rescued.

Now that we have standing-order programs in Ohio, we've had reports of patients' visitors coming in, engaging in use of illicit substances with the patient and the visitor, and then the visitor reversing a patient's opioid-induced respiratory depression with their own supply of naloxone. Then that goes unreported to the acute care team.

While I don't have a good mitigation strategy for this other than potentially developing some screening protocols for visitors -- but then again, acute care facilities are very sensitive to patients' rights, ethics, and patient satisfaction scores -- that may be something agencies need to consider as well as increased access permeates across the country.

DR. BROWN: Dr. Krebs?

DR. KREBS: This is a clarification personally, a comment. The question is about

naloxone co-prescribing, and clearly, naloxone is currently labeled that it can be prescribed to anyone who might be at risk.

So it's not about the naloxone label. I think the question here is about whether the opioid label ought to be changed to encourage co-prescribing.

This question, is it about potential unintended consequences of naloxone prescribing, or is it about unintended consequences of labeling opioids to recommend naloxone co-prescribing?

DR. HERTZ: What we're trying to ask is if the labeling on opioids was changed to recommend co-prescribing to all or some, what are the unintended consequences there?

DR. KREBS: Excellent. So that's what I'll address is the labeling of opioids. I already co-prescribe naloxone sometimes, but that's an on-label prescription decision for naloxone. This is about opioids.

I think if this is part of the opioid label, an unintended consequence is that becomes the

standard of care that all of us primary care docs are supposed to uphold. And if it's based on risk, again, that requirement that we're assessing risk, we're assessing risk accurately, and that we're going to be held to some sort of standard of prescribing it, I think that could be a problem in all the ways we've already talked about.

DR. BROWN: Dr. Meisel?

DR. MEISEL: Steve Meisel. This is an unintended consequence or risk or whatever regardless of whether it's co-prescribed or the community-based distribution or over-the-counter. And I think the agency and all of us probably need to be prepared with our response to this because just like there is a segment of the populace that says that we should not be distributing birth control in high school because it's going to encourage sex, or HPV vaccine because it's going to encourage unprotected sex, that sort of thing, there will be people that will say don't give out or make readily available antidotes to narcotics because that will just encourage the use of illicit drugs.

Now, I don't personally believe that model. I think we ought to be making this available, but I believe that there's going to be a significant segment of the political establishment and others who will take that position and lobby in that space. I think we need to be prepared and the agency needs to be prepared to address those kinds of questions head on.

DR. BROWN: Dr. Amirshahi?

DR. AMIRSHAHI: I just actually have two brief comments. Number one, as an emergency physician, I administer naloxone very regularly, and I have seen firsthand the effects of precipitated withdrawal. Not to discourage people from administering naloxone, definitely not, but at the same time, I think that we need to address this and maybe provide some education for bystanders that patients may, in fact, become violent; just something to consider for bystander safety.

The second comment I had relates to medication shortages once again. We know from prior history with regard to medication shortages that when

you do have a drug shortage, what can happen is you develop a gray market, which drives costs up. So one of the unintended consequences could potentially be that this drives up the cost of naloxone, which could particularly impact the community programs, so just one other thing to be mindful of. Thank you.

DR. BROWN: Anyone else?

(No response.)

DR. BROWN: This is what I have. The unintended consequences of co-prescribing for all include the cost to the healthcare system and the effect that could have on prescribing. This cost could affect the cost of other drugs as capacity is transferred to naloxone.

The standard of care could be changed by changing the labeling, increasing the liability risk to clinicians. Some will take the position that co-prescribing extends the risk of addiction to a larger population. In addition, we heard that we may need to educate the population about the acute effects of opioid withdrawal from the administration of naloxone.

Can we move to our vote question, number 5? I'm going to read the question.

Would labeling language that recommends co-prescription of naloxone, for all or some patients prescribed opioids or more targeted prescribing for patients otherwise at high risk for death from opioid overdose, be an effective method for expanding access to naloxone and improving public health? If so, which populations do you believe should be included in such labeling?

Is that clear? Dr. Zacharoff?

DR. ZACHAROFF: Hi. Kevin Zacharoff. Just a clarification of the question, so when we get to the vote part, I know exactly what I'm voting for.

If I believe that targeted prescribing could be beneficial for people other than the patient, meaning other members of the household, for example, if there's a high-risk member of the household, would that fall into this wording? Because it says "or more targeted for patients otherwise at high risk of death from an opioid overdose," which to me implies that I'm only thinking about patient-level risk, not

other risk.

DR. HERTZ: That's a good point. I think that if you think that co-prescribing with that in mind would be good and you want to vote yes, then in the A discussion part, you can clarify that.

DR. ZACHAROFF: Thank you.

DR. KREBS: The opioid label, not the naloxone label.

DR. HERTZ: Yes, labeling for the opioid label about co-prescribing naloxone with that opioid.

DR. BROWN: Dr. Macher?

DR. MACHER: I guess another point of clarification for Dr. Hertz. This is one label, not two different labels targeted to two different populations.

DR. HERTZ: This would be language that we would include in opioid analgesics. It would go in the package insert, and then possibly/probably, the medication guide, which is considered patient labeling, and then there would be a ripple of other documents where it would be mentioned.

DR. BROWN: Discussion? Questions?

Dr. Krebs? No, you have to ask a question.

(Laughter.)

DR. BROWN: Yes, ma'am?

DR. SHOBEN: You're talking about this like in general, so in some time in the relatively near-term future? Are you talking about doing this right away? Does that make sense as a question?

DR. HERTZ: I don't know how to exactly answer that. I think that if you feel differently based on timing but ultimately at some point, it should be you would recommend that we do that, you could vote yes and then explain it. Or if you think other things need to be in place before you could consider it, you could vote no and then explain it.

I say, in general, vote if you want something about this done, and then you can put qualifications or explanations in the after part.

DR. BROWN: Everyone that votes around the table will have the opportunity to explain their vote after all the votes are in. Dr. Ballou?

DR. BALLOU: I think that there's just a lot of pieces to this question, so it's hard to say yes

or no, because if you say yes, are you saying yes to the whole thing? I realize we can clarify our response, but I think there are too many pieces to this one question for the answer to just be yes or no.

DR. HERTZ: Perhaps you can think about it as would labeling for co-prescription be a useful tool to expand access and improve public health? The assumption is connecting, I guess, the expanded access with improving public health. Sometimes if we don't put enough in the question, then it's too ambiguous, and sometimes, apparently we put too much in, and then it's -- so it's hard to balance sometimes.

DR. BROWN: Sharon, could you repeat that, what you just said? Because I think that makes things a lot more clear.

DR. HERTZ: The first part of the question is some form of co-prescribing language in opioid labels, then it's something you would recommend as a way to expand access and improve public health. And if there's somehow a yes in your mind to that

concept, no matter how extensive or limited, you can describe when we go around after the vote.

DR. CICCARONE: I have a radical idea. What if we continue the discussion before we voted? Because it seems like there's still -- what if we voted to see -- are people clear?

Do they have a clear answer in their head and they want to vote right now, or are they still fuzzy about it? Because I'm definitely going to say that I'm on the fuzzy side. I have to choose black or white, yes or no, and then explain myself later.

DR. HERTZ: If you want to ask questions to your peers here at the committee or want to engage in conversation -- I got to ask the big boss. Yes, that's okay. So feel free to -- don't preview your vote. Keep your vote close to the chest, or vest, but if you want to discuss the issues to help you decide how you want to vote, that's okay.

DR. BROWN: Dr. Garcia-Bunuel?

DR. GARCIA-BUNUEL: Martin Garcia-Bunuel. A comment and maybe a question related to how we all get to a point to make an answer. But on another

topic, the question of language and the language we use to communicate with patients has come up I think as a significant point in these discussions, whether it's communication between the healthcare provider and their patient or how that information is shared in a variety of settings.

One comment I have about where we are now -- what matters to me, a bit, is the labeling language because I think that's where we start to think about its potential implications, downstream effects, what's the message.

What I've heard and what I've gleaned over the last couple days, and many important and significant things, is I have picked up on some themes around the whole idea of engaging patients, engaging family, engaging friends, engaging the community around risk; namely, as we discussed, the risk of overdose and death and how co-prescription and/or supplying naloxone may very well have a significant benefit to decrease the risk of death from overdose.

How that would be stated in a label of an

opioid and how that's framed actually I think is a significant part of this.

DR. HERTZ: If you have thoughts on the messaging that you think would accomplish a yes vote, meaning if you think that there could be a positive impact, based on specific language, I would consider that a yes with an explanation.

DR. GARCIA-BUNUEL: Right.

DR. HERTZ: Unless you feel really strongly that it's a no with a small exception.

DR. GARCIA-BUNUEL: Right, yes.

DR. HERTZ: These things can go either way. If the labeling tool -- that's our primary source of communication, is our labeling. That's how we get the word out, and we can work off of that.

If you think there's a role for us to put information in opioid labels about co-prescription of naloxone, you can tell us exactly what you want us to say. You can share any of that as well after the vote.

DR. GARCIA-BUNUEL: In our comments?

DR. HERTZ: Yes.

DR. GARCIA-BUNUEL: So I'm not trying to couch this. I'm trying to maybe get a little bit farther into it because I do think those words and how it's framed could -- and I say that because the struggle I'm having from the excellent opinions that we've heard from all around the table is -- and maybe being a primary care physician as well, it's the engagement, it's the discussion, it's the listening, it's the understanding the context of an individual, their family unit, their community unit, and how this is playing out around our country.

If there's a way -- and maybe this is a big reach for me, but if there's a way to use the label to help form or begin that conversation, I might find that quite helpful. Thank you.

DR. BROWN: Ms. Numann?

MS. NUMANN: Sabrina Numann, patient representative. I think I'm expanding on what they are saying. I don't feel like we've had much of a discussion on opioid labeling as much as we have on the crisis of naloxone distribution. I don't feel like I have enough information. I don't feel like I

have enough information to really even make a decision on this vote.

This is coming just as a patient representative. If we could get into a little bit more detail of what that actually means and that impact, I would feel much better with that decision. Thank you.

DR. HERTZ: Product labeling has defined sections, and it's a very clear format. We have the opportunity to put information that we think is useful. Then there's the part that's really intended for the prescriber, and then there's the part that's focused on patients, and opioid labels have both.

So if you think that the prescriber should be co-prescribing naloxone, for some reason -- if you think they should be co-prescribing naloxone to achieve what's in the question, and you think that for some reason, then you would vote. And we don't typically label here at the table because I'd need to keep you for a week.

So if you think the labeling needs to be improved with regards to risk communication but you

don't particularly favor co-prescription, then tell us that. Vote no about co-prescription. You don't think it's going to achieve the goals, but you would prefer this other communication element to be included.

That's why the actual language is not specific here because labeling takes us a really long time. This is really about should we include in the labeling something to tell prescribers to co-prescribe to achieve that goal.

Is that the tool that would be useful to help achieve that goal? And if that's not the tool, the co-prescribing, if there's something else you want to use the labeling for, that would be a no, but this is what we'd like you to add to the label.

MS. NUMANN: Thank you.

DR. BROWN: Dr. Meisel?

DR. MEISEL: Steve Meisel. I'm going to take a contrarian view. In this case, I usually have a lot of problems with the way the questions are worded and in the past have suggested the agency go to question writing 101 school. But in this case, I

think the question is perfect because as I unpack it --

(Laughter.)

DR. MEISEL: Well, I do. As I unpack this question, the first thing I want to ask myself is, okay, would co-prescribing expand access and improve public health? And if the answer to that is no, then I would vote no. And if the answer to that is yes, would labeling -- putting in the package insert some suggestions to the provider that either for a large population or a targeted population, that they do so, if the answer to that is yes, then I'd vote yes.

To me, it's a relatively simple question here. The first part that I unpack is do I believe in co-prescribing, that it's actually going to achieve an outcome here. And then if the answer to that is no -- but if I say yes, okay, well, then how do we get there and would labeling the product be an avenue to get there; or maybe I think that would be ineffective, so I would say no. It's a good goal, but labeling is not the way to get there. There are other mechanisms to get there.

So from my point of view, I think it's a relatively easy and simple question to answer.

DR. BROWN: Dr. Krebs?

DR. KREBS: I think we all have this belief that sometimes physicians should co-prescribe naloxone, and I suspect everyone agrees that that's sometimes the case. Also, I think we probably all agree that most patients should know more about the risk of opioid poisoning, meaning inadvertent sedation or respiratory depression.

Being both in VA and in primary care and having been involved in the CDC guideline development process, I remain concerned about how things -- the most subtly worded things, the most carefully parsed recommendations to consider something, or potentially do something, or evaluate, as soon as they're out there, the world would like to turn it into a quality metric. Did it get done? Yes/No?

A label recommendation on a drug that recommends another drug with it is just such an easy yes/no. Did it get done or not? So I am just very concerned about how aggressively this will be

enforced on many levels and the unintended consequences we've all described for labeling language that recommends co-prescribing; so just separating that labeling language that recommends co-prescribing from the general concept of should we sometimes co-prescribe. I think that's a very important distinction here.

DR. BROWN: Dr. Ciccarone?

DR. CICCARONE: Thank you, Chair. Dan Ciccarone, UCSF. This is good. Thank you. I'm glad we're discussing more instead of moving right to a vote.

Thank you, Dr. Krebs. I think this notion of unintended consequences, which was raised earlier today, is very important. If I break up Dr. Meisel's simple question, which is now two questions, does one believe in co-prescription, I think there's some evidence that you can either accept or not accept about co-prescription.

But really what would be underlined here is the labeling language. And what I'd like to have more conversation about is does labeling move

practice. Does it change how prescribers move? Would it also -- if it does work, does it move them too far? Because I think there's also some concerns -- and I'd like to hear more conversation about this -- that if we got lots of co-prescribing to happen, that we might get shortages, and we might get other inadvertent effects.

So I'm still trying to stimulate that conversation. Thank you.

DR. MEISEL: If I can just respond to that, I think you've set up a model to answer the question. Because if you think that co-prescribing is good in some cases but you think that labeling, thereby proscribing it, has unintended consequences that offset the value, then you vote no.

DR. CICCARONE: [Inaudible - off mic].

DR. MEISEL: No. It's a no vote, because what the agency is asking is, should they put recommendations in the package insert for oxycodone that some people should be co-prescribed naloxone? That's what they're asking for. They need guidance from us as to whether they should put that, in one

language or another, into the package insert to push the envelope to prescribers, please prescribe more naloxone in some cases.

DR. BROWN: Dr. Bateman?

DR. BATEMAN: I'd say there are lots of ways the label could be written. It could be consideration should be given to co-prescribing in naloxone in circumstances where the patient's at heightened risk for overdose because of high milligrams of morphine equivalent co-prescription of benzodiazepines.

I don't think it has to be so cut and dry and necessarily have all of the effects that Dr. Krebs alluded to regarding performance metrics and the like.

DR. BROWN: Dr. Dasgupta?

DR. DASGUPTA: Are there previous examples of labels that have co-prescription that's mentioned, and if so, in which sections of the label would that be in?

DR. HERTZ: There's Leucovorin for methotrexate -- am I getting that right? -- but not

sure of an antidote to the primary action. That's more of avoiding unintended effects. I think that if there is, it's pretty rare, and we certainly can't come up with it very easily.

The labels do have a mention of naloxone or an antagonist in Section 10, which is overdose, which is different. This might go into a couple of sections of labeling. It's a big deal, so it would probably require some association with the risks, so the respiratory depression, the risk for overdose. And there could also be some instruction, possibly, which would be dosing and administration.

So it could potentially go somewhere like Section 5, warnings. It could go in Section 10, overdose, something additional. And it could go in Section 2, which is dosing and administration.

DR. DASGUPTA: Section 5 is also the REMS section, right?

DR. HERTZ: The REMS is listed in the Section 5 and in the box, and Section 17, which is information for patients, and the medication guide, which this also has, which is part of labeling,

although not the full prescribing information.

DR. DASGUPTA: So one avenue could be to put it in 17 as a patient communication thing, so it's not as much of a strong directive for co-prescribing as in higher in the label?

DR. HERTZ: No. Generally, it is in the label, and then it's the recommendation to convey that information from elsewhere to patients, so that's what listed in 17.

DR. DASGUPTA: Would you guys consider something like this to be an element to assure safe use? Would you want to go that direction, or would that create so much --

DR. HERTZ: We really didn't want to ask that question. Thank you for bringing that up. If you feel strongly enough about co-prescribing that you think it should be somehow part of a REMS, you can say that separately when we go around. Right now, we're really just talking about labeling.

DR. BROWN: Dr. Zacharoff?

DR. ZACHAROFF: My personal opinion is that in 2018, even in a primary care setting, based on all

of the different guidelines and recommendations I see from pretty much every regulatory agency and every association, that at least consideration of offering naloxone to patients needs to be considered in 2018 if an opioid is being prescribed for anything other than acute basis.

To me, we're only talking about when you're prescribing opioids. So if all the recommendations -- the Federation of State Medical Boards clearly defines inappropriate prescribing of an opioid, and they talk about the fact that if naloxone is not considered as part of that package, then that is considered inappropriate prescribing.

From my personal opinion, it's already standard of care, and if it's already standard of care, then it belongs in the label when these medications are prescribed. Thank you.

DR. BROWN: Dr. McCann?

DR. McCANN: I don't have anything.

DR. BROWN: Ms. Robotti?

MS. ROBOTTI: Hi. Suzanne Robotti. I guess this is more of a question. What I would like is a

label that didn't say naloxone should be prescribed. I would like a label that says a conversation should ensue with the patient about naloxone and opioid overdose possibilities.

My point is to encourage conversation, but mostly to increase the patient's self-awareness of being an opioid overdose risk, and for the patient to be brought into the consideration of what level that risk is.

So my question is, am I suggesting co-prescribing? I'm suggesting a conversation. Can one suggest a conversation on a label?

DR. HERTZ: It depends what conversation you're suggesting. If you think that it's important for the label to say engage in a conversation about shared decision-making concerning risks associated with opioids, possible opioid overdose, possible use of -- if that's what you would like, that's not recommending/requiring co-prescribing.

If you think we should be doing something specifically about co-prescribing, and if you don't but you still want to comment on the other, if you

don't want the label to have something to say about co-prescribing but you want that further engagement, you can certainly let us know that.

DR. BROWN: Are there any other comments or questions prior to the time that we take a vote on this very clear question?

(No response.)

DR. BROWN: If not, we'll be using an electronic voting system for this meeting. Once we begin the vote, the buttons will start flashing and will continue to flash even after you have entered your vote. Please press the button firmly that corresponds to your vote. If you're unsure of your vote or if you wish to change your vote, you may press the corresponding button until the vote is closed.

After everyone has completed their vote, the vote will be locked in. The vote will then be displayed on the screen. The DFO will read the vote from the screen into the record. Next, we will go around the room, and each individual who voted will state their name and vote into the record. You can

also state the reason why you voted as you did if you want to. We will continue in the same manner until all questions have been answered or discussed.

Now we can vote.

(Voting.)

LCDR SHEPHERD: For the record, the vote is 12 yes, 11 no, no abstain, zero no voting.

DR. BROWN: We are going start down at this end with Dr. Faul.

DR. FAUL: Mark Faul here. I voted yes because it's part of the CDC guideline. The guideline sets forth the risk populations and the MME. It was really not gray for me. It was pretty straightforward.

DR. BRAND: This is Paul Brand. I voted yes because the wording, as a couple people here reworded how it could appear, I think it opens a conversation with a patient. So I asked myself the question, will this improve the well-being and health of the public, and my answer to that was yes.

DR. BALLOU: This is Jordan Ballou. I voted yes because I tried to simplify the question as much

as possible. Would labeling language that recommends co-prescription, for at least some people, be an effective method for expanding access to naloxone and improving public health? I do believe that it would be one of many potential effective methods, and as many have discussed, that it would require at least a conversation to happen with the patient.

I would be in favor of language that not necessarily -- it does say "recommends," not "requires," so that's one thing to think about as well as an offer to co-prescribe, not necessarily co-prescription, but at least an offer, which again reiterates that need for the conversation.

DR. MACHER: This is Jeff Macher from Georgetown. I too took a similar approach to answering the question, would labeling language that recommends co-prescription of naloxone be an effective method for expanding access to naloxone and improving public health?

The caveat is I believe it should be targeted to those high-risk categories that we've discussed for the past day and a half, those that have

concurrent prescription of other opioids, pain management, history of substance abuse disorders, mental health, and any other medical issues.

I was also convinced by Dr. Zacharoff's point that it's already a standard of care. If it is, then I think the benefits far outweigh the harm.

DR. GARCIA-BUNUEL: Martin Garcia-Bunuel. I voted yes, and I came to the conclusion for a couple reasons. One, I thought of my clinical self, and actually thought of my clinical self years ago, trying to understand how we all evolve in terms of our knowledge, and how we take care of patients, and how do we respond to changes both in our patients' lives and what's going on around us.

I think the labeling, if done properly, will help create a conversation, standardize as a conversation, that protects patients who aren't getting this conversation. So it may help bend some behaviors and some interaction, even if the motivations may not be completely patient centered, but it might help some clinicians have that conversation.

I think this brings it one step closer to the center of the fold as we continue to confront a very complex situation. Thank you.

DR. PISARIK: Paul Pisarik. I'm going to be the first no. I voted no in this question. It's not to me that it wouldn't help, but part of the question that hit me was "be an effective method." I think it'd be a method. I don't know if it'd be an effective method for expanding access to naloxone.

The whole idea of improving public health, improving public health isn't so much one-on-one, it's more casting a huge net over everything, and then trying to get as many people into the net as possible. That's what public health means to me.

It would help some people for sure, but I don't think it'd be an effective method for improving public health. I think having some sort of public distribution program for naloxone the government might provide at a reduced cost for public health centers, for community health departments, that would be an effective method of expanding naloxone.

DR. KREBS: I voted no, and I've mentioned

some of the reasons. But importantly, I do think there's a great deal of difference between considering co-prescription, which is what the CDC guideline recommends, and labeling language that recommends co-prescription, which I think creates a standard of care that will be implemented in a way that could potentially undermine public health by directing resources away from the most effective approaches to expanding naloxone access while generating a great deal of cost, and potentially less time for consideration of other more effective strategies to improving the safety of opioid prescriptions in the primary care office.

DR. BROWN: Dr. Krebs, state your name.

DR. KREBS: Oh, sorry. That was Erin Krebs.

DR. CICCARONE: Dan Ciccarone, UCSF. I have to say this vote is the hardest decision I've made in a long time and I'm not one to be shy about decisions. I usually get it and go with it. And I didn't decide until my finger was about an inch away from the button. Perhaps I should have chosen abstain, really.

The positives, the reasons why I voted yes, 51 percent was the evidence presented by folks in San Francisco and Rhode Island, showing there's some evidence co-prescribing will have public health benefit. It enhances the conversation. There will be spillover effects to the community, including -- and I think this is probably the extra salt on one side of the balance scale -- increased pharmacy stocking. Pharmacies don't always stock. This will push that momentum. Most pharmacies will start stocking.

In public health, access is important. When you increase access, you have increased access, and you usually see a benefit. It's almost always a good thing.

Having said that, the ways in which it might not be a good thing were weighing on the other side of the scale. We have language questions that persist, how to label this but also what goes out to the community. It may compel the medical community to move too far, and then the idea of shortages come in.

As the pendulum is swinging, there is a little bit of opioid-phobia; maybe not a little bit, maybe a moderate amount of opioid-phobia going on there. Will prescribers overdo it? We see effects of people overdoing it in this epidemic because it is a crisis and there's a lot of fear.

Co-prescription can happen whether the FDA labels it or not. If it's a good idea, it can be promoted, CMEs and all that stuff. What we really need is to support our friends in the community who are doing great work over multiple years. We need OTC switch. We need federal stockpiling. We need parity in the injection versus intranasal labeling. We need generics. Thank you very much.

MS. NUMANN: Sabrina Numann, patient representative. I was splitting my vote kind of into two. Bear with me here.

I voted no, I think because there wasn't like a to-be-determined later type of vote. I feel like co-prescription does already exist out there, and I don't know if that necessarily addresses the crisis. I don't feel like I have enough information to say

yes.

On the second part regarding labeling, I would have abstained because I feel that I would worry there are additional barriers yet that I don't understand myself, i.e., standard of care.

As for A, had I voted yes, then I feel that the high-risk group would be where I would address this crisis. It does seem logical to at least start there. Also, I believe this discussion needs to continue. I just don't feel like a vote today really resolved much.

I ask that the FDA consider the excellent VA model, very impressive presentation' VOA; the Fiduscript ideas; educational media campaign for education, definitely an option there; and language to discussions to lower the stigma. Thank you very much.

MS. ROBOTTI: Hi. Suzanne Robotti. I voted no to co-prescription, but I do vote yes to a label that lists the profile of high-risk patients with a recommendation to discuss the risk of opioids, particularly when used with other respiratory

depressive drugs in order for the patient to understand and evaluate his/her own level of risk.

Somebody mentioned that naloxone should be offered by doctors and pharmacists all the time, much like would you like fries with that. That type of normalizing naloxone and maintaining awareness of ongoing risk and changing risk is exactly what I'm in favor of. I think it's also another good reason to move naloxone to OTC status.

DR. GOUDRA: Basavana Goudra. I voted yes. To make the decision, I went both by the published evidence that is out there and by whatever the discussion that happened between today and yesterday. I think there is no debate about the fact that this will benefit the method for expanding access.

In terms of improving public health, I'm not so sure about it, whether it will be the discussions surrounding, or education element, or availability of the actual drug. It doesn't matter what it is, I think it is going to help in resolving or addressing the crisis to some extent.

DR. BATEMAN: Brian Bateman. I voted yes. I

think this is just one more approach that's available to heighten awareness of the potential role for naloxone in a targeted high-risk population. We know there's a segment of the opioid-prescribed population that are at greatly heightened risk, those on high doses, those with a history of overdose, those on certain concomitant medications. And getting this medication to them I think is important. It's really become the standard of care, and this will just reinforce that message.

I'd also agree with some of the comments made by others that this is not really the most important issue with respect to naloxone. I think what's emerged from the discussion is we need a way of getting inexpensive naloxone to community-based programs and finding a sustainable model for funding that and lowering all of the barriers that might impede that.

DR. McCANN: Mary Ellen McCann. I voted no for several reasons. I think the evidence was weaker that co-prescribing is efficacious compared to the community programs that are out there.

I'm very, very concerned about mission creep. I think the opposite of public health would be somebody going to the emergency room with a broken arm and ending up with $30 worth of some codeine product and an autoinjector at $4,000 plus. I think that's a problem.

I think for the generic versions of naloxone, I think that there's a possibility that there would be a diversion of resources from community-based programs away from them, so that would be another point.

I would like to make the point that it may be standard of care to co-prescribe in very high-risk groups, but I don't know that we need a label change to do that. We've never done it before. You couldn't even come up with another example. I would think responsible prescribers would already be co-prescribing for their vulnerable high-risk groups.

DR. ZACHAROFF: Hi. This is Kevin Zacharoff, and I voted yes with some wording recommendations, which I'll get to in a minute. But I voted yes for reasons already stated by Drs. Ballou and Brand and

things I've said before.

I think it is worth mentioning, despite the fact that I'm often educating primary care providers about what guidelines and recommendations say. It always comes as a surprise to them, even though it's 2018, almost 2019, and that really scares me. I look at this as a message to healthcare providers that are prescribing opioids.

My wording recommendations would be "recommends considering offering co-prescription of naloxone for targeted prescribing for patients and/or households and communities at high risk for death from an opioid overdose." That's my recommendation for tweaking the wording to go along with my yes vote.

Certainly, I would never recommend prescribing -- I removed "for all or some patients prescribed opioids" because I think it needs to be, as we've heard mentioned by many people, something that promotes the discussion, the idea of offering.

We heard one of the public speakers today talk about the ethical analysis of this whole thing,

which unfortunately, I don't hear enough discussed about. There is no ethical pendulum with respect to autonomy and with respect to the fact that patients get to have things offered to them and make their own decisions about what happens to them. Ethics pendulums don't swing.

If we think it's an autonomous right of a patient to know what's available to them; to know what could potentially impact the risk-benefit analysis of them, their households, and their communities; that's inalienable scenario as far as I'm concerned and that's why I think it needs to be in the label of all prescribed opioids so it will promote clinicians to offer this and promote the discussion. Thank you.

DR. BROWN: I'm Rae Brown, and I voted no. I think that as a healthcare system, as a nation, we're dealing with broad issues, one of which is limited resources. And there are very limited resources to address the public health problem of 100 or so people dying every day.

Focusing the agency to get their attention

directly on providing the most efficient method of managing naloxone distribution will require time and money, and it would be detracted from by taking the eye off the prize of co-prescribing. Co-prescribing is the least efficient method that we talked about in terms of actually providing product to a patient.

A couple of things that it would do, it would allow for the maintenance of the status quo in terms of the price point, which is not going to be helpful in providing the naloxone to the 80 percent of people that are dying because of illicit drugs, and it doesn't address the issue of capacity.

We're living in a healthcare emergency. We need to be thinking along the lines of providing more product rapidly to our community programs. I agree with Dr. McCann that making a hard stop declaration in the label could turn into unimaginable legal creep and regulatory creep, and those are very important unintended consequences that I personally don't want to have to deal with.

DR. HERNANDEZ-DIAZ: Sonia Hernandez-Diaz. I voted yes, but I was completely neurotic about what

to vote. And I voted yes with two huge qualifications, and if I had voted no, I would have had qualifications as well.

I voted yes because I think it might be effective in increasing a little bit accessibility, and for some very specific groups like those prescribed buprenorphine, it might help. But just to be very clear, I don't think this is the most effective strategy.

As we discussed, the first strategy that would be most effective is probably going after those who know they are at risk, like Dr. Krebs put it, those abusing or injecting opioids, by lowering the barriers through OTC and other potential ways that we discussed today.

Strategy number 2 would be to go after those that are unaware, like the first prescription of opioids for pain, with information, education, and as we mentioned, offering, which takes me to my second qualification, emphasis on offering, when we say recommending, so that is not taking us mandated co-prescription but just offering.

If going after strategy number 1 is not done, then I will not go into labeling. I will first after strategy number 1 and then take care of the labeling. And if the labeling is going to impair strategy number 1, then I will not do it.

So I vote yes as long we go first with what we have discussed might be the most effective first step.

DR. SHOBEN: Abby Shoben. I voted yes with some of the same qualifications that have been previously discussed. I think what I want to emphasize here is that my vote yes was on strict interpretation of the question, that it would be an effective strategy, not the most effective strategy.

Part of the reasons I think it could be an effective strategy is more widespread distribution than some of the community-based programs. This would get it out to communities that don't necessarily have community-based programs. It would encourage discussion with the provider and with education as we've discussed previously.

I do have significant concerns similar to

Dr. Hernandez-Diaz and others about unintended consequences on more effective strategies, so that's part of my concern about doing it right away versus waiting until some supply issues can be resolved.

DR. BESCO: Kelly Besco. I voted no, and I had a little bit of a different interpretation of an effective method than what Abby had. While I don't necessarily disagree with the concept of co-prescribing as an access method, I believe that medication labeling in general is a passive strategy

So I think a more effective, active strategy would be to adopt and develop risk stratification algorithms that we could embed in electronic health records to guide providers on appropriate patients and families that would qualify for co-prescribing selection.

Lastly, just like others, I just want to restate that we do need to remove barriers and provide a greater government funding stream and procurement program for our national naloxone distribution programs that were overwhelmingly shown to be effective during this meeting.

DR. MEISEL: Steve Meisel. I voted no for a lot of the reasons that others have stated. A public health problem requires a public health solution, and an individual one-patient-at-a-time approach is not going to get us to anything near improving public health.

As others have said, all of the attention on whether we should put something in the label, as Kelly just described, nobody reads the label anyway.

DR. BESCO: I didn't want to say that.

DR. MEISEL: It's passive, and there's got to be -- none of us would disagree that there are going to be individual situations; that it's the right thing to do to co-prescribe. I think that's a given. But whether we should put it in the label and set the expectation that it will happen under these circumstances, and then what happens when it doesn't, I think is problematic.

Risk groups, of course, are going to be evolving. Yes, we can use what the CDC says. We can use what Dr. Oliva talked about yesterday, but it's going to be a changing landscape for quite some time

and therefore subject to interpretation.

What all of this focus on co-prescribing does is takes away focus on what we know and really believe. I think if we had a vote on should we make this product OTC, we wouldn't have a 12 to 11 vote here. We'd probably have a 18 to 5 vote or maybe even higher than that, I would suspect.

Something like that and enhancing the community partnerships that we heard so much about today, that's what's going to impact public health, an inexpensive, readily available product without barriers through community health, through OTC programs, through government stockpiles, through whatever. That's what's going to impact public health.

All of this discussion and all of this angst about whether or not we should be putting co-prescribing as a recommendation in the product labeling for oxycodone sort of misses that point, and misses the big picture, and really won't impact public health.

DR. BOUDREAU: Denise Boudreau, and I voted

no. This was a difficult vote. Clearly, access needs to be expanded, and while a labeling change may increase access some, for certain patients, this didn't seem to rise to the top of the list, as many have stated, as far one of the biggest barriers.

In looking specifically at the question and breaking it down, yes, it may improve access for some patients, but I'm not sure about improving public health. I had concerns that have already been stated of what this would do to the community programs, prices, the healthcare system, the burden on providers, and there's nothing preventing it from happening now, anyways.

So as others have stated, I think the efforts for putting efforts with our finite resources towards things that we've heard in the last couple of days, that are probably the top things that are barriers, would be a better effort.

DR. GERHARD: Tobias Gerhard, Rutgers. I voted no. I believe the co-prescribing approach is a fairly inefficient way to get naloxone to the people that need it the most. However, that being said, I

think a carefully targeted co-prescribing approach or recommendation is likely useful at some point in the future if many other things are already in place. So I think there's a place for it, but it's not the primary place.

Most importantly, I didn't want to vote yes and give the impression that we vote yes here, and this really is something that addresses the problem because I think that's not the case. I think what we need is a response that's appropriate and proportional to the challenge that we're facing, which is a major and unprecedented public health crisis that kills tens of thousands of people every year.

While that response is incredibly complex and difficult, one key component of it is to assure a stable and affordable supply of many millions of doses of naloxone for various distribution channels that's procured by the federal government.

I think this is purely a question of political will. This is entirely feasible. Naloxone is a product that has been on the market for many

decades. It is not expensive. This is doable and can save a lot of lives, but it requires a concerted effort that goes outside of the usual approach to regulate prescription drugs.

DR. DASGUPTA: This is Nabarun Dasgupta. I voted no. Since 2007, I've been helping pharmacists and doctors co-prescribe, and I've been waiting for this vote for 12 years, and --

(Laughter.)

DR. DASGUPTA: -- to my great surprise, I voted no, in large part because the impact on the harm reduction programs has not been adequately explored.

I found the failure to acknowledge the programs in the sponsors' presentations was shameful and deceitful and exploitative. I think the absence of the harm reduction programs more deeply in this conversation is so inadequate that I cannot vote to change the status quo without taking their wisdom directly into account.

Since Dan Bigg died in August, I've often wondered what would Dan vote, what would Dan do with

this situation. Since he's not here to talk to my heart, I'm going to have to talk from my head. So looking at where the data are that were presented, the benefit, the people who use these medications are often not the person who they were prescribed to.

I firmly believe that the U.S. Food and Drug Administration's drug label is one of the most important public health documents in the world. The information contained in there has a level of objectivity and direct relevance to the biological and clinical aspects of a drug.

To include in the label someone who is not the intended recipient, I feel like would create a precedent that I don't know that I would be willing to endorse at this time.

DR. AMIRSHAHI: Maryann Amirshahi. I voted yes. While I don't feel that co-prescribing is the most efficient way to improve naloxone access, I do believe that it does start a dialogue between the provider, and it serves as a reminder to the provider to bring it up.

Additionally, I feel that by starting that

conversation, perhaps we can identify patients that may be at risk that we didn't initially think about. I think that the effort should be targeted specifically to high-risk populations, at least initially. I also think that we should try to gather data as to how efficient it is moving forward so that we can re-mine [indiscernible] our interventions. Thank you.

DR. BROWN: Before we adjourn, Dr. Herring, do you have any comments about any of the discussions that we've had here today and yesterday?

DR. HERRING: Sure, yes. This is a tough issue and presents a lot of challenges, particularly given the situational differences between illicit and prescribed drug abuse. I think that was really clearly illustrated by the discussions.

I want to commend FDA, the sponsors, speakers for their thoughtful views that were expressed, and I think one thing we can agree on is that we need a multiprong strategy; that no single intervention is really going to solve this very complicated problem, and that regulated industry fully supports and

endorses the continued dialogue and collaboration on this front to stem the opioid crisis.

Along those lines, regulated industry's participating with NIH and the public-private partnerships that have resulted in the HEAL initiative, Helping to End Addiction, with Long-term strategy. There's industry-sponsored research and development that continues, as you know, for the abuse-deterrent formulations to try to make it harder to overdose on opioid medications, as well as efforts to produce non-opioid analgesics that can helpfully provide patients with effective treatments for their pain in the future.

DR. BROWN: Thank you, Dr. Herring.

Any last comments from Dr. Hertz or others in the FDA?

DR. HERTZ: Well, thank you. I often say that the discussion is more informative sometimes than the vote, and that's clearly the case today, so thank you. Thank you for taking the time to come help us with this. The discussion was really excellent, and we'll be poking through this for some

time. So thank you all.

DR. STAFFA: This is Judy Staffa. Can I just add one more thing? In addition to thanking the committee, I'd also like to thank the unprecedented number of guest speakers who came and took their time to share all of their relevant work with the committees and also the outstanding participation in the open public hearing. I think we learned a lot, and I'm very grateful for the time people spent in coming.

(Applause.)

DR. MEISEL: I'd like to acknowledge that I believe this is Dr. Brown's last meeting as chair. I'd like to acknowledge his strong leadership of this committee, and we thank you very much for your leadership and skills.

(Applause.)

Adjournment

DR. BROWN: Thank you.

We kindly ask that all attendees dispose of any trash or recycling in proper receptacles. Please remember to take all your personal belongings.

Please leave your name badge on the table so that it can be recycled. All other meeting materials left on the table will be disposed of.

Thank you, and we will adjourn the meeting now.

(Whereupon, at 3:49 p.m., the meeting was adjourned.)