Centers for Medicare & Medicaid Services
COVID-19 Call: Lessons from the Front Lines- Theraputics
Moderator: Alina Czekai
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OPERATOR: This is Conference #: 9409959

(Alina Czekai): Thank you for joining our call today. CMS Lessons from the Front Lines on COVID-19. Today's topic is therapeutics. I'd like to turn it over to CMS Administrator Seema Verma. Administrator?

Seema Verma: Thank you (Alina) and thank you all for joining our CMS Lessons from the Front Lines and COVID-19 call today. I'm the Administrator and I'd like to begin by thanking all of you for the work that you are doing day in and day out to care for patients around the nation.

You really are the heroes on the front lines of this war and our nation is grateful for everything that you are doing. We know that this has been extremely disruptive to the healthcare system and we appreciate these sacrifices that you're making, like not performing elective surgeries and rapidly implementing telehealth.

Today CMS will announce that we are making accelerated payments to Medicare providers that may have cash flow issues and tomorrow or very soon we plan to make additional announcements around a range of regulatory (inaudible) to make your jobs during this unprecedented epidemic. So, stay tuned.

I speak for the president, the vice president, the task force, FEMA and our entire Administration when I say we are here to support your front line efforts and we want to make sure that we keep an open dialogue with providers, as well as facilitate conversations across the country so we can learn from one another about what works and to drive innovation in our response.

Today's call is part of our ongoing series, CMS Lessons from the Front Lines on COVID-19. Our first call in the series took place earlier this week and we were joined by (Dr. Colah) who talked about testing and then we also spent some time on telehealth.

Since then we've heard from many of you that you found this forum to be helpful as a learning network for best practices and information sharing. Around the nation providers and local communities are innovating in response to COVID-19 and at CMS our goal is to bring local innovators together to share best practices that can be scaled at the national level.

Today our discussion is going to focus on treatments and we are joined by FDA Commissioner Dr. Hahn. But before that, Ambassador Dr. Birx is with us as well and you all know who she is. And so, I will turn it over to her to give a few comments and then she will turn it over to Dr. Hahn. Thank you.

Deborah Birx: Thank you Seema. And really, again, I just want to echo the Administrator's incredible words of thanks to you all. I guess many of you don't know me, but I am one to both thank and ask. So, you are – we are experience a different profile of admissions than many of the other countries that have confronted this virus in the last month.

Certainly the average age in both admissions and the ones going to the ICU were older in both China and Italy, because their population, particularly in Italy is a decade older. So, a lot of their recommendations come from working with a much older population in the hospitals.

We're really looking to you all to provide us insights that we can share broadly across the nation as your metro areas become engaged in this epidemic to really ensure that we're learning from you about the issues confronting, particularly people under 55. On the average age of the admission, I think many of you know in Italy was over 62, the average of the individuals who succumbed to the illnesses were in their mid to late 80s.

So, we need to really understand what you're seeing and how our patients will respond maybe different than Italy and China, both from clinical care and what would be important related to therapeutics. So, I just want to plead for

your wisdom so that we can get that into a broader context as new cities confront what New York is seeing currently.

So, thank you for your work and thank you for the information you'll be giving us to really help disseminate new findings and particularly around people under 55.

Seema Verma: And may I please ask everyone who as an unmuted line to mute their lines. We're hearing some background noise. Again, please mute your line if you are not speaking. Thank you.

Stephen Hahn: Thank you Dr. Birx and Administrator Verma. This is Steve Hahn, the Commissioner of Food and Drugs. I want to echo what Deb just said, it was three short months ago that I was also a practicing physician and I can only imagine what you are facing out there in this country. My many, many thanks.

One of the wonderful things that our country has is doctors who are compassionate and skilled and we all very much appreciate what you're doing on the front lines. One of the major returns I'd like to seek in this call is input from you so that we can give that input to the task force as well as to our response through Seema and Health and Human Services. Your input is critical so that we can adapt and adjust as needed to what's happening on the front lines in this very quickly moving situation.

I just want to briefly talk about FDA's role here, what we do in these situations and then turn it on to Dr. Anand Shah, who is Deputy Commissioner for Medical Products, to talk about some of the experimental therapies that we have available for patients across the country.

So, we're focused in two major areas. One is facilitating medical countermeasures to diagnos, treat and prevent the disease, but also and very importantly surveilling the medical product chains for potential shortages or disruptions in that supply chain. And we've all seen that those have occurred.

We have anticipated that those occurred and we have had an amazing response from manufacturers in the private sector, as well as the public sector, to try to fill the gaps that we're seeing in medical products.

We've engaged across the government in this effort, and as you probably know, this information goes to HHS and to FEMA. And so, for many of you, your local FEMA representatives are who your hospitals can contact with respect to questions about the supply chain, particularly around personal protective equipment and ventilators.

We have been balancing the need to ensure safe and effective treatments and safe and effective medical products like personal protective equipment, with reducing red tape so that we can move as quickly as possible. I want to give you a couple examples why I think this balance is really important.

One is we, last night, approved a point of care test by Abbott Laboratories, they have an installed base in many of your offices, similar to the flu and strep test and that is a five minute test for a positive and a 13 minute test for a negative. It's a very rapid in-office test that should expand testing capacity.

The CEO and I have spoken about this and this is a situation – this is a test that normally takes them 9 to 10 months to develop, and they have collaborated very closely with the FDA and this took between four and six weeks. So, it really is an all of America approach to do this.

The other thing I want to point out is that with respect to PPE, I know as a front line provider when I had to don and N95 mask, I was confident that that mask provided the protection that was necessary for both patient and provider. And we've seen unprecedented demand for these masks and other personal protective equipment.

And what we want to make sure is, if we – if we allow into the country N95s, for example, that we have not looked at ourselves, that we are making sure that the (laboring's) appropriate, so you understand what the best uses are for those personal protective equipment. And the folks at FDA are working around the clock in that area.

The other big issue that's come up is hand sanitizer and we are also working around the clock to expand that as well with the manufacturers. Compounding pharmacies now have guidance from us on how to make it. One thing I want to point out is, that diversion of hand sanitizer is a major issue.

If denatured alcohol is not used, so if conventional alcohol is used and it's not denatured, that is a hazard to toddlers and we've seen diversion in one teaspoon of hand sanitizer that does not have denatured alcohol could kill a toddler. And so, we're very cognizant of the fact and we've been expanding the list of denaturants to try to get that into the – into the community as quickly as possible.

And the last thing I just want to mention from our perspective is the prevention of fraud. Many of you have heard the reports of some individuals who have taken over-the-counter chloroquine products that are used for cleaning fish tanks.

That – we've made it clear that there are no over-the-counter chloroquine products that are approved by FDA or safe for use by anyone. Getting that message out to your patients and to Americans is really important, because, of course, taking that is potentially lethal.

And my final word here is that we are expediting a broad range of therapeutics with manufacturers and developers, we hope to bring out into the medical community and through clinical trials. And it's important to remember that there are no FDA approved therapeutics at the moment for the treatment of COVID-19.

So, thank you again for all the terrific work you're doing. It's so impressive to see American medicine at work. I realize that the system is stressed, but thank you for what you're doing. And I'll hand it over to Dr. Shah.

Anand Shah: Good afternoon. Thank you Dr. Hahn. Thank you Administrator Verma. I'd like to start by discussing how we're accelerating the development availability of new treatments and vaccines.

Currently, clinical management includes infection, prevention and control measures and support of care, including supplementary oxygen, mechanical vent support when indicated. That said, there are an array of drugs approved for other indications as well as several investigational drugs that are being studied in several hundred clinical trials underway around the globe.

As we move forward in the study in use of these products, it's essential that we understand and continue to develop the safety profile and understand the evidence associated with these drugs.

For example, chloroquine and hydroxychloroquine, these are being studied as potential treatments for COVID-19. But we know the safety and effectiveness of these drugs for treating the diseases for which they were approved. What we don't know is how safe or effective these drugs are for treating COVID-19.

Similarly, FDA has granted access to hundreds of patients to the investigation anti-viral remdesivir. This drug has broad anti-viral activity that inhibits viral replication and we know that it has in vitro activity against SARS-CoV-2 and also in vitro and in vivo activity against related beta coronaviruses.

Currently, there are four options for obtaining remdesivir for the treatment of hospitalized patients with COVID-19 and pneumonia in the United States. First is an NIH sponsored adaptive, double-blinded placebo control trial. There are two Phase III randomized open label trials. And in areas without clinical trials, COVID-19 patients in the United States have been treated with remdesivir on an uncontrolled compassionate use basis.

Importantly, Gilead, the manufacturer, is currently transitioning the provision of emergency access to this drug from individual compassionate use request to an expanded access program. And this is being done in tandem with FDA. Gilead and FDA will have more information available shortly on this expanded access program.

Another promising treatment the FDA is taking the lead on is facilitating the development and use of therapies, such as plasma from donors who have recovered from COVID-19, such as convalescent plasma, as well as hyperimmune globulin.

These products use antibody rich blood products that are made from blood donated by people who have recovered from the virus, that can then be administered to individuals diagnosed with COVID-19. Both of these products have the potential to shorten the length or lessen the severity of illness.

Even as we are heartened by the promise of some of these products, we also must be weary of and responsive to developments that bring unintended consequences to other patients.

For example, we've seen a surge in the demand of chloroquine and hydroxychloroquine, which has led to an impact on patients who are dependent on these medications for the treatment of malaria, lupus, rheumatoid arthritis.

We're doing everything possible to work closely with manufactures to increase production. We're working with manufacturers to access their supplies and are actively evaluating the market demand for the patients that are dependent on these medications.

But as prescribers, please understand that this is a fluctuating and dynamic situation. Regarding these drugs, we've received several offers of donation from drug manufactures for millions of chloroquine tablets. The FDA is working closely with these companies to ensure the quality and safety of the donated product. We're also in touch with companies on their efforts to accelerate production of chloroquine.

For example, one manufacturer aims to increase chloroquine production by 25 percent over the next month. Companies are also working to produce millions of additional chloroquine tablets in coming months by importing more active pharmaceutical ingredient or API from abroad. And we're working to make sure that this can happen as expeditiously but also safely as possible.

A few words on clinical trials, we're working with a number of companies to rapidly advance the development and availability of vaccines and treatments for COVID-19. There are many investigational COVID-19 vaccines and

treatments that are being studied in clinical trials but all of these are in early stages of development. FDA is working closely to ensure the safety and effectiveness of any products developed through these trials and by facilitating expanded access to individual severely ill patients of clinicians without access to a clinical trial.

On this point I want to mention the challenge we face in terms of medical treatment of affected healthcare workers. Specifically there are some questions regarding whether these frontline workers can have immediate access to drugs or whether they should ne enrolled in clinical trials. And these are admittedly very complex and nuance questions that we as an agency are working through with our provider community.

A few words regarding supply chain, another important aspect of our current focus at the agency is also vital to your work making sure that Americans have access to safe and effective medical products, making sure that we're keeping a continual surveillance of the global supply chain to identify concerns and access or assess the availability of products that Americans need most.

We are partnering very closely with FEMA or the Federal Emergency Management Agency on supply chain issues including importation of necessary medical products. Let me give you a quick update on some of the details that we've taken there and also on diagnostics.

We don't as an agency develop tests but we do engage with developers in the private and public sectors. We've accelerated the development of a number of COVID-19 tests and helped to rapidly increase the testing capacity in the United States. We've done this by providing maximum flexibility to labs as well as commercial manufacturers.

FDA has authorized more than a dozen commercial tests, many of these at record speeds. We receive applications and often times we're able to make a decision within days including the point of care diagnostic that Dr. Hahn mentioned. This was approved last night and can provide results in less than an hour in a doctor's office.

We're also working very closely with states to authorize certain laboratories within their jurisdictions to begin patient testing and this is all without needing authorization from the FDA during the pandemic. We've granted that flexibility to New York, Nevada, and the state of Washington. We've also been researching and mitigating the shortages of laboratory testing components including the identification and sharing knowledge regarding scientifically acceptable alternatives for testing components. We put those on our website.

We've established a mailbox and a toll free number for quick responses to questions. That toll free number is 888-INFO-FDA. We've also provided recommendations for test developers who may wish to develop serological tests during this outbreak. Serological tests measure the amount of antibodies or proteins present in the blood when the body is responding to a specific infection. We recognize these tests are generally less complex than molecular tests. And they are solely used to identify antibodies.

This limits their effectiveness for diagnosis; however they can provide very useful information to providers and also to patients. We have taken a posture that we do not intend to object to the distribution or use of serology tests to identify antibodies where this test has been validated where a notification has been provided to the FDA and when appropriate warning statements are including – included with these tests.

I want to thank my colleagues from the FDA (Dr. Burnfrand) and (Dr. Murray) both of who are leaders in the – our division of antivirals. And also (Dr. Nicholos) was one of our leaders in the rheumatology branch. And with that, I want to turn it back over to Administrator Verma.

Seema Verma: Thank you, Dr. Shah. And I believe – why don't we just take a few questions at this point and then – before we move on to the next portion.

Alina Czekai: Operator, please open the line for questions. Thank you. Operator, please open the line for questions. Thank you very much.

Male: Operator, question here.

Operator: Go ahead.

Male: Hi, this is (inaudible). Can you guys hear me?

Operator: Yes we can. Thank you.

Male: OK. Hi. So, the lupus patients that need their plaquenil that have been on it for years, just yesterday two of our patients called saying they can't get it from their regular pharmacy whether it's Walgreen or – and two of them actually are healthcare workers working in either a hospital or nursing home setting.

And so, sort of talk about the double, triple whammy for these people who are going to frontlines and already made a compromise. So what can we do to get that refill? These are not people getting new prescriptions that could be questionable; these are people (that have been it) years. So, how can physicians ensure their people get those refills?

Anand Shah: Doctor, thanks for your question. This is Anand Shah from FDA. We are continuing to watch that supply chain very closely. Just over the past ten days we've seen a surge in the number of pharmacy prescriptions for chloroquine, hydroxychloroquine products.

This is coming from a number of different avenues. One is an uptick in demand from the American consumer from patients who want to have a dose ready and available on a prophylactic basis at home. We've also seen a surge and have been working with the medical licensing boards. We see a lot of self prescribing from healthcare providers.

That said, taken together there is a run on the pharmacy so to speak for these products, we're working with the manufacturers who produce these drugs both domestically and overseas to make sure that that supply is replenished and available for patients who need it for chronic disease management like your patients. So, we're watching this closely and we are engaged multiple times a day with manufacturers. We hope that that supply should be smoothed out in the next few days.

Male: Thank you.

Seema Verma: Operator, we'll take our next question please. Thank you. (Alina), if we don't have questions we can move to the next section.

Alina Czekai: Operator, do we have any questions lined up in the queue? Hello?

Seema Verma: OK, why don't we move along? We also have a section here that we're going to talk about experimental drug therapies. We have a presentation from Dr. Khalil and Dr. Mehta. They're going to be talking about the NIH remdesivir clinical trial. Dr. Khalil, Dr. Mehta, are you ready?

Alina Czekai: Dr. Khalil is going to join in ten minutes. Administrator Verma, perhaps we turn it to Dr. Debbie Birnkrant at FDA to share some updates on the experimental drug therapies.

Debra Birnkrant: Good afternoon. Thank you very much for inviting us to participate. My comments actually add to what Dr. Shah and Dr. Hahn had addressed. So given the significant impact of ongoing – of the ongoing COVID-19 pandemic there is great interest obviously in developing new therapies or repurposing existing therapies to treat and prevent COVID-19.

However, as we said no drug has yet been shown to be safe and effective against this or any coronavirus disease. Furthermore, because of the variable and complex nature of the disease and of proposed therapies in many instances it's difficult to predict whether an intervention could actually be harmful rather them helpful even if you're biologically stealing (inaudible).

We are committed to supporting all scientific (inaudible) to attenuating the clinical impact of COVID-19. And we believe there's a shared priority among patients, clinicians and pubic health decision makers including regulators to have the best information possible to guide treatment and minimize harm from therapeutic interventions.

So, it's essential that we get key information to be able to provide advice and guidance to ensure the safe and effective therapeutic intervention can be developed for those in need. How do we at the review division do this during

a pandemic? Well, we not only provide advice on drug development and clinical trial design but we review data to be able to make a determination whether the benefits of the use of the investigational drug as well as repurpose therapeutics for COVID-19 out weigh the risks.

For investigational therapeutics we would minimally like to see (inaudible) data with related viruses or the SARS-CoV-2 virus before trials are initiated in human patients. In addition, we would like to see animal model data with related viruses or with the current virus causing this outbreak.

However, these are not rigid requirements and we are open to discussion of the rational for introducing candidate interventions into human trials. Well, what else do we need to see any available toxicology data to have an idea of what to monitor in the clinic and any available data from previous human experience with the proposed therapeutics. Also, we would like to see a justification why the purported mechanism of action and dose would be appropriate to evaluate in patients of COVID-19.

I also wanted to let you know that we have a special (inaudible) program where we will rapidly review your proposal and questions to enhance the efficiency of interactions with us and any preparations you need before you submit a protocol under an IND that would actually initiate a clinical trial after our review.

What are we looking for? We're looking for pilot trials to begin with that are randomized and placebo controlled compared to single arm trials which may be intrinsically unable to differentiate either beneficial or detrimental drug effects from the variable and complex natural course of the disease. The pilot trials will provide more interpretable data on exploratory endpoints and safety and mortality before exposing larger numbers of patients to investigational therapeutics and later stage randomized trial.

Well designed randomized controlled trials are the highest priority to guide improvements in patient care for the sake of everyone involved in this rapidly evolving situation. But we're also open to discuss different mechanisms for

additional access if needed for patients who are unable to participate in clinical trials.

We have a newly formed multidisciplinary office of new drugs team that manages all incoming COVID-19 drug development inquiries and their e-mail address is COVID-19-productdevelopment@FDA.HHS.gov. In sum, I would like to say that we are patient advocates at the FDA foremost. And we are committed to supporting all scientifically sound approaches to attenuating the clinical impacts of COVID-19. Thank you very much.

Seema Verma: Thank you, Dr. Birnkrant. Do we have our operator on the line to help us open for any questions please?

(Dr. Toroth): I have a question.

Alina: Sure. Happy to take your question.

(Dr. Toroth): Hello?

Alina: Hello, we can hear you.

(Dr. Toroth): Oh, you can hear me. Oh, wow. OK. My name is (Dr. Toroth). I am doubled licensed in Ohio and Michigan, I live on the border, and there are a lot of us primary care doctors, I'm private practice that we're ready to fight and help decrease the flow to urgent cares and ERs. But we have no PPE and we don't have the funds to even get the ones that are available that are at very high prices and places like (Melina) are claiming that they're not even going to pay any doctors until after April 15th if not later.

So, it's kind of hard of me to keep my doors open but also try to fight on the front line without the funds or the access to the PPE.

Seema Verma: This is Seema Verma, so a couple of suggestions there. Number one I know that a lot of providers are concerned about payroll because you're see patients or some of your staff may be at home taking care of kids and not being able to help, have the clinic be at full capacity. So, one of the things that we announced at the beginning of the call is that CMS is making accelerated

payments for Medicare so that'll will be based on your historical spend. You're welcome to go on our website to find some more information on that.

In terms of PPE, we've been hearing a lot about that. The best thing to do is to talk your local officials. There is a distribution channel where FEMA is distributing supplies but they go to the state and then the state's responsible for distributing those supplies. So, if that's a concern …

(Dr. Toroth): Right.

Seema Verma: … the best place is to go to your local health officials.

(Dr. Toroth): They're not sending it to anybody but hospitals, still.

Seema Verma: OK. We can look into that but I think that they're in control of where these supplies go. So we'll continue to take a look at that, but I think then trying to communicate with the hospital about what your role could be and those local health officials.

Stephen Hahn: And Administrator Verma this is Stephen Hahn jumping in. I think that's really good feedback and we'll as Administrator Verma said we'll provide that feedback to folks at FEMA regarding that request. Maybe there's some communication we can give. I'm sure they're prioritizing where they're giving the PPE. But it's a really good thought and suggestion.

Alina Czekai: Thank you. Operator, do we have other questions lined up in the queue, please?

Seema Verma: OK. I think we're also going to hear from Dr. Murray from the FDA as well. He's the Deputy Director of the Division of Antiviral Products. Dr. Murray.

Jeffrey Murray: Hello, this is Jeff Murray. So we have numerous clinical trials up and running for some antivirals and immunomodulator drugs and I just wanted to make a statement that I think we need to manage our expectations regarding the therapeutic field. Because largely what's being study are repurposed drugs including the anitvirals and immunomodulators. And the track record for repurposed drugs has been plus or minus.

It's best if you have (rationally) designed agents against for specifically for antivirals against a specific target. But in the past in both Deborah Birx and I have been working in the antiviral field since early on in the HIV epidemic. A good example is (APC) was repurposed for HIV approved. And it did work but it wasn't optimal and (inaudible) thing from that example was a randomized control trial was done even at that time of great need and showed a mortality benefit. At the same time that we were having expanded access program.

So, that's what we're trying to do now. Also, as far as managing expectations as far as antivirals, there's not really a good track record for treating hospitalized critically ill patients with antivirals. We really don't have one approved even for influenza for that. And it may be better early on in disease seems to work well. So it would be great to have oral drugs for that and that's where the hydrochlorthazide, I mean hydroxychloroquine, sorry. Hydroxychloroquine studies may take a role. But, maybe the greatest need for therapeutics could be for the immune response to treat things like (inaudible) syndrome and there are some trials up and running for that.

So of the IL6 blockers, there's at least three trials and you can find two of those trials up on clinicaltrials.gov. So, we're very hopeful that maybe some of the immunomodulators and products could work. But, again those are sometimes a little scary to think about some of them because we don't yet know if they could be harmful or helpful. We all know that the immunologic cascade can go either way and sometimes have paradoxical responses depending on dose.

And, so, that's why we are strongly encouraging for these immunomodulators randomized controlled trials before even really thinking about just giving them to individual patients. Because if we don't have those set up basically you might be giving just leaking out something harmful to people without ever having a chance of getting the results. So that's been our approach and we've trying to strike a balance between the randomized clinical trials and expanded access as we have a long history of doing back decades ago with HIV. Thank you.

Seema Verma: OK, any questions? We're going to open the line up for questions.

Operator: Yes, we have next question from (Virech Mahachan). Your line is now open.

(Virech Mahachan): Hi, it's (Mahachan) again. This question was not related to the drug so I can wait until the end of the call. It's more about nursing homes and referrals of positive cases.

Alina Czekai: Operator, are there any more questions?

Operator: The next question comes from the line of (Gary Laroy). Your line is now open.

(Gary Laroy): OK. This is (Gary Laroy) from Dayton, Ohio and I was actually not asking question but just responding to one of the previous callers about whether we're trying to get the PPEs from the County Health Department as opposed to just the hospitals. Because they are doing collections for some of this devices and things from various sources and they're send them to collection entities. And so possibly they could get these PPEs to the (physician) offices and where they're most need (inaudible) without sending them to the hospitals. Anybody heard anything about that?

Seema Verma: This is Seema Verma. I think it varies in every single community. Just to give you a sense of the way it's supposed to work is that locally executed state managed and federally supported. So FEMA's sending materials to the state level and then it goes to the local level. But it may vary in your particular community. I think per Dr. Hahn's suggestion we can follow up with FEMA and in your state, Ohio, and just flag that that's still an issue for those of you on the ground not knowing exactly where to go for supplies.

But, I appreciate you bringing it up.

Female: In Detroit, Michigan, which is one of the hotspots, that's where I am.

Seema Verma: Thank you, we will do that. Appreciate you flagging that.

Anand Shaw: This is Anand Shaw from FDA. Just to add on to the Administrators comment, we're in direct contact with the Governor and Lieutenant Governor

in Ohio (inaudible) specifically on PPE. So, I know the state is working very actively to make sure that PPE gets directly into the doctor offices.

AlinaCzekai: Next question, please.

Operator: And your next question comes from the line of (Robert) (inaudible).. Your line is now open.

(Robert): Thank you. I'm in Reno, Nevada and I've been doing studies in metabolism to try and understand the metabolic basis of chronic disease. I do believe that some of that work has led to an understanding of how Vitamin D regulates it's affects on the immune system and have a thought on a medication that maybe quite useful, it's been around for a long time but is not currently available. I don't want to say what it is because I don't want to create a hydroxychloroquine type response to this.

But I do want to engage and I've sent emails to (Fauci) and (Collins) and of course I'm not getting any feedback. But I would like to discuss the potential for using a very safe drug as a clinical trial and I'm not in the position to do clinical trial. So I would like to have a contact.

Stephen Hahn: Yes, this is Commissioner Hahn, we'll give the contact information at the end of the call so that you can either call or use our website. Really appreciate the suggestion as you can imagine we're getting quite a few and we're looking at these certainly with a scientific and medical eye, but we welcome all opportunities to look at those things, Doctor, and at the end of the call we'll give the contact information.

(Robert): Will I be able to personal talk to somebody, because my attempts to contact have not gone through. I just get back form letters basically.

Stephen Hahn: Yes, well there's a long line of people bringing information to us but if you call in at the 1-888 number which we'll give at the end you will actually talk to a human being. And they triage the calls to the appropriate place.

(Robert): OK, thank you.

Operator: And your next questions comes from the line of (Ray Lorenzoni). You may ask your question.

(Ray Lorenzoni): Hi, this is (Ray Lorenzoni) from New York City. I had a question about in comparison to HIV where we decreased our physical sensitive for a lot of the (ramide) controlled trials. Is there talk about decreasing (RP) value to .1 instead of the typical .05 in order to explore tiers and save lives more quickly? Thank you.

Operator: And your next question comes from the line of …

Female: We need to respond. Dr. Hahn, do you want to respond to that before we take the next question?

Stephen Hahn: Yes, for sure. I was going ask either Dr. Murray or Dr. Birnkrant to speak to what we do at FDA with the respect to clinical trials (inaudible) which I think this question is related to.

Jeffrey Murray: Yes, (inaudible).

Debra Birnkrant: I can start it off, oh, go ahead, Jeff.

Jeffrey Murray: OK. I think we're very flexible with T values, I'm not going to give you the necessarily exact cut off. It really depends on the study. I don't think that we would necessarily call a study failed because it exceeded .05, if all the rest of the data and some other supportive data show (it's) going in the right direction and multiple endpoints going in the right direction. So, in the setting of this pandemic we are very – going to be very flexible and the interpretation of some of these trials because we know that they can be difficult to enroll and it's hard to choose (inaudible) what the best endpoint would be for the statistical analysis. So, we take that into account and will be very flexible.

Debra Birnkrant: I think also this is Debbie Birnkrant, this is why we're asking for a more rigorous pilot study to being with. Because we're asking for placebo controlled trials upfront. So, at least we have a better chance at hopefully getting interpretable data although limited that will help to plan the larger

clinical trials. And as Jeff mentioned we're very flexible, we don't necessarily know the right endpoint at this point and time either.

So, we're looking forward to actually getting some data so we can be able to review those results and possibly learn something that we can pass on to the next clinical trial that comes in for review.

Alina Czekai: Next question, please operator.

Operator: And your next question comes from the line of (Chris Birch), you may ask your question.

(Chris Birch): Hi, can you hear me?

Alina Czekai: We can, thank you.

(Chris Birch): Hi, this is (Chris Birch), I'm a (dairiatritian) in Philadelphia. It's (inaudible) in mind of the questions that you've been getting regarding PPE.

Specifically about the N95, right now for getting a supply for N95's we're having difficulties, but we're able the equivalent N95's from other countries; like the KF94, the KN95. Is there any comment about using those?

Stephen Hahn: Yes, this is Steve Hahn from FDA. We've issued broad guidance around this as most recently as yesterday and certainly have flexibility around those, in particularly the K95 that you've brought up.

If there's a specific brand or a specific company, you all can go to our website or that 188 number that I'm going to give out, you can call as well with specific questions around those.

If they aren't an FDA certified produced (inaudible), we haven't inspected their plant, et cetera, we're just asking you to make sure that you verify that the chain of custody et cetera, the certification is appropriate.

And just one last thing, not to get too technical; if any of these products have a CE certification doctor, that is a good to go from our perspective.

And just let me shout out real quick the number here – its 1-888-INFO, I-N-F-O-F-D-A. 1-888-INFOFDA, and that's manned 24/7.

(Chris Birch): Thank you so much.

Alina Czekai: Thank you for your question. We'll take one more question in this segment and again, there will be plenty of time for Q&A later on in the call.

Operator, next question please.

Operator: Yes, we have next question from (Mark Sherman), your line is now open.

(Mark Sherman) You may ask your question.

(Mark Sherman): Hi, (Mark Sherman) from Chicago, a question regarding hydroxychloroquine. Is there – do you envision any current indication for treating high risk out-patients with hydroxychloroquine with or without azithromycin?

Or do you recommend against it?

Male: (Inaudible).

Debra Birnkrant: (Inaudible).

Male: Go ahead.

Debra Birnkrant: I'll start off this time. It's not that we're making a recommendation either way, the recommendation is for clinical trials and we can refer you to clinicaltrials.gov where the University of Minnesota has an interesting internet based clinical trial looking at hydroxychloroquine for past post exposure prophylaxis as well as treatments.

We've seen other clinical trials for pre-exposure prophylaxis, so I personally would recommend that you go onto clinicaltrials.gov and see the landscape of clinical trials that are being conducted with hydroxychloroquine.

Jeff, anything else?

Jeffrey Murray: Yes, we know a lot of doctors are using hydroxychloroquine kind of routinely or perhaps chloroquine.

One consideration with the azithromycin, we don't really see a necessarily a lot of rationale, certainly in vitro data to support the azithromycin component. And one thing that we're concerned about as an outpatient for that combination, is a potential prolongation of QT interval.

In the hospital that can be monitored better, but as an outpatient that could be a potential toxicity that could be monitored as well, since both drugs have the potential to prolong the QT interval that chloroquine more than – a little more than azithromycin, but together it's unclear if that would be a worse combination for that safety risk.

So we heard from some of the physicians, critical care physicians, that they were not using the combination anymore because they had too high a proportion of patients with unacceptably prolonged QT intervals, so that's just one caution for that combination.

Male: (Inaudible).

Male: This is…

Male: (Inaudible).

Male: No, go ahead.

Andre Khalil: This is Andre Khalil, just to let you know, I'm logged in for the talk.

Stephen Hahn: Thank you, and just in follow up to what Dr. Murray and Dr. Birnkrant just said, this is Steve Hahn, FDA. CDC has issued on their website, it was last weekend, a state of knowledge paper for physicians for providers regarding some of the questions that are being asked around hydroxychloroquine in particular.

And so much of what Drs. Murray and Birnkrant said is stated in that document. But it's an easy and pretty handy document, I'd just refer you to that if you have questions about the drugs.

Male: Thank you.

Alina Czekai: OK. I think we are ready to talk about our NIH remdesivir clinical trial and that'll be a joint presentation from Dr. Khalil and Dr. Mehta.

Andre Khalil: Hi, this is Andre Khalil. I'll give you a summary of the trial and a little bit of – about what we are doing here in Omaha, Nebraska. The – so the trail is an adaptive randomized trial in which, as you know, we're going – we started with remdesivir and the goal here is to move with adaptations to other therapies through the process of conducting the trial.

We start with the first patient here at the University of Nebraska, now we have over 100 patients and getting to close to 200 patients pretty soon. And so the goal is to reach about 400 patients – around 440 patients to complete the trial. And the prediction is that probably in the next few weeks, the trial will be completed based on the (enrollment rate) that we've had speeding up almost every day following the outbreak in the last week or so.

The trial is a double-blind randomized trial in which the – all my patients and myself and my coordinators and nobody else knows exactly what the patient is receiving. So frequently, I get questions about if we know any progress. And the first (thing we analyzed), it's going to be done probably very soon (in the) next few days or next – probably this coming week.

And that's going to be critical for us to understand the – how to proceed with the trial. But this is something that is right now being validated because we need the full follow-ups of all the first 100 patients before the DSMB make the evaluation and the decision to proceed ahead.

The trial is definitely running much faster than when we started. We have about 40 P.I.s here in the United States. We have sites in Singapore and South Korea as well. And so the idea is to try to really have as many sites as possible, we think, the in context of the trial and trying to complete the trial also in an efficient and safe way.

The – I think that's important, I think, for the listeners to understand too, how we have approached here at the University of Nebraska, the general approach to these patients (ordered) in the trial. As you know, the trial only enrolls moderate to severely (ill) patients. So these patients have to have not only the presence of the infection but also pneumonia from COVID-19, from the SARS-CoV-2. So – and that's about 20 percent or so, 15 percent/20 percent of the patients.

Most of the patients will not fit the criteria of the trial because the trial really requires that kind of severity. We've had many patients also that were severe but did not fulfill the criteria for the trial, or because they had renal failure, or because had liver function test elevation, or they – we couldn't consent for different reasons.

And what – the way we have approached all these patients is supportive care. We decided that it would be a safety issue to give hydroxychloroquine or azithromycin. A lot of these patients already have chronic cardiac disease, they also – we've had patients with myocarditis from COVID and hepatitis from COVID, so these are all potentially side effects that can be – it can be really serious in these patients.

So based on what we know from chloroquine or hydroxychloroquine and that has – these drugs have failed in every outbreak for the last 20 years against any virus, literally every outbreak people start on chloroquine or hydroxychloroquine and the (history is) really a very poor track record. And then you add the safety issues, especially cardiotoxicity and liver toxicity.

At the University of Nebraska, we decided to completely avoid the drugs because we don't believe it's safe to our patients. And by the way, we've had patients come in after a week taking these drugs and getting very severely ill as well, both from COVID or side effects. So we – unless these drugs are going to be tested in a clinical trial, we are not going to be advising any of our clinicians or patients to take these medications.

So basically, we are (in the) trial and whoever (is going in) the trial is getting the supportive care. And that's kind of a quick summary of the situation in Omaha.

Aneesh Mehta: Good afternoon, everyone. My name is Aneesh Mehta. I'm an infectious disease physician at Emory University Hospital and the site P.I. for the adaptive clinical trial that Dr. Khalil just mentioned here at Emory. I'm also a faculty member of the ASPR-funded National Emerging Training and Education Center, NETEC.

And I just want to echo a lot of what Dr. Khalil has just mentioned. We are strong believers in examining the correct methods of taking care of patients with COVID-19 through well-developed clinical trials. And I will just start by saying Dr. Khalil has written a very nice editorial in JAMA recently. And I would refer people to this document as a really good rationale for why we need to examine scientifically what we're doing prospectively so that we can take care of our patients without causing harm.

So here at Emory, we are managing – here at my hospital – almost 45 patients with COVID disease, and throughout our system close to 140. We have several severely ill patients and moderately ill patients. We have been approaching all of these for clinical trials. We have not only the NIH adaptive trial, but we have another clinical trial for an IO six receptor blockades that's also placebo controlled.

And we strongly, again, believe that's the method to figuring out the right countermeasures for our patients. But I will also comment that we have taken care of dozens of patients that have not been receiving any medical countermeasures, but have been receiving very good supportive care, whether that be on our medical floors or in our ICU's, and we have been able to successfully treat them and get them out of the hospital.

We have had patients that have been on a clinical trial, and have been ventilated and proned and got them out of it and got them home. We've also had patients, not on the clinical trials, that have been proned and ventilated for several days and got them home. So, I think that we are learning a lot from

these experiences and again, I think the clinical trials will give us the answers. I will also mention we have apprehensions about hydroxychloroquine as a general countermeasure, as Dr. Khalil has mentioned.

I can tell you personally, I have had two patients who've come in the hospital who have been on hydroxychloroquine, and again, that's just two patient experiences, but one had been on it chronically for rheumatoid arthritis, and developed COVID-19, ended up in the ICU, and is now better. We've had patients on prophylaxis that have developed – with hydroxychloroquine that have developed COVID-19 as well.

So I, again, this has underscored the reason to do good examinations, good clinical trials to figure out the right ways to approach these patients, whether it be for treatment or for prophylaxis and I would encourage everyone to participate in some sort of study to get these done. Thank you.

Stephen Hahn: Administrator Verma, this is Steve Hahn, can I jump in?

Seema Verma: Please.

Stephen Hahn: I just want to congratulate both of you for the terrific work that you're doing. FDA depends upon this sort of data being collected in a rigorous way to make decisions about safety and efficacy. And the message we just heard from our colleagues on the phone here, I think are really important for practioners to communicate to their patients that we don't know, we don't have any FDA approved countermeasures for COVID-19.

We have terrific folks around the country gathering data to try to help us figure that out, but there are dangers associated with therapies and that has to be a doctor-patient decision, and just really strongly encourage the work that we just heard being done in Chicago and Nebraska, and we thank you both for your terrific efforts.

Male: Chicago? I am not doing any work.

Female: OK, well with that, do we want to open it up for questions?

Operator: Again as a reminder, if you would like to ask a question, please press "star," "1" on your telephone. And we have a question from (Patas Romenian). Your line is now open.

(Patas Romenian): Good morning. This has been very interesting, and thank you. I have a question. Are we using data from EHR? Because I'm a (hemologist) from Anchorage, Alaska, and the reason I ask is we have several EHRs like CancerLinQ and Flatiron where we're supposed to collect data that will hopefully treat patients in real-time from experiences from other patients. So are we using the EHRs to collect data and see how patients are doing? Say even in Italy or New York?

I'm concerns about our patients with cancer who were already receiving immunotherapy, and if they develop COVID, do we continue with the immunotherapy and how do they respond? Do we have data on that?

Stephen Hahn: This is Steve Hahn from (FDA), I can speak to the first issue. I know of no data with respect to the immunotherapies, and of course being a cancer doc, I likewise have similar concerns. We are partnering with EHR companies and also university systems to try to obtain some of the real world evidence that you're talking about. The infrastructure for that isn't as robust as it could be, but we're rapidly gaining experience and trying to help inform our decisions on the task force. So it's a really great suggestion that you've made, and it's an ongoing project.

Andre Khalil: This is Andre Khalil. If you'll allow me to just add to a response to your question is that, electronic records are going to be – they're going to be very important for us to understand the natural history of the disease and the natural history of different hosts, like patients with different situations like patients that are (immune compromised) from either cancer, from transplant. But the electronic records are not going to help us understand what works and what does not work, so they are really useless for efficacy.

They may help us a little for safety; let's say if you have more patients with (kidney) prolongation, cardiac arrest from chloroquine and (inaudible), that's going to be important, and that can be actually that can been seen in electronic

records. So this kind of electronic record cohort can be very useful for safety, can be very useful natural history, but unfortunately it cannot help us in terms of efficacy. So just trying to understand the strength and limitations of the electronic records. Over.

Alina Czekai: Thank you. We'll take our question please.

Operator: And your next question comes from the line of (Kevin Ohike). Your line is now open.

(Kevin Ohike): Yes, my name is (Kevin Ohike), I'm a surgeon in the Cleveland area and I think some of the data has definitely been shifted (towards) some of the medical frontlines folks in terms of therapies for healthcare workers, things of that nature. Have there been any discussion about the operating room and potentially some prophylactic measures for the O.R. staff and surgeons and patients for potentially COVID positive or even patients that are asymptomatic?

Andre Khalil: This is Andre Khalil. I can tell on our experience in Omaha here in Nebraska, we take all the precautions that are needed to be taken in terms of quarantine and PPEs. But I just want to remind you there are absolutely no treatments for COVID. Not only no proven treatments, there's no safe treatments.

And I truly believe that in some places people are using either hydroxychloroquine, chloroquine or azithromycin preventive. I truly believe this is way more risky than beneficial because these drugs have very poor activity against any of these viruses and they have a lot of side effects; and if you're going to (prophylaxis) everyone with these drugs, we're going to harm people.

So we have – we literally have nothing at this point and we cannot – you cannot really start to do prophylaxis on the basis of what potentially can do or not, because I really think that we're going to be misleading ourselves with these drugs, that the healthcare providers are going to be protected or are going to be safer, while the only thing that we know that can really protect him is PPEs and quarantines and make sure that you know exactly what the

situation with each patient. So we are not giving any kind of prophylaxis in terms of medications to any of our healthcare providers here in Omaha.

(Kevin Ohike): All right, just a quick follow up. I think there have been a lot of recommendations and guidelines of varying types for testing patients preoperatively before undergoing aerosolizing procedures, intubations, various laparoscopic procedures, but there's really – I think we don't really have that much guidance on the patients who again are asymptomatic, potentially have a cancer diagnosis that can't wait for three months for proceeding with surgery. I think some federal guidance may be helpful to decide when we can potentially do some preoperative testing on patients as to potentially increase our PPE, what we wear during the operations.

Female: That's a great recommendation, we will take that back to CDC and other partners at HHS, but appreciate that suggestion. Thank you.

(Kevin Ohike): Thank you.

Operator: And your next question comes from the line from (Chris Peterson). You may ask your question.

(Chris Peterson): Yes, good afternoon. I joined the conversation a little late, but I'm curious as to if there's thought of pursuing the drug Avigan, which is the Japanese influenza drug. Apparently it showed some promise and some use I think in China, and I just haven't heard of any ongoing interest in doing some trials regarding that medication.

Andre Khalil: This is Andre Khalil. I can tell a little bit about – we – this (cited peer review) has also been given to patients with Ebola and we just – we don't have really any substantial results, because there were controls. The only study published with (that drug) that I'm aware of, and somebody can correct me if I'm wrong, because anything can be published (I mean at the go) in today's situation, but the one that has been in the media, it's basically – it's just a retrospective small – literally, I mean it's a very small cohort in which they just compared a peer review with lopinavir and ritonavir.

There was no controls, there was no really kind of a clinical or survival data that was meaningful. So basically (case serious), to be honest with you. We just don't have any data besides the peer review. I think that it's a drug that has had (intravenous activity) a lot or drugs, but I'm not aware of clinical data in COVID. So I think if we have more clinical data, COVID-19, it's a drug that potentially can be part of a clinical trial. But I'm waiting to see more clinical data. I really didn't see (anything) other than that very small case series. Over.

(Chris Peterson): I would just say mechanistically, it seems to make more sense than hydroxychloroquine, to my way of thinking as being both a pharmacist and physician.

Aneesh Mehta: This is Aneesh Mehta from Emory University. It is a direct acting antiviral agent, so I would agree with you, it has probably better theoretical potential than something like hydroxychloroquine. But this underscores what Dr. Khalil said, we need good preliminary data so that we could potentially include this in the NIH adaptive clinical trial.

As Dr. Khalil had mentioned before, the adaptive trial, once the first 440 patients are enrolled, we'll analyze which agent – which are is superior, and the inferior arm will go away, and then one or two arms will come in, and we will look at all potential countermeasures that could be included, including combination countermeasures. But to get to the point to include them in a second phase, we need good preliminary data.

And so I would encourage those who are thinking about developing clinical trials to really formulate good, controlled randomized clinical trials, even if it's a pilot study so that data could be used into inform these larger adaptive clinical trials so that we can get these agents anaylyzed in a prospective comparative manner. Over.

Debra Birnkrant: Hi, this is Debbie Birnkrant. I think this also points to the fact sometimes in-vitro data and animal model data don't always translate into efficacy in human clinical trials. So that's something else to keep in mind. But it doesn't mean

that it shouldn't be further evaluated at least pre-clinically in an animal model to start off.

Alina Czekai: Thank you, next question please.

Operator: And your next question comes from the Thad Waites. You may ask your question.

Thad Waites: Yes, this is Thad Waites, I'm representing American College of Cardiology. And I just – of interest to everyone, we would be having our annual session at this moment in Chicago with more than 20,000 people, and we cancelled it of course. But we're doing it today virtually and it's proving to be a huge success.

Within the College of Cardiology, we have a list-serve and they're circulating about what to do about the thrombosis that's going on with COVID-19. It originated from New Orleans, where they're saying young people who are having thrombosis, preliminary embolism and so forth, so far and (a multiple messaging) back. Nobody really has any experience or any suggestion of how to handle this, and I was wondering if anyone in this audience could help with that.

Aneesh Mehta: So this is Aneesh Mehta from Emory University. We are also concerned about the potential prothrombotic potential as a COVID-19 infection and we have seen a few clots have developed in our patients. For our inpatients, we are giving them DVT prophylaxis and trying to ambulate them as early as possible, but also giving them guidance when they go home to watch out for symptoms of both DVTs and P.E.s and to report back to us if they're having any of those symptoms.

We've also educated our E.D. providers to know about this risk, so that they can evaluate patients with suspected or confirmed COVID-19 coming in with an onset shortness of breath for P.E.s as well. So I think the educational component will help us recognize these early and get the patients treated early and diminish the ramifications of acute P.E. and DVT. Over.

Thad Waites: We had a webinar with a Chinese cardiologist, and there was at least some suggesting that D-dimer could be associated with the risk of any thrombosis or a market for it maybe. Any comment on that from anyone?

Aneesh Mehta: Again, this is Aneesh from Emory. We are monitoring D-dimers. I will say many of our patients do have D-dimers during the acute phase of illness, but we are monitoring those. We have not had enough data to correlate a D-dimer lever either in mild, moderate or severe disease with a risk for DVTs yet, but the data is still quite early, but that goes to the point of collecting the data on these patients so that we can understand what the risk are moving forward.

Thad Waites: Thank you, I'm a fellow Emory grad.

Aneesh Mehta: It's always good to hear from someone from Emory. Thank you.

Alina Czekai: Thank you, next question please.

Operator: your next question comes from the line of (Adino Dougi). Please ask your question.

(Adino Dougi): My question centers on the DVT and pulmonary emboli. There is a clinician who put out some information from New Orleans saying that they were not treating for DVT or pulmonary embolism primary because most of the critically I'll patients had thrombocytopenia and also elevated liver enzymes and probably also had acute renal failure. So the question is, if you're using prophylaxis, are you using very low dose lovenox, are you Eliquis, what are you using?

Aneesh Mehta: This is Aneesh Mehta from Emory University. We are using our standard protocols. So depending on the risk factors, dictates what modality of DVT prophylaxis we're using, whether that be (SEDs) versus lovenox versus other agents. And then as far as treatment goes and what treatment we use for these thromboses, that is made on a case by case decision.

(Adino Dougi): Thank you.

(Alina Czekai): Thank you, we'll take one final question in this segment please and then we'll move forward with our agenda. Thank you.

Operator: And your next question comes from the line of Willie Underwood, your line is now open.

Willie Underwood: Yes, how are you doing? This is Dr. Willie Underwood, I also do a lot of population health things and clinical trials. So we know previously that we've been unable to accrue at that diverse population of patients in clinical trials. Is there anything that we're doing specifically here to assure that we bring in health systems that may or may not do clinical trials, but have a diverse population of patients who have been infected with COVID-19?

Andre Khalil: Hi this is Andre Khalil from University of Nebraska, Omaha. So very good question, as you realize, this is a very difficult situation which we are literally just trying to offer the trial in all the areas that are most needed in the country. And so it's in part the site selection that has been influenced by the need in different regional areas in the United States.

And so it's diversity, be it, it's something that hopefully it's going to be part of the whole process, but it's not something that, like in a regular elective, planned with primary (dormice) trial in which you're going to try to really understand the (diverse of operation). This is – we just didn't have time to really get into what normally would do with a more kind of as low paced (renovized) trial. This is a fast pace, we had to design and get up and running in matter of weeks and days.

So it's a very important question, but how (diverse of operation) we're going to get is going to depend on where you're going to enroll. At this point, you're enrolling patients pretty much in every corner of the country, so I hope that we'll have a well represented (population) of the whole country.

Aneesh Mehta: And just to add to what Dr. Khalil said, this is Aneesh Mehta at Emory. We've gotten a lot of questions from our partners in community hospitals and critical access hospitals, and unfortunately, we can't have the adopted clinical trial at every hospital, but I would encourage people to look at

clinicaltrials.gov, contact the representatives for the study that may be of interest to your centers, and try to get them on board at there.

There are multiple of these studies that are not as cumbersome as they – the NIH adopted clinical trial to onboard, and that will generate good data that will help us in the long run. So I would encourage people to try to find those studies if at all possible, and many of those have been launched at small community hospitals and critical access hospitals to date, so over.

(Alina Czekai): Thank you, Administrator Verma, I'll turn it back to you. Thank you.

Seema Verma: All right, thank you. And if there are additional questions, we'll open it back up to all the speakers, but we're going to move to the pulmonology and critical care treatment and therapy, and that's going to be led by Dr. Brian Stein, who's pulmonary critical care physician at Rush Hospital, and then we'll hear from Dr. Josh Benditt, medical director of respiratory services at the University of Washington medical center. Thank you. Dr. Stein, go ahead please.

Brian Stein: Thank you. Thank you for having me today. My name's Dr. Brian Stein, I am a pulmonary critical care provider at Rush University medical center, also the Associate Chief Medical Officer for hospital operations and I've been working fairly closely with our teams and our incident command center to search our capacity at Rush as well as working on the various protocols that are both COVID specific and not COVID specific for our intensive care units.

Rush is a tertiary care academic medical center in Chicago, and I was asked to speak on our experience, some best practices around managing COVID patients, and some specifics really around (proning) and tracheoscopy. So, our experience has been certainly a little more limited than the coasts since the ramp up really occurred mostly on the east coast and the west coast, but we are currently seeing our numbers increase rapidly.

We are also a high volume critical care transfer center, and so we've seen an influx of these patients as well and currently have upwards of 70 patients in the hospital and 30 COVID patients on mechanical ventilators at this time. I think, again, I think we're a little different than the rest of the city of Chicago

in the sense that we have a little bit of an enriched critical care population, but I anticipate everyone is going to be seeing more in the coming days to weeks.

So, again, I was asked to speak on some of the best practices, and one thing to point out is that, well, COVID-19 is new, the disease we're seeing in the ICU is not. From a pulmonary and critical care perspective, we manage this all the time as a condition, that condition being acute respiratory distress syndrome, or ARDS, just typically not on this scale. And the general recommendations for ARDS really apply to COVID type ARDS as well with a couple caveats.

So, I think the – and I'll go through the general recommendations, initially around managing these patients in the ICU, are if you have an ARDS patient with COVID is to use the standard lung protective strategies, low pressure, low volume, typically at 6 cc's per kg title volume and keeping the (platco) pressure in the place where we typically like to keep it. Also recommended, and again not isolated to COVID, are conservative fluid (to granities).

Now, one thing that did come out early is that these patients don't tend to respond, or respond more poorly to increased fluid administration. And so when we're faced with patient with low blood pressure, we're actually giving less fluids than we have traditionally to this type of patient, so we're kind of, it's (enacted) even more, can just – restrictive fluid strategy and move to what we call vasoactive medications or vasopressors, blood pressure – blood medication to keep your blood pressure up earlier on than giving liters and liters of fluids, which we typically do in the setting of concurred sepsis, which we do see with this disease as well.

The other thing that has been noted, and again there's not a lot of published literature on COVID patients, there's just case series sitting out there, I think we'll see a lot more of them coming to light. But they tend to like a higher back pressure or (peak) on the ventilator, and their lungs don't seem quite as stiff as we have seen in typical ARDS. Other recommendations have been to avoid systemic steroids, and again, as it could be controversial in the pulmonary critical care world, but many people avoid steroids initially anyways for ARDS unless you're using it for a different indication such as refractory shock or adrenal insufficiency in those circumstances.

With regard to prone positioning, and that was one topic that I was asked to talk about. So prone positioning is taking a patient who's on a mechanical ventilator and flipping them onto their stomach and ventilating them basically on their stomach for an extended period of time. Benefits have been seen in the population of doing it over at least for 12 hours when you're flipping someone.

And again, prone positioning's not new either for us, it has been recommended by most critical care societies as part of routine severe ARDS management, and that's based on data from roughly seven years ago demonstrating the mortality benefit, although there are those that still argue about that trial, given several prior negative trials that didn't show benefit in similar populations before that.

So, the question then comes down to, OK, if we're – if we are doing (proning), why do we want – why would it potentially be beneficial. And so we know that, again, from an (Alkem) perspective, there are – there's (Alkem) data that demonstrate survival benefit, but we know that you improve your oxygen levels, or improve your oxygen requirements through multiple possible mechanisms when you take someone and flip them from their back to their stomach.

As I mentioned, there are – there's a potential survival benefit in doing that, though there is no COVID specific data around survival. There are some case series demonstrating perhaps some improved lung compliance in very small case series, but again, no COVID specific data around (proning), and again, this is endorsed by most critical care societies as the standard around managing severe ARDS.

And so the questions are, why might it even be controversial if it's recommended, it improves survival, it improves oxygen saturation. And it's because it hasn't been widely adopted across the county for several reasons. So, one is it's not risk free, so when you flip someone onto their stomach, you can deal with the complications of potentially developing pressure wounds

from having those areas of the body in contact with the bed or other medical devices over time, so you have to be very cautious with that.

You can run into problems with blood pressure when turning patients and we would abort if that happens. Another concern is the loss of endotracheal tubes or the breathing tubes or the loss of IVs, or central venous access or basically anything attached to the patient when you're trying to turn the patients. It's just a mechanical complication of turning someone with lots of lines and tubes attached to them.

Another concern, again, is obstructing the actual breathing tube when you do that, so there is risk to doing it, but what has been demonstrated that if you have an experienced team doing it, that it can't be done safely with no increase in complications. The other reason it hasn't been widely adopted across the country is it's very labor intensive. It takes a team of six or more people to flip someone and keep all the line and tubes intact, and that's maybe even six or more people at times.

And if you think about a patient who might weigh 300 or 400 pounds, to turn them over on a mechanical ventilator with a team and not lose anything, not have a complication, is a really daunting task. And while the studies have demonstrated that there may not be any increased complications, all of the trials that have looked at this have had very experienced proning teams or they were intensive care units with years of experience in doing this.

So it wasn't like they – we went out to the community and said OK, start proning people, and didn't have these sorts of complications. And so – so at Rush, what are we doing currently? So we are proning people, we haven't had this many ARDS patients on ventilators at the same time, and if you think about proning 30 people every 12 to 16 hours or if you get up into 60 or even 100 people, that's a real daunting task to implement this kind of therapy.

So what we're doing currently is developing or creating a team basically that's going to have to go around to do it, because it would occupy the entire ICU's team time to go from room to room otherwise and perform this procedure. So

I think another important question still to answer is whether it's making a difference or not.

I know we'll get a fair amount of observational data out of this and that may help to answer the question. But it might be an important question to answer with the number of patients who we're going to see in current states in ARDS on ventilators.

And then, the other question is can it be safely performed in the community. And I think that's a really difficult question to answer and it really depends on how many patients you have and what kind of support staff you have in a community hospital. And so, I'll move on.

For a tracheostomy, this is a work in progress even for us. I have a team that have kind of put together guidelines based on communications with China, with folks that they know there. And I haven't seen the – there may even be a guideline statement.

But in current state, the last recommendation I saw was waiting until day 21 with two negative COVID tests. I'm not sure I would endorse that recommendation yet, I think it needs more discussion around – again, if you're going to have to wait that long and they have – and they have negative testing on repeat testing whether you even need to wait that long or you could go earlier if need be.

And then the last area I wanted to talk about a little bit was ECMO, or extracorporeal membrane oxygenation, which is kind of a salvage therapy for ARDS and done by only specialized centers which are ECMO centers, which is for patients with refractory ARDS. And there are, I think, cautionary tales out of China with respect to just go ahead – moving ahead with ECMO routinely with really high mortality rates in this population.

However, in the – if you have enough – a tight enough selection criteria, there still may be patients that we want to implement this modality on. Again, that's even for academic tertiary coronary care centers, it's very labor-intensive from

that perspective and I think there's going to have to be some careful thought about who we are actually putting on ECMO as we move forward.

And that's all I had and so I'm happy to hand off to the next speaker and answer questions.

Seema Verma: Thank you, Dr. Stein. That was terrific.

Dr. Benditt, do you want to go ahead and give your presentation? And then we can just open the line for questions for both speakers.

Josh Benditt: Great, thank you. I'll go ahead and present now. First of all, I'd like to go ahead and thank the organizers for inviting me. Not only am I presenting but I have learned a tremendous amount already.

My name is Josh Benditt. I am a pulmonary critical care physician at the University of Washington School of Medicine in Seattle. I am the medical director for respiratory care services at our main academic center and work very closely with the other three medical directors at our other three hospitals.

And what I'm going to talk about today – I think Dr. Stein has done a beautiful job talking about the (direct) critical care. I'm going to talk about some issues that we have been dealing with here with regards to respiratory care and ventilators and – which I think might be helpful for other places around the country.

So the three areas I'm going to talk about is managing our ventilator supply here at the University of Washington, the second is managing the respiratory care practitioner personnel supply, and then the third is an idea that is being worked on right now about load sharing between hospitals in the Seattle area. We're a large and very growing metropolitan area and there are number of private – large private hospitals around and we are working with them.

So the first point, management of our own ventilator supply, so the first thing that I have done is an inventory of each of our hospitals in terms of the ventilators that we do have. And I was very surprised to find that we had ventilators in areas that you would not necessarily expect them to be.

So for instance, in our outpatient day surgery arenas, in outpatient clinics, they have anesthesia ventilators as well as some portable ventilators and I did not realize that. We've got them into our database. We then spoke with our anesthesiologist about operating room ventilators. And this may be a topic about which there are questions that I'm happy to answer.

We found that at my hospital alone, we had 60 O.R. anesthesia ventilators. And given that we have about 60 ICU ventilators available, we were able to double our ventilator supply almost immediately.

We then – and I came up with this, about establishing what I am calling a conceptual tier categorization of the types of ventilators that we have. So for those of you in pulmonary critical care, this will be obvious to you, but for other folks maybe not so much. We have standard ICU ventilators that most ICUs have. They've been designed for taking care of critically ill patients and they have been treating people with ARDS, as the COVID-19 patients are, for decades.

That is the major supply for us. However, there are other types of ventilators available. There are anesthesia O.R. ventilators and the more modern devices have every capability of a standard ICU ventilator and can be moved out of the operating room.

We have a large number of transport ventilators that we have brought into our database. They are generally used in transporting people either from outside hospitals to us or from O.R. to ICU, but they are capable of ventilating patients with ARDS.

We then have a supply of home ventilators and these are ventilators that would be used at home by people with neuromuscular disease, tracheostomized patients, et cetera. Again, there may be questions on those as well. I'll tell you how we are using them.

Lastly, we have many, many BiPAP and CPAP units and we have a lot of calls trying to donate those to us. I'll tell you how we utilize those in a moment.

So in this kind of tier system as a conceptual framework, we are using our standard ICU ventilators for intubated patients with COVID-19, assuming that they are likely to develop ARDS which is seen in many of these patients. We're also using it for other critically ill patients with ARDS but we're trying to conserve those.

We are going to be using our anesthesia O.R.-ventilated patients for intubated COVID-19-negative patients. That is somebody who comes out of the O.R., needs ventilation for a day or two. We'll use it for them. Obviously, we have patients coming in with pneumonias, severe asthma. They will be used for them.

We are going to need to train our respiratory therapists and we've developed a one-page review sheet for the types of anesthesia ventilators that we have. Also, our anesthesia techs are helping out our respiratory therapists. Because we're doing less operations, they can come up to the ICU.

The transport ventilators would be used next. We're using it generally for COVID-19-negative patients and also have negative testing. They are a little bit less solid than the other two types of ventilators. They're much smaller. They're a little bit harder to do (exhalatory) filtration on, meaning to not blow secretions into the room.

Home ventilators, we are using those only for COVID-negative patients with negative testing. They also have some issues with filtering the (exhalatory) ports on the ventilator, so we're using them on patients who are not positive. The same thing with all the BiPAP units and we hope not to ever need to use those.

The difficulty with both the home ventilators and the BiPAP units, again, is that they don't have all the capabilities of the ICU ventilators and they also are a little bit more difficult to make sure that the exhalation side of things is filtered with respect to the room.

And if we end up having to treat COVID-19-positive patients with those lesser ventilators, we are going to make sure that the rooms and everyone going into

them use full PPE. And especially – there's been a lot of debate about using non-invasive ventilations for COVID patients.

I've worked with non-invasive ventilation for many, many years and, although there's debate as to whether it is truly an aerosolizing procedure, I think at this moment in time there's not enough data and we really need to say that it probably is. So if you're going to treat people with a BiPAP or CPAP who have COVID, I would say that you need to use full PPE.

Split ventilation, meaning using one ventilator for multiple patients, here we have decided we are not going to do that. For those of you who are physiologists out there, there are some real issues around two patients on one ventilator and who will get the lion's share of the ventilation. And we decided we are not going to do that. I know that has been in the news, we're not going to do it.

Point two, the management of our respiratory care practitioner personnel, so the first thing that we have done – and I think most places have – is cancel all outpatient respiratory care activities. That means we've shut down our pulmonary function test lab, where we have about six respiratory care practitioners. We've cut out our respiratory care practitioners in any clinics. And we've taken our practitioners who are involved with home care and brought them into the main hospital for surge capacity.

My excellent manager for respiratory care has actually designed a three-level of R.T. assignments in the ICU depending on the surge numbers. I should mention, we're predicted to have our surge here in Washington state somewhere in the second week of April, we don't know exactly.

But our usual for a respiratory therapist is about six ventilated patients per therapist in the ICU. If the surge were mild, that's probably where we'd stay. If we have a moderate surge, we're going to have 12 to 14 ventilated patients per respiratory care practitioner. If we had a severe surge, there would be 20 ventilated patients per respiratory care practitioner. Obviously, that has loosened up our hospital policy, but it is what it is.

So far, thank goodness, we have not entered the surge and we haven't had to go to those very high numbers per practitioner.

The last point I wanted to make was about load sharing between hospitals. At our center we have what's called an infinite command center, I would guess many places have that. We have twice a day phone calls with the directors of the hospital and people from various departments. We know every day, twice a day where all the COVID patients are in our system as well as the city of Seattle. And what we have done within our system is that we are doing load sharing.

So if somebody is coming in to our emergency room and it looks definitely like they're going to have COVID we will send them to the place that has the most capacity. We have actually transferred one or two patients who developed the very severe disease from our community hospitals to the university center, and it's balancing the numbers of patients that we have. We obviously can't do that on an hour by hour basis, but we look at the trends.

Then, we are trying to develop a system for load sharing between all Seattle region hospitals. So we have a number of large private hospitals, we are speaking with them regularly, and what our hope is is that if one hospital gets overwhelmed we will bring patients over to other hospitals that are less busy.

You may remember at the beginning of this the life center nursing homes had this gigantic number of positive patients, they went to a small – well relatively small community hospital who did a fabulous job with them. But basically once they were full we said all further COVID patients are coming to the main centers.

So that's a lot of kind of information – I've tried to make it as practical in preparing for the numbers of patients that we see. I will stop there, and I guess we can entertain questions.

Seema Verma: That was terrific Dr. Benditt, really appreciate it. And we'll probably have somebody follow-up with you on your use of the ventilators, I thought that was very interesting…

Josh Benditt: Sure.

Seema Verma: … and I think something that a lot of folks could benefit from. With that, why don't we open it up to questions at this point? I know we're running (out a little bit of time), but we're can try – we're going to try to do these calls more frequently so that people have an opportunity to present more information and ask questions.

But we'll just use our remaining time for the questions, and then I think there is a few words – I think we were going to talk about the rheumatology patients. So if we get time for that, that'd be great or otherwise we may do that on our next call. Thank you.

So Operator, if we could open it up for questions?

Operator: And we have a question from (Sharon Keane), your line is now open.

(Sharon Keane): Yes, thank you for taking my question. First of all I'm about to become a frontline telehealth provider for a new app, (COVIDMD), so all of this information is very helpful to knowing what's happening across the country.

But I am also a friend and colleague of a former Surgeon General Rich Carmona, and I queried him about the possibility of a (topical) approach to the COVID-19 infection, because we know as a surgeon we always look at things anatomically. We know that this virus goes in through the nose and the mouth.

Has anyone looked at nasal sprays and throat gargling as a means to reduce viral burden? Because that is a cheap and easy way that we could add to hand washing to potentially reduce a patient's risk of infection and reduce somebody who is infected, reduce the transmissibility. And there have been two small studies that I know of that showed a reduced viral burden with these maneuvers, has anyone studied this?

Seema Verma: Is there anybody from FDA on the line that wants to take that question?

Male: (I'd say if Dr. Khalil is still there).

Andre Khalil: (Well thanks for passing about). Now, I'm not aware of – I think it's an interesting question. I think the – but to be honest with you, as I mentioned there were very – what we know even from just regular pre-op studies we know very little. We have just not enough data to have a (safety issue) in terms of know.

Because even if let's say, even if – honestly if I just – if we're able to provide a solution that has antiviral capacity, even something that's not so irritating as alcoholic solution, but something that could reduce the amount of virus in either the nose or the mouth.

It's biologically interesting, but the reality is it's – that alone wouldn't be enough (for us) really to provide a safety for the operating procedure because besides reducing (a load) you want to make sure that whatever is left in the upper (airway) is not going to be contagious to healthcare professionals and to other patients.

So I think it's an interesting idea, but we have not seen the fruition of this either in the past, or currently. It doesn't mean it shouldn't be looked at, I think it's an interesting idea but I'm not aware of any data that could support (it) to moving forward at least during the outbreak. I think it's something that can be studied, but I'm not aware of anything (that can bring any changes).

(Sharon Keane): Well, I mean there is data to support a reduced viral load, it's been studied for the common cold which included coronavirus. They're small studies, but…

Andre Khalil: Great, but the – reducing…

(Sharon Keane): … I (cannot) agree with you – it would be dangerous to do in an operative setting, but for prophylaxis, and for the general population reducing viral load could conceivably reduce infection and maybe even symptom severity.

Andre Khalil: It's – I think that theoretically you're absolutely right, but we also know that the viral load – it's quite unreliable especially in the upper (airways), it's very hard to know the clinical significance of viral load, so I'm just trying to play the devil's advocate here in the sense that I agree with you, that that's a very interesting concept, that it should be evaluated.

I'm not against, but I'm just saying that I'm a little bit (skeptic) about the viral load being predictive of things, because it's very much a consequence of the collection of the data, the (inaudible) – so there are a lot of variables that they have to account for. But I'm not disagreeing with the concept, I think it's an interesting concept.

(Sharon Keane): So who would I talk to about conceivably getting such a study done? Because just telling the public to wash their hands is a great idea, but if we could tell the public to also spray their nose, and gargle and reduce the risk that asymptomatic carriers could spread their infection, this seems like a simple no-brainer if we know that it can reduce viral load.

Seema Verma: Thank you. We'll pass that on to the CDC as well. Operator, can we go to the next question, please?

(Sharon Keane): Thank you.

Operator: Yes, and the next question comes from the line of (Joanna Baeskurl), your line is now open.

(Joanna Baeskurl): Yes, I do have a question. I am a family physician in Wisconsin, and I'm also a public health – I'm a local public health official, and so one of the things that all of us have been working so hard to get right is the dissemination of accurate information. I want to – I know he's not on the call, but I really want to tip my hat to our surgeon general who has been working day and night to make sure we get the accurate information out there.

I guess my question is from the more general standpoint, because a lot of the information that's come out has been confusing, especially with regard to treatments and what would work, and what doesn't. I've heard so much information on this call regarding medications that we should not be doing.

We've been trying so hard to get the right message out there, I'm almost – I think I'm asking and pleading for just (inaudible) centralized guidance from the government to help us get the right message to the public. So, what can we expect?

Seema Verma: Thank you. That's a great suggestion, and we have a lot of government officials on the lines today. So that will certainly give us, certainly some things to do (in task) and you're absolutely right, and we appreciate the advice.

Can we go to our next question…

Debra Birnkrant: Hi, this is…

Seema Verma: I'm sorry, go ahead.

Debra Birnkrant: Hi, this is Debbie Birnkrant. I'm aware that the Department of Health and Human Services is starting a treatment guidelines panel, similar to the ones that they have for antiretroviral use and treatment of adults and children with HIV. So they're starting an HHS panel on COVID-19, so I think we all have to stay tuned for that.

Female: I have a question.

Seema Verma: Go ahead, please.

Female: Me? OK. I was (curious as) – so I'm frontline primary care doing telehealth, I already do a lot of it. And so I have a lot of patients that are coming to me saying things like they'll lose – loss of small and taste, and I'm managing them at the house, they're not critical, they don't need to go to any sites.

But (we supposed to one), be reporting these patients because in both Michigan and Ohio none of them are able to be tested because they're not critical (and lack of pressing things), but I also feel like the information would be needed for public health stats, hey we have these people are sheltering in place (inaudible) with COVID-like symptoms, especially the – (he) had nausea and stuff. And so just curious on guidelines on that, and if the whole loss of taste and smell truly is a real thing (scene)?

Brian Stein: So was the question whether we should test them…

Seema Verma: (Maybe from – go ahead).

Brian Stein: … test more people? I'm – this is Dr. Stein, I didn't…

Female: No, so testing (in-home) – yes, so I'm in Ohio and Michigan, I'm on the border so I work in the poorest parts of Detroit, and then also in Toledo. And I have a lot of patients that I'm having shelter in place, take – and it's just they're having COVID URI symptoms with it, but the thing that makes me think they have COVID without any exposure is the loss of taste and smell that you keep hearing about in the news and different (inaudible) saying that this is COVID.

I've had – I've talked to both health departments and they said yes, send them to these places to be tested. The patients called to get set up for testing and they got turned away because they are not considered a moderate or severe case and there's not enough testing.

So am I supposed to be reporting these patients, since we can't get testing? And then on top of that, is the whole loss of taste and smell truly something that has been found to be unique to COVID now? So it's like a double-sided question.

Brian Stein: Well I think that – again, I can't speak to the local testing, but I think that's an acceptable general recommendation is to really test your higher risk patients and make the recommendations you are making, to keep those who are lower risk and likely do have COVID infection, at home, from that perspective. And we know that'll be – (any epidemiologic measurement) we're typically not going to have data on those patients.

Female: (Inaudible)…

Seema Verma: Thank you. We'll take our next question, please.

Operator: And you next question comes from the line of (Dr. Cheyanne Hart), your line is now open.

(Cheyanne Hart): Thank you so much for taking my question. I had just one a couple things, one was related to the favipiravir. I do believe there's a Chinese study with

340 cases out there, so I did send some info to the fda.gov address, so thank you so much for giving us a way to communicate, I'd like to get that to Dr. Khalil.

I am in West Lake Village, California, west of – I'm in Los Angeles County. One of the things I'm doing is as a small private practice owner is trying to help small practices adapt as quickly as we can to doing only essential care, and to providing the ability to reduce the flow to ERs and Urgent Care.

But what I'm finding in the sense of things that we can take care of community so that urgent care and ER can take care of respiratory diseases, well one of the things I'm finding is clinical practices are quite far behind. Like two months maybe – sorry – two weeks or four weeks behind in how to deal with these things.

So I'm still seeing practices taking people's temperatures or having staff go up to people's faces, take their temperature; checking travel history. At this point we are – with the number of cases in the world and the number of countries, we're far – we're far along in that sense.

So I was wondering if the FDA or CDC was planning to give some instruction to small practices so that we can avoid putting our staff right in the face of people who are presumed COVID positive.

Additionally when we're looking at one percent of people with – asymptomatic people in Iceland testing positive for COVID-19 and 6 percent in the Netherlands. I presume that we should be instructing all practices to presume that ever patient is positive if we're having any sort of in person visits.

So as we transition to telemedicine and work our way down in these inpatient businesses to urgent care, I just hope that we can remember the small practices that are trying to help reduce the burden to the urgent facilities. So I'd love any commentary on that. Thank you.

Female: I know I have my practice in Down River, Michigan; which is the poor part of Detroit that no one realize they're talked about. And we have a very big

practice that's able to have a great triage center and help take the burden off ERs.

But we can't get our access on to any PPE. So we want to help be the front line but if we can't get PPE, we can't help. And so that definitely limits. And then you also have other providers that aren't believing that this is real still and are still seeing patients and putting their staff at risk without PPE.

So just getting that more out there. But I see what you're talking about with being far behind because I've seen it in some of my colleagues.

Seema Verma: Great. I think we just have a few more minutes here. We're a little bit over on time. (Dr. Nicolade), do you want to make some – just a few comments on the impact on rheumatology patients.

(Dr. Nicolade): Sure. So I'll try to be brief because I know we are short on time. But first off, I would like to thank the organizers for recognizing this important topic and the opportunity to share some thoughts and considerations on how COVID-19 situation affects patients with (rheumalogic) conditions but I would also include transplant patients because some of the considerations are pertinent to that population as well.

And – but first I'll start with a fact that he rheumatology and transplant patients are immuno-suppressed for the most part due to either their disease or treatment of their disease and by default they're at higher risk for infections and potentially more serious disease and death related to COVID-19 even though some of the published literature (all be it) limited, suggest that they may fair similar to the general population.

On a different note, immuno-suppressants and immuno (inaudible) therapies use rheumatology and transplant patients have received significant attention as potential treatment options for patients with COVID.

And as a result, these treatments are getting diverted to combat COVID-19 and are or may soon be no longer available to these patients and that became apparent from the very first question that we received from this call today about the hydroxychloroquine shortage.

Even as we consider the promise of some of these products, we must also remain cognizant of – and responsive to the development that could bring unintended consequences to other patients.

As it was highlighted, we have seen a significant surge in demand for chloroquine and hydroxychloroquine, which has had impact on patients who are dependent on these treatments like patients with systemic glucose and rheumatoid arthritis.

And for systemic glucose this is a corner stone of treatment. As Dr. Shah has shared in his response to the question before, this shortage has been on the FDAs list to address and FDA has been working and will continue to work with all the stakeholders to mitigate the shortage.

In addition, a contingency medical treatment planning may be in order for patients, prescribers and professional organizations to consider in the setting. And I just want to point the audience to the American College of Rheumatology that has issued guiding principles to scarce resource allocation during the COVID-19 pandemic, specifically talking about the case of hydroxychloroquine.

There has been also some publicity on the use on non (steroid) anti-inflammatory drugs, which are used by many of the (inaudible) of the rheumatology patients but also general population.

And the FDA has also published an advisory on this topic, recognizing that there have been news reports stating the use of a non steroidal anti-inflammatory drug such as ibuprofen could worsen COVID-19.

However, at this time FDA’s not aware of scientific evidence connecting the use of (house aids) like ibuprofen with worsening of COVID-19 symptoms and the agency continues to investigate this issue and will communicate if we have more information.

There are also a few additional considerations that are not specific but are relevant to the rheumatology and the transplant patients and the first one is

that we have to recognize the impact on – (with the medical fair) which was already shared by many of the callers where some healthcare services are now only performing emergency visits or procedures.

And some healthcare services have shifted to virtual visits. COVID-19 epidemic has also impacted families, emotional, social, and financial well being and this is clearly a stressful time and this has various impacts on families and health patients and their families.

And last but not least, COVID-19 has had an impact on the clinical trial enrollment and participation such as potential suspending enrollment, changes to (inaudible) participation and assessments, and the resources have been diverted to COVID-19 clinical programs.

And to guide the considerations for the conduct of clinical trials, the FDA has proactively issued in the last week a guidance for industry investigators and institutional review boards on conduct of clinical trials of medical products during the COVID-19 epidemic.

So again, I promise to be brief and with this I would like to thank you for the attention and more importantly to thank you for being in the front lines of managing our patients in these challenging times. We are humbled. Thank you.

Seema Verma: Thank you. And why don't we just have a couple questions for (Dr. Nicolade). That was a great presentation. And then I know there are still probably more questions and this is just the beginning of the discussions that we need to have around COVID. So we will be having more calls.

And if you want to send questions in advance, we can try to make sure that we have speakers in lined can answer those questions. And I really do want to thank all the speakers today. I think you guys have done an amazing job today getting information out.

Again, just to echo everybody's sentiments about those of you that are working on the frontline and appreciate the suggestions that we got from the

government as well and we will go to work on those. But let me just open it up for a couple more questions. Thank you.

Operator: OK. And we have a question from (Earlby Door). Your line is now open.

(Earlby Door): Thank you very much. We already talked – I'm a rheumatologist. We already talked about the shortage of hydroxychloroquine. The other problem is because of using the aisle six drugs to treat the cytokine storm, my patients have not been able to get their (subcutaneous and intravenous actemra) and my local hospital is actually taking the actemra that they've ordered form their supplier and saving it for their COVID patients of denying my rheumatoid patients access to therapy.

So I wanted to make certain that the FDA was aware of this shortage as well. I've talked to the company and they say they're not able to keep up with the demand. So if the FDA could also work on the actemra in addition to hydroxychloroquine, I would really appreciate that.

(Nicoli Nicolov): This is (Nicoli Nicolov). We certainly appreciate you comment and I just want to assure you that this potential shortage is also on our radar. Aisle six targeted therapies have been one of – some of these therapies that are considered for investigation and potentially on the shortage list and can impact particularly rheumatoid arthritis patients. But we are aware of this and we'll keep working on trying to address this.

(Earlby Door): Thank you. I appreciate very much because I'm – my patients (are now kind of going from infusion center to infusion center) trying to find a place for them to get treated so there RA doesn't flare terribly. So I appreciate it.

(Nicoli Nicolov): Yes. And we heard about also (inaudible) who need actemra for their disease that there could be potential shortages for them too. So that's another consideration.

(Earlby Door): Thank you.

Operator: And your next question comes from the line of (Michael Manterino). Your line is now open.

(Michael Manterino): Good afternoon. Thank you for that presentation, it's very helpful. I'm (inaudible) position in Pennsylvania. And again, we're not able to get testing kits or personal protective equipment. So I know you're going to work on that. I appreciate that.

But what are your thoughts about pediatric patients – we didn't talk about that – and their parents as potentially – if we're assuming they're asymptomatic carriers – should we convert everyone over to virtual visits.

And as you know that could be difficult with newborns and infants. Thank you very much.

Operator: And your next question comes from the line of (Juliet Presensky). Your line is now open.

(Juliet Presensky): Hello, can you hear me?

Seema Verma: Yes, we can hear you. Go ahead please.

(Juliet Presensky): Hello. Hi. Yes. (Juliet Presensky), Michigan. I basically have – and it kind of – there's some duplication with one of the previous callers is the issue with universal masking for healthcare staff. There are some issues with critical access hospitals.

A lot of the rural health regions, many of my colleagues and friends who work in healthcare and medicine are hearing a lot of backlash for wearing even standard masks in clinical settings.

And I just wonder will there be a mandate soon that will require that hospitals and clinical environments require everybody to wear at least a minimal standard surgical mask. In addition to that, obviously higher level PPE when t's called for with direct patient care.

(Argen Transosen): This is (Argen Transosen) from (CDC). Do you mind if I jump in on this one?

Seema Verma: Please do.

(Argen Transosen): We – it's an outstanding question. We already do have a recommendation for this healthcare worker masking. Is it universal healthcare working masking as a source control strategy in nursing homes. And it's a great question.

We are having discussions about moving that direction and issuing some recommendations on it in other types of settings. The biggest challenge of course is with PPE supply. We've been reluctant to make these types of recommendations because of the – of some of the supply limitations that we are hearing about and know about.

However, we are hoping that as supplies begin to become more available that these other types of uses of masks as source control could come into play, we think they could be helpful. So it's a great question and I think more to come pending what happens with the supply chain issues.

(Julie Presensky): Great. Thank you.

Seema Verma: Well again, I want to thank all the participants for joining us today. I think this was a great discussion. A lot of questions still out there that we'll try our best to make sure that those questions or try to get answered as much as we can.

Also we will be converting this discussion today into a podcast. So if there are – if some of your colleagues out that didn't get a chance to participate in this, we'll make sure that that opportunity is available.

We will be continuing these calls and so would appreciate any suggestions you have on topics or speakers. And again, very thankful to our speakers. You guys all did a fantastic job. Thank you.

Operator: Ladies and gentlemen, this concludes today's conference call. Thank you for participating, you may now disconnect. Speakers, please stay on the line.

End