

Tom Kraus: Good afternoon. Thank you so much for joining us today. I'm Tom Kraus, Vice President of Government Relations at the American Society of Health System Pharmacists. Today, I'm joined by my co-moderator, Amy Cadwallader, Director of Policy, Development and Quality at the Institute at US Pharmacopeia (USP). As a former FDA Associate Commissioner and Chief of Staff, I'm proud to continue supporting the agency through the Alliance for a Stronger FDA. We are delighted to have you all for today's webinar on drug shortages with Val Jensen. Val leads FDA's drug shortages staff.

There's been a tremendous response to today's webinar, and I think that probably reflects the current interest in supply chains and drug shortages. And I want to thank all of the Alliance members and guests and media for joining us today.

But before we begin, I want to just briefly talk about the Alliance for a Stronger FDA. The Alliance is a multi-stakeholder coalition of advocates. We advocate for appropriated resources for FDA and have been an important force in doubling FDA's budget authority funding from \$1.6 billion to more than \$3.3 billion. We also spend time educating policy makers, the American people, and media about FDA's growing mission and responsibilities.

We're the only advocacy organization that focuses resources on both the food safety and medical product side of FDA, as well as other parts of FDA's jurisdiction. Our members include consumer groups, patient groups, research advocates, health professionals, societies, trade groups and industry. We have about 160 members and continue to grow. So, we welcome other new members to further strengthen our advocacy and our educational efforts about FDA. So, please consider joining the Alliance, as we start a new year – particularly as FDA's responsibilities continue to grow faster than its budget.

So, for today's webinar, we're going to focus on drug shortages and the format's going to be split between an initial period where Valerie will take about 20-25 minutes to introduce the roles and responsibility of the FDA drug shortage staff, and address several questions that Alliance members have provided her in advance about shortages. And then Dr. Cadwallader and I will moderate a Q&A session. We encourage you to submit your questions for Q&A and you can do that by clicking on the Q&A button on the bottom of your screen. Please don't use the chat section. We won't

be able to see those as moderators, so please do use the Q&A button.

I now have the privilege of introducing our speaker, Valerie Jensen, Associate Director of FDA's Drug Shortage Program. I know many of us in the audience have worked with her on shortage issues in the past and know that she is an outstanding leader in addressing these issues. Valerie received her degree in pharmacy from the University of Iowa in 1990. She completed an ASHP specialized residency in ambulatory care at White River Indian Health Service Hospital. She's worked as a clinical pharmacist for Indian Health Service Hospitals in Arizona and New Mexico before joining the FDA. She was a member of the US Public Health Service Commission Corps and became Associate Director of CDER's Drug Shortages Staff in 2012. So, Valerie, thank you so much for joining us today. We look forward to your remarks.

Valerie Jensen:

Thank you so much, Tom. And thank you so much to the Alliance, for inviting me today. And I agree, this is a very, very important topic. A very timely topic. And it gives us an opportunity really to talk about all that FDA is doing in this critical area.

So, I wanted to start out, really I continue to get questions quite often about the types of shortages, we're seeing, what we have seen and just bring everyone up to speed with what types of shortages are occurring and have occurred; so, the types of shortages that, in past years and even currently, mostly shortages of older sterile injectables and mostly related to quality issues. And that's really been an ongoing issue.

And then, of course, during the pandemic, we've been seeing new challenges. Challenges related to increased demand and that's been a really new area that has been challenging. During the pandemic as well, we had competition on manufacturing lines and that's still occurring due to vaccine production and other COVID-19 related products. So, the same products being made on those lines are making the vaccines and COVID related products, and that creates a competition situation.

One other really new area is the increase in demand for commodities due to the large-scale vaccine production. So, things like glass and filters in manufacturing and vial toppers and all those type of things that we really haven't had those types of

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supply chain issues like we have currently been seeing. And so, it's really brought on new challenges and ones that we're definitely addressing. And then, I think recently, what we're really seeing is, and this Fall, we're seeing again some more increased demand, unfortunately due to increased respiratory illness. We're continuing to monitor all of that really closely and do everything we can to work with the firms to address these issues and to talk about numbers of shortages.

So, our website where we continue to keep that updated daily with new shortages and then of course, when a shortage resolves, it goes into the resolved section. There are 123 current shortages posted on our website, and that is a little above normal. It's fairly consistent though, from year to year, keeping about- around 100 shortages at any given time for the past many years. That sounds like a lot. Some of these are more intermittent situations, where a company is continuing to produce, but not in the complete volumes required to meet total market. So, it's varying as far as different stages of recovery and you can see that on our website.

Which firms have product, which ones are continuing to produce and release. So, the number of new shortages changes each year. In the past couple years, we really would've expected numbers to be much higher than they were. There were 38 new shortages in 2021. We would've expected higher than that. However, the challenge really is the ongoing shortages. So, the ones that started in 2021, we're still dealing with them today during 2022. So, these ongoing challenges are the ones that we are continuing to really focus on and develop ways to address those.

So, what is really our role in the drug shortage staff that I manage? We really are a coordination role; We're mitigating, preventing shortages. We're bringing in every expert in FDA that's needed to address a particular shortage or prevent a shortage. We're really the hub of the wheels, as we like to say. So, we're dealing with our industry colleagues. So, the pharmaceutical industry, really having close communications with them on any given supply situation or shortage situation. And of course, bringing in our Center for Drug Evaluation and Research (CDER) experts. So, whatever the particular issue is, if it's a chemistry issue, a formulation issue, or a manufacturing issue, we have folks that we can call on at any time, really. They're on call 24/7 to come in and help, so that's really important.

Also, we really value our relationships with outside stakeholders. So, professional organizations: ASHP is also a great partner. They have a drug shortage website as well and we trade information daily. We also communicate regularly with professional organizations and patient groups, really trying to get communications out on supply chain shortages. So, another area where we have really good, important relationships is our international counterparts, too, our regulatory authorities in other countries, so that we can trade information on what's happening in our countries. Sometimes shortages do cross over and it's helpful to hear what's going on elsewhere in the world.

But when a shortage occurs, or when a shortage notification comes to us, what are the steps that we take? So, as you probably know, there's a requirement in the 2012 FDASIA legislation that requires companies to notify FDA if there is going to be a supply disruption. So, that is really important. Early on and getting as much detail as possible, as far as what is happening, what's causing this supply disruption, what's the duration – getting all of that information. So, those notifications come into us daily and it may just be a preliminary potential issue, and that's fine. It doesn't mean it'll go on our website, but it means that we'll investigate it and work with the company and anything to do to mitigate and prevent an issue.

So, once that notification comes in, we first do a market assessment. So, we're looking at the total market of that product, all the manufacturers in that market, what're they able to do, what is their inventory, all of the information that we need to put together, that current market picture. And we can also compare that against historical sales data that we purchase. Looking at, is there a supply gap or is there expected to be a supply gap? When we put all that together, we also are doing a medical necessity determination. So, that is a determination made by our clinical experts in FDA. So, we go to the relevant clinical division and they're answering basically a question of: is this a drug for a serious disease or medical condition? And are there appropriate substitute products that could be used? So, we're looking at that as well. So, we're looking at the impact of that shortage – are there alternatives and can those alternatives meet demand? And so, we're putting together that entire picture of whether this is a shortage issue or are we going to be able to fill the gap. So, then when we're looking at what tools we can use, we really have a very complete well, a good set of tools that we use.

And that's been consistent through the years, so we work obviously with the company that's having an issue. Working with them on any particular mitigation strategy that they have and working with the other companies in that market. And of course, expediting review of anything that any of those companies need to increase supply. So, if it's a new raw material supplier or a new component or a new glass vial supplier that they need. Any of those issue, we'll work with them closely and we'll work with our chemistry group –our Office of Pharmaceutical Quality or whatever group needs to be involved – and we'll expedite review of anything that needs to be approved to help with the shortage.

So, the other area where we are routinely involved is in regulatory flexibility issues. So, this is when I mentioned earlier that most shortages are related to either quality issue in a plant or quality issue related to a product itself, such as a defect, like an out of specification or a product suddenly has a new impurity or things can happen over time, even with older drugs. So, when that type of thing happens, what we'll do is have the firm put together a proposal and we'll have our experts evaluate that proposal and see if there is any risk to patients, any significant risk to patients from whatever that defect is.

So, I can give you an example. Particulates or some particles in a sterile injectable should not be there. So, a sterile injectable that's given intravenously – you can't have any type of particles in that product. And sometimes things happen during manufacturing, or something happens, or sometimes glass can get in there. There are things that could possibly get in a product – this is something that's happened through the years. For a critical drug, a medically necessary drug, we would want the company to look at ways that they could potentially mitigate that. So, one way has been to use an inline filter at the patient bedside or even using a filter to draw up the product when product is being prepared by pharmacy.

So, if the company can actually prove that a mitigation, such as a filter, could deem the product safe for patients, we would review that and, of course, if we agree with that it's a critical drug, it needs to be available, but this is a temporary mitigation strategy. We would have a "Dear Healthcare Professional" letter developed by the company and then shipped out with the product and posted on our website. So, that's an extreme example but there are many different examples of many ways we'll be flexible in keeping

product available while the firm works to correct the problem.

So, if we don't have these types of options. So, if our US manufacturers, our approved manufacturers aren't able to address the issue in a timely manner, then we need to look to our overseas counterparts. I mentioned we have good relationships with our counterpart regulatory authorities in other countries, so we will reach out to them in that case and see what's being marketed in their countries, and contact the manufacturers of those products and see if that's a potential for temporary importation. And that's something we've done more commonly than in past years, I think when we've had some of these issues where it's a drug that's absolutely needed for patients and it's something that we can use as a mitigation strategy.

As I said, these are temporary importations. So, once we have approved product meeting the total demand, then we end the import. Also, we try to encourage the importing firm to get approval so that we have another manufacturer on our market.

But an example of this type of mitigation, step by step, is fludarabine injections. So, we had a critical shortage, or we still do have a shortage of fludarabine injection, and that's a critical cancer drug, and it's used for a lot of promising new therapies as well. It's an old drug, but it went into shortage when two of the manufacturers were having some manufacturing delays and then the other one was having a raw material issue. So, we had to work closely with- well, we're still working closely with all three firms. But the company that had the raw material supply issue, they needed to qualify a new raw material supplier. So, we're working with them, and they ended up making product with unapproved raw material, which we were able to use our regulatory flexibility to review the data about that product being made with that raw material, and it was deemed safe to be used. There's really no difference from the approved product. So, that drug is posted on our website now, and the availability is posted, and then that company, of course, will get that raw material approved, too, and we'll expedite review.

So, another step that we've taken with fludarabine is a temporary import. So, we want to make sure that supplies are available for patients. So again, a temporary import was identified, and that overseas product was very closely looked at, very closely reviewed and made sure that there are no risks with that product for US

patients. And that product is being imported now, that's on our website as well. So, those are examples of really, the types of things that we will do, I mean, to make sure that the product is available for patients. It's really always our goal to ensure availability while also ensuring no risk to patients.

So, I also get asked: how have shortages really evolved over the years and what do we really anticipate going forward? So, I think one thing that we really see going forward is these demand increases. This is something that is fairly new to us. It's something that we really are looking at closely. We really want companies to inform us if they're seeing spikes in demand because that's currently not required. So, the requirement that I mentioned earlier about notification of supply disruption does not actually include notification of increased demand. So, it's something that we did put out a guidance during the pandemic, I believe March of 2020. So, that's still in effect. And that guidance does encourage companies to report increases in demand to us. Because again, if we can know about those spikes in demand early on, then we can work with the tools that we have to prevent shortages. So, that's something that we're continuing to look at closely. And we're also looking at other ways to use supply chain data, to look for potential signals of shortages.

So then, I also get asked about our approach to addressing a shortage versus preventing a shortage, and how is that different. So, some shortages are really not able to be prevented. Either there was a sudden issue, like a plant shutting down or a manufacturing line shutting down, maybe a sudden issue with a raw material supplier. Those are sometimes unforeseen by companies, and so by the time we get notified, it's too late to prevent. However, in those cases, when we can prevent, we are using those same tools to prevent. So, we're expediting review, we're looking at potential ways that we can use flexibility to allow product to be on the market while the company fixes a problem. All of those tools are really the same for prevention and mitigation, but I think that the key is early notification. The earlier companies let us know about an issue, the earlier we can deal with it.

So, as far as our role, not just what I've talked about, but a lot about our Center role in the Center for Drug and Evaluation and Research. We also have other agency components working on shortages. Our Center for Biologics has a shortage program. We have our Center for Devices. And I should mention, Center for

Biologics deals with vaccines and blood products, and then we have Center for Devices, which we deal with device-related products. So, empty syringes and those types of things, which do cross over into drugs- our drug realm as well. So, we have very close communication with them, with both of those Centers, on shortage efforts.

So, we trade information. We work on products that jointly affect us. And then our Center for Veterinary Medicine also has a shortage program as well, and we communicate with them on anything that crosses over there too because sometimes- obviously, human drugs are sometimes used for animals as well.

And some of the new types of investments – or, I think, the new types of endeavors that we're really involved in, there are several, actually. But one that we really think is important is the recent CARES Legislation which actually requires companies making certain products to have risk management plans. And that's something we've really talked about for years, is having if companies are able to build redundancy and resiliency into their system and be able to identify vulnerabilities early on, and be able to react to those or to be able to mitigate anything related to those. That could really help prevent shortages. So, this is exciting to us, to have this requirement for RMPs– risk management plans. There was a recent guidance put out by our Office of Pharmaceutical Quality telling firms really what they should be looking at for vulnerabilities and really how those plans should look.

So, that's something that we really do believe will be helpful going along. I think, really, all of our efforts really have been heightened during the last couple years. I think we've had many more challenges to face than usual, but I think our team is a very dedicated team and the agency really considers shortages to be a priority. So, we're really glad for this opportunity to talk today. Thank you.

Amy Caldwell: Thanks so much, Valerie, for those comments. We really do appreciate the detail you provided. One of the things that stuck out to me is, you mentioned a significant number of shortages arise from manufacturing quality challenges, and that you do work with the Office of Pharmaceutical Quality. Could you comment a little bit more about the role of OPQ and how they work with you preventing and mitigating shortages?

Valerie: Yes, absolutely. So, our Office of Pharmaceutical Quality really contains- so, that's the group that really will help us when we have any type of quality issue. So, whether it's a product quality issue – so something, a defect with a particular product – and commonly, those types of things we've seen just across the board. I mean, things can happen. I think in manufacturing, it could be something very, very minor. It could be just even a labeling error or something in the packaging, or it can be something more serious, like I mentioned. Particles or a sterility issue would be extremely concerning.

So, I think any of those issues, we get the information from the manufacturer, get the firm's assessment on the risk as far as what do they believe the risk to patients is, and then have all of that together as a package. And our Office of Pharmaceutical Quality reviews that, and we also bring in others too. We'll have our clinical experts review as well, as far as patient impact. We may need our pharmacology, toxicology experts depending on what the issue is. But it's really important to have that team of experts on hand. And believe me, they will- they'll drop everything and help when it's a shortage issue.

Tom: Great, thanks. Thanks, Valerie. We have a question from the audience about the Public Health Emergency. And I think there's interest in that coming to an end at some point, in the presumably not too distant future. Are there particular authorities that you have that are tied to the PHE, or is there something about the way you work that will change when that PHE is over and affect your ability to respond to shortages?

Valerie: I think, so for us, I don't believe it'll – it will not affect our ability to respond once the PHE is over. I think our role remains the same throughout the PHE and beyond. We're going to do a revised guidance. I mentioned the guidance that we issued in March of 2020 about notification and what we want firms to notify us of. And I think we'll need to modify that. That was really a COVID specific guidance, so we'll modify that. And we will need to include some provisions from the CARES Act. So, there's a new provision about notifying us about API shortages. And so, we'll include that. So, I think that will be one thing.

I know another part of the PHE is having these Emergency Use Authorizations. So, some drugs have been available under EUAs, or Emergency Use Authorizations, during the pandemic and during

the PHE. So, once the PHE is over, then I think that'll be something to look at: how to work with companies on gaining approval of those products that they are seeking approval for and then making sure that there's still access.

Amy: Thank you for those insights. Another question from one of the panelists: supply chain and drug shortages have been in the news a lot over the past couple of years, and there have been a lot of suggestions and proposals and recommendations made in published reports to increase resilience. And some of these reports come from the White House, from the national academies. Are there any particular recommendations that you've read in any of these reports that you or the drug shortage staff feel could truly be helpful in mitigating or managing shortages, or is there anything missing from your perspective in these conversations?

Valerie: Definitely, there are potential solutions for shortages, for sure. We continue to investigate as well on our end. I think I can refer back to- so in 2019, we had a congressional request for a report. And that request was really for FDA to look at, what are the root cause of shortages, as well as enduring solutions. And so, we knew a lot of that was beyond FDA, so we involved a lot of stakeholders. I know many, many, many groups came in and we listened and had listening sessions. And our economic staff was largely involved with this as well.

Some of the root cause really came down to what I talked about as far as mainly quality issues, and especially for the older products, which are maybe less economically viable. And so, looking at what would incentivize firms or how do you incentivize companies to maintain quality. And so, that's really something we are focused on in the agency right now. So again, I'm going back to our Office of Pharmaceutical Quality.

And so, they have an endeavor right now called Quality Management Maturity, where they are looking at ways to develop possible ratings systems for companies, where companies would be incentivized really to have a quality maturity- a mature quality system and be able to get rated and be able to show that rating. And I think that's one area where we're really looking strongly at.

Tom: So, another question from the audience related to coordination with other agencies. You mentioned coordination that's required with other components of the agency, but we would love to understand

coordination with other agencies, like DEA in particular. If there's anything you want to share around particularly how you coordinate with regard to shortages for controlled substances, that would be helpful.

Valerie: Yes, that's a great question. And if you look at our website, there are some shortages currently of controlled substances. However, those are not related to quota- to DEA quota. And as you know, DEA does grant the raw material allowances, which are the quota allowances for companies that make controlled substances. So actually, in the law that I mentioned that requires the notifications that was enacted in 2012, it also requires an interaction with DEA if there's a company that needed quota to address a shortage or mitigate- prevent a shortage. Then FDA would interact with DEA, and we'll assess the market, we'll assess whether that's a shortage concern, and work closely with DEA.

So, we have an MOU with DEA. And that's how we would work through that issue. And I can tell you, we've not had shortages related to quota. We work very closely with DEA on those issues, and they take that very seriously as well. So, it's been a very good relationship and it's worked really well.

Tom: Thank you.

Amy: Thanks, Val. During your talk, you mentioned shifting in shortage driven from spikes in demand versus supply chain disruptions due to quality, and how this is new for the agency and that you're figuring it out as it progresses. Can you comment a little bit more about that and maybe what the difference is in management of the shortage versus the spike versus a disruption might look like?

Valerie: That's right. So, I think really- so again, I think one ask that we have of industry is that they notify us of those spikes, because that will help us early on. And I think when they do notify us, they're seeing a trend. And of course, we can monitor too using data that we have to watch: are there trends occurring? And that's something we're really looking closely at, too. But then, I think then it's really, really important even if we're seeing a trend on our end, then reaching back to the manufacturers and asking what they're seeing, and just having that continued communication. I know right now, with the increased respiratory illnesses, we're seeing increased demand. And as you know, probably the amoxicillin oral suspension is currently in shortage due to

increased demand. And so, in that case again, we're having very close communication with the manufacturers and using all of the tools that we have available to help them increase production and resolve the shortage. So, definitely working very, very closely on these issues.

Tom: Can you just elaborate on that a little bit, around some of these ongoing shortages that we're experiencing. How does the agency think about anticipating shortages when there is this anticipated uptick in RSV? How do you not just engage the manufacturers, but also communicate with healthcare providers and consumers to try to avoid hoarding of product and other concerns like that?

Valerie: Yes, that's a good point. So, to your first point, I think the ongoing shortages— these ones that are difficult, they're challenging for us. Those, it's really taking just more of an effort of hand-holding and working with companies on what else can they do, what else are they able to do to resolve this shortage. And then these new issues that we're seeing now, knowing that there is an uptick in respiratory illnesses.

And then, it's just a matter of really reaching out. Monitoring the market, seeing what companies are experiencing and then downstream as well. Working closely with pharmacy associations as well and other trade groups and seeing what's being experienced out in distribution and at the pharmacy level. So, it's really important to get all of those pieces together and so, seeing what's actually happening on the ground is really important too.

Amy: Thank you for that. I'm going to shift gears a little bit and talk about some devices, or just ask a question about that. I know that over the past several years, and as you noted when you were speaking earlier, that we've seen shortages of tubing and syringes and things like that. Specifically, how does the drug shortage staff coordinate with the Devices Center and other agency groups to address those that might not necessarily be the drug, but is something really necessary for administration of the drug?

Valerie: Yes, absolutely. And so, during the pandemic, so we had shortages of diluent. So, the drug- the liquid – either it's saline or sterile water that's used for diluting other drugs. And so, we had a very severe shortage of that occurring and a lot of that was related to an increase in need for the vaccine. So, needing that same diluent that was used to dilute drugs for vaccine as well. So, that's an area

where this crossed over into our Center for Biologics because they are managing the vaccine issues. And then it also crossed into our Center for Devices because pharmacists were having to- so to dilute, they were having to use either empty bags and dilute in a bag, or they were using empty syringes, pulling solution out of larger IV fluid bags to dilute drugs. And it really crossed over into our Center for Devices where they were ending up experiencing shortages of some of those components. And so, keeping that information flow and continuing to work as a team between the Centers was really important during that time, and it still is.

Tom: I'm seeing in the Q&A that we have several questions that relate to geographic risk and geopolitical risks of onshoring. So, can you help us think about, how does the agency, when it's assessing risk of a shortage or responding to a shortage, think about these geographic or geopolitical risks? So, that's Question 1. And then Question 2: does the agency have a perspective on the impact of sourcing raw materials from particular geographies, or the benefit or not of onshoring? I think I'm seeing several questions that relate to those- those topics.

Valerie: Sure. Sure, so of course during the pandemic and beyond, we've been looking at potential areas where products are being made in areas of the world where there were shutdowns – maybe there were labor shortages. So, looking at what are the vulnerabilities and identifying the factories and also the drugs that're being made in those areas and looking for potential vulnerabilities. And I believe another important piece of recent legislation is the CARES Act, where we have now a requirement for companies to provide us manufacturing volumes data. So, companies will be providing the amount of product being produced at their sites. And so, I think that's a new piece of data that will really be helpful at piecing together where things are being made and looking for potential vulnerabilities; looking at maybe where there are concentrated markets, or maybe similar to back in 2017, where a lot of our IV fluids were made in Puerto Rico and then we had the hurricane and that caused a shortage. So, I think looking at those types of things, where vulnerabilities might be, being able to think ahead about that type of thing is important.

Amy: Another question from the Q&A chat function. You mentioned earlier of importing drugs from other markets to potentially alleviate shortage. Can you comment on the requirements that those drugs are held to? Is it similar to FDA approval or are there

any exemptions?

Valerie: So, when we identify a company overseas that's ready and able to help with a US shortage, one thing we do initially is make sure we're not going to cause a shortage in another country. So, we do end up importing from Canada quite a bit. They have a much smaller market than us, so we want to make sure that our demand isn't going to cause a problem in Canada. So, we work on that aspect and then as far as the product itself, all of the attributes of that product, the formulation, the labeling. Sometimes the labeling is in another language. So, that has to be addressed too.

So, anything that is different about that product, and it is very closely evaluated by our teams. So, anything that's different gets put into the "Dear Healthcare Professional" letter that gets sent with the product and also ends up on our website too. And another thing to note too is, we do make sure that we evaluate the facility-the facilities that the product is made in as well. So, if we didn't perform an inspection, then we can rely on a foreign inspection and get all the information that we need to ensure that that site doesn't pose any risk for patients nor does that product.

So, I shouldn't say it's a long process. We've done it really pretty quickly and efficiently. But I think it's a lot of effort, but I think it's absolutely worth it when we can make product available for patients.

Tom: Val, you mentioned in your opening comments that there are some shortages that are demand driven, but there are those that are just persistent shortages and have been in existence for several years. I know from the health system pharmacy side, we see that a lot with sterile injectables. What is driving those persistent shortages? And what is it that prevents the market or existing manufacturers from resolving those shortage, bringing more supply online?

Valerie: Yes, and I think that goes back a little bit to our 2019 report, especially for these older sterile injectables. Just, the economics are not really incentivizing firms from entering these markets. So of course, we hope to have firms interested in entering the market for these drugs that if you look on our shortage list, have been there awhile. And it's not that they're completely out of stock. There is product being made, it's just not being made to those levels that we can resolve it. So, there's not inventory buildup. There is not consistent supply and I think that goes back

to, too, with a lot of these, especially with older drugs, that there are many drugs made on the same lines- same manufacturing lines, and so they're competing with other products. And so, it's difficult for companies, especially with low revenue producing drugs- they're trying to prioritize, they're trying to shift things around and keep availability, but there just has not been the capacity to really resolve, especially some of these older drug shortages. And I think we're there in that same place for quite a few drugs right now that are on our list. So again, I think what we hope is that other companies, at some point, will be interested and submit applications for some of these products, and those would be expedited.

Amy: Yes, a follow up to that as you were speaking came in the chat. Just wondering if there are considerations of incentives for companies who fill in a gap when necessary or add redundancy where there isn't. Has there been any thought or consideration for that?

Valerie: Yes, I think that would probably require legislation, but I think it's something that's being looked at and what would incentivize firms. From our end, in FDA, of course we'll definitely expedite anything that we can to address a shortage. So, that's really our incentive for firms.

Tom: Is that handled on an ad hoc basis or is there- can you just talk about how you would consider whether some things should get an expedited review?

Valerie: So in our Office of Generic Drugs and Office of Pharmaceutical Quality, they have, definitely, a policy on this and how things get expedited. But if something's in shortage, that's in policy – that will be expedited. So, medically necessary drugs that're in shortage, they do receive expedited review. We ask companies to notify us when they're submitting those submissions and then we'll help coordinate as well.

So, that's very routine. So, I think if something is more risk for shortage, then the company can let us know that they believe there's a risk of shortage and state what that risk is and tell us about it and I think- well, we would investigate further and see if there is there a risk for shortage of that product.

Amy: A question from an attendee on the White House's use of the

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Defense Production Act to reallocate resources. Has that impacted your Office at all? Have you been able to utilize any of the authorities from that? Is there any involvement that you've had with any of that reallocation or of those resources?

Valerie: Yes, so the DPA group in our ASPR, in HHS. We've had close communication with them throughout the pandemic and I think when there's been issues where the DPA has been utilized and then there's potential for maybe a shortage of another product that might be impacted, they've been really, really collaborative with us and worked to make sure that that didn't happen. And I think it's been a good collaboration, as far as the DPA- use of that and addressing some of the supply chain issues and then also, preventing shortages as well.

Tom: Val, you mentioned some of the provisions in the CARES Act and some of the traditional transparency provided there. Can you give us a sense of what the status of the implementation of those is by the agency?

Valerie: Sure. So, I mentioned, so the requirement for the risk management plans, that the companies are required to have those. I think that's something that is- they're working on that. And then, I believe for the implementation of the submission of the volume data, the amount of the product being manufactured at each site. So, that's also- that data is coming to us. So, we're working on our development of how we're using that. And I think, again, it'll be helpful for us. I think it's something that's really going to help us pinpoint where there might be some weak points in the supply chain for certain products. So, I think it's an ongoing effort.

Amy: Val, you mentioned the 2019 report that FDA published about drug shortages and the root causes and enduring solutions, and you talked about some of the findings in context of the questions. Is there anything else from that report that you would like to highlight or that you think is important for us to recognize or realize as we're thinking about drug shortages?

Valerie: Yes. I think there are several recommendations and several potential solutions. I think one recommendation, or one observation, is that I think sometimes, especially for hospital drugs, the public really doesn't sometimes know when there's a shortage of a hospital drug because pharmacists have workarounds, and they can use something else. And I think it's a concern in

many ways because people don't often realize the impact of shortages. So, the hospital is having to deal with a shortage of a certain drug and they're having to develop workarounds.

And that creates all kinds of trouble at the hospital, as far as risk of medication errors and having to use a drug that maybe you're not as familiar with. And also, having to substitute something that maybe wouldn't have been the first choice. And I think a lot of times, I think that does not get out to the public, that these shortages do have a lot of impact. And in FDA, we realize that. And so absolutely, we're doing everything we can to resolve them, even if they don't receive the public attention.

Tom: So, another question we received in the chat relates to some of the comments you made about when you can turn to or identify other facilities that can manufacture a drug that's in shortage. Is there a process by which you can do- prospectively do some of that identification? And how does that work? Is there a way to know the next place that you can turn to for manufacturing capacity?

Valerie: Sure. First, of course, working with our current, approved manufacturers that are marketing, and seeing what they can do for a particular shortage. We'll also go to companies that maybe used to manufacture, especially for these older, generic products. We end up with fewer and fewer firms making those products through the years, so companies will see them as not as viable over time, especially for older products, and discontinue. So, we will reach back to companies that used to market and see if they would be interested in resuming production or resuming their application. That's usually- hopefully, that's usually not a long process to do that. If they haven't made many changes to the plant or they've been recently inspected, that could be a quick comeback.

So, those are where we start and then, if we don't have those options, of course, we're also at the same time looking at anything that's in the queue that's currently being reviewed. Any generic drug applications that're being reviewed, we would make sure that those are prioritized.

And then, looking for outside the US, one thing we do first is we ask the currently approved firms if they market outside the US because a lot of times, our US firms will have a different version overseas. It may be labeled differently, or it may be a slightly

different formulation. But that's been successful, too, where even though a company- they're marketing here, they can't meet the demand, but they also have an overseas version that they can help. And then again, that would be a temporary import.

So, that would be where we're evaluating that overseas product as a temporary import until the approved manufacturers can meet full demand. And then, a large success has been these imports- getting those approved. And we've had a lot of success with that too – encouraging them to get approval because they've helped out during the shortage but now, we'd like them to continue to help. Because especially for the very limited markets – the markets where we only have two or three manufacturers – we want more stability there.

Amy: You've mentioned a couple of times, the economic impact specifically regarding some of the older, generic drugs that are very inexpensive. One of the questions in the queue is asking for you to comment a little bit more about the role of the marketplace and potential incentives that might help prevent some of these generics from going into shortage, specifically because of the lack of profitability or the economic landscape. Do you have any additional details about that?

Valerie: Yes, I think the FDA- to offer incentive, we really just don't have that capability. That would really take outside help. But I think, besides the expedited review, that's all we can offer. But I think as far as companies and what would entice them to enter these markets, I think that's going to definitely take some additional efforts.

Tom: We have a question about API and how do you assess when API is a shortage of an API or disruption in API manufacturing is actually going to flow through the system and become a threat to supply of a finished dosage form. How does the agency think about that, anticipate that and work with manufacturers to respond accordingly?

Valerie: That's a good question. So again, I think looking at where – so, when we do, as I mentioned- so, early in the pandemic, when we were starting to think about supply chain and reached out to all the manufacturers to assess their own supply chain and looking at where the vulnerabilities might be. And then, if there is an API supplier or an API issue with one firm, we're going to

definitely look at who else could be impacted by that. Now, with the CARES Act notification requirement for API supply disruptions, again, that gives us additional tools to find out early on about an API issue, and then trace that back to who could be impacted by that API and making sure that we're having those conversations. And of course, if a company is impacted by a raw material issue, API issue, if they want to qualify a second supplier. And they may be doing this as part of their risk management plans as well, to prevent shortages.

So, I think those are all good conversations. We want to have those conversations and have companies coming to us with those issues. And as we go along, I think we're continuing to look now with the CARES volumes data too, looking at where there could be concentrations, even in raw material markets. So, that's another area where we can look ahead.

Amy:

I have a question about- when you were talking earlier, you mentioned the differences between addressing a shortage and preventing one, and I think that's a pretty important concept. And you mentioned that earlier notification is one of the key things that would help with that. Can you comment about, in your work, is it a 50/50 split? Do you find that you're doing one versus the other, and are there other tactics or other things, different tools that you use to address versus prevent a shortage? Does that make sense?

Valerie: Yes. That's good. So, during we'll say, 2021, last year, we actually prevented a record number of shortages. We had 303 prevented shortages, which is way higher than previous years. It was 179 the year before. And it had been around that level for previous years. So, the 303, I think, was really- that was due to really increased collaboration. I think companies were coming to us much more often with potential issues and as I mentioned, especially with all of these various component issues. So, that was a new thing that was occurring where companies needed to think creatively about if they only had a certain number of manufacturing filters that're used in the process, how could they reuse those, or how could they propose to lengthen the time that they use those? And things that the companies came to us with, proposals to prevent shortages. And so, we want to see more of that. We think that was a very beneficial thing for all of us, I think being able to work with them on those issues. So, a prevented shortage, I'll just tell you, is one that FDA did something to intervene. So, it's something where we were able to help the

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company in some way or either give that flexibility or give an expedited review or some action that we took that helped prevent that shortage. So, really that was a huge success to have that many and we hope that continues.

Tom: Well, thank you Val, for engaging in this conversation with us. I think this probably generated the most questions in the Q&A that I've seen, and I apologize that we haven't been able to get to all of them. But before we close out, I do want to turn to Steven Grossman, executive director of the alliance to close us out.

Steven Grossman: Okay. I want to again thank Valerie for her time with us today. It's been an informative talk and shown us what an impressive job her office is doing. I wanted to ask her what happens on Thanksgiving.

I also want to thank our moderators, Tom Kraus of American Society for Health System Pharmacists. And Amy Cadwallader of the US Pharmacopeia. They both contributed to the success of the webinar, which I thought was very impressive.

Finally, I want to encourage our guests to consider joining the Alliance. We have about 160 members. Our voice would be even louder if we can grow that to 200 and beyond. Our website, www.StrengthenFDA.org, has additional information on our priorities and activities. Please get in touch with us to discuss how your organization or company can contribute to a stronger FDA. Thank you again to all of you for your time.

Tom: Thanks, Val.

Valerie: Thank you.

Amy: Thank you all.

[End of Audio]

Duration: 58 minutes