FOOD AND DRUG ADMINISTRATION (FDA)

CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)

Electronic Submission of Adverse Event Reports to FDA Adverse Event Reporting System (FAERS) using International Council for Harmonisation (ICH) E2B(R3) Standards

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Moderated by Suranjan De, MS, MBA

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Food and Drug Administration

White Oak Building #22

10903 New Hampshire Avenue

Silver Spring, Maryland 20993

Reported by: Jean Tompane

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A P P E A R A N C E S

List of Attendees:

Suranjan De, MS, MBA, Deputy Director Regulatory Science Staff (RSS), Office of Surveillance & Epidemiology (OSE), CDER, U.S. FDA

C O N T E N T S

P R O C E E D I N G S

THE REPORTER: Good morning. Today is Tuesday, November 7th, 2023.

MR. DE: All right. So good morning, everyone. My name is Suranjan De. I am the Deputy Director of Regulatory of Science in the Office of Surveillance & Epidemiology in CEDR FDA.

So, good morning. And today's topic is a topic -- is a topic on reporting premarket and postmarket safety reports to FDA using ICH E2B(R3) Standard.

So this is a follow-up of the presentation that I had in April of this year. And so this is the second one and one of the last ones before FDA -- and it goes into making this a live interaction system.

All right. So this is my standard disclosure. So, next slide, please.

All right. So what is the FAERS session overview? So this session will review updates to requirements for submitting safety reports for,

INDs, IND_Exempt BA/BE studies, and approve drugs and therapeutic biologic products, but excluding vaccine, using the ICH E2B(R3) format.

Also, we will discuss about implementation plan and progress and that's the most exciting thing probably everybody is looking forward for as to where we are with it and when will FDA be ready with this.

We'll give you something on testing updates. So we know that we -- you know, as sponsors, you would want to invest with us to make sure that, you know, your submissions are good.

And of course, we will also talk about FDA's readiness and submitter preparedness. So FDA readiness would be more of our FDA's, some timelines that we will share with you. And of course, with submitter preparedness, we want to give you some tips on more things that a submitter will do from their end to be prepared for submission ICSR using the E2B(R3) format.

So as for the objectives, so we will

have basically three objectives. And this is something that many in our organization would like to understand and know what the objective is of this presentation since they are attending this. Is we recognize that FDA will require reporting of IND and postmarket safety reports to be submitted in the R3 format to FAERS to the Gateway or Safety Reporting Portal.

And then also, understand updated regional extensions that are key for postmarket, IND, and IND_Exempt. And of course, we communicate our implementation status and readiness.

As for the second, regional extension, I won't go into too much detail of the regional extension because I did that in the April meeting. Today, I will just talk about a few updates that we had with regional extension based on the testing that we did on some of our industry models.

All right. So today's agenda -- so today's agenda, we're going to recap from the previous public meeting. We will talk about the implementation

plan and progress, external and internal testing updates. We'll take a break for 15 minutes. We'll talk about the regional extension updates, FDA readiness, submitter preparedness, and we'll go into a summary.

Now, to recap from the previous public meeting. In the recap, we'll also go over some of the questions that were asked at the previous meeting which we were unable to provide an answer during that meeting. So many of these kind of slides, which will talk about some of the questions that you had asked, and we have prepared some answers and responses for these questions.

All right. So the recap from the previous public meeting. We had that meeting on April 4th. It was a six-hour meeting. All right. And six hours of my talking. And the meeting agenda, presentation, and slides, and recordings are available at this link. So you can always go back and look at the recordings of the previous meeting.

Before I get into the next slide, I

just wanted to let you know, I actually have a little record. My voice may sound that I have a cold. So I'm trying to stay away from everyone. So just excuse me if my voice cracks. All right. Let's go to the next slide.

So some recap from previous public meeting. So what did we talk about last time? So we talked about the implementation of R3 submissions of both premarket and postmarket at the same time. We still have the same plan. We will have a new date for voluntary reporting and we will communicate that in the future slides that you will see.

And we will also communicate all of that in the FAERS Electronic Submission web page. We have not done that yet. I know our plan was as we go through the final implementation date. We know the month, just final date in that month, and then we will update the FAERS Electronic Submission web page.

I'll also be referring to the -- one of the important documents, which is a Core and Regional Data Elements document and everybody needs to be using

that to understand all the core and regional elements. We talked about Controlled Terminology, the Separate Submission -- Separate Submission Path, and the rules.

So one of the paths for IND vs. IND_Exempt vs. postmarket. It's very important because that helps us in different shading in the reports such that premarket reports to market published publicly versus postmarket published publicly. The submission methods and mechanisms are based on the AS2 header and Routing ID. Also, we had talked about Safety Reporting Portal, that is also another option that companies have. All right. Next slide.

So as for the rules of triaging of ICSRs via ESG, so we had talked about how the reports would come. So we have the premarket ICSRs submission and the postmarket. In the premarket side, now you have the AS2 Header. And for the premarket, CBER. So those XML files will come and it appears in the reporting system, so this -- the left-hand side, all

you will see is basically the submission that you will do and then how will it show up in our FAERS System, so we know that that's a premarket report.

Same thing for CDER INDs. And the reason why we have these two separately because there are some IND numbers which coincide, we can see that in CBER, so to differentiate whose report is for who. And then to send it to the right reviewer. We have that routing and the XML file and the destination already set.

Then we go into the postmarket. Postmarket, we have kept it as the same as we have today as we do with R2. So none of those headers and the IDs have changed. And that report gets sent there and now we are able to differentiate between premarket and postmarket reports.

And within the premarket reports, we are also able to differentiate who the safety reviewer is and see they are in CBER. And this reports that accordingly. Published or not published and accordingly sent to the right reviewer. Okay. Next

slide, please.

So the Submission Path Business Rules. This is, again, very important while we were doing system testing and while we were doing investor testing. We had to review this and make sure that everybody understands. So that's why I have to point us back again.

If you look at this table here, we have the premarket ICSR, if it is 4CDER_IND or CBER_IND, or IND_Exempt_BA/BE, viability -- ICSRs, then in that case, the values are provided. For AS2 header, for routing IDs, and N.1.4 should be inside the XML file, which means the values of N.1.4, and within a batch, you will have messages which is N.2.R.3 and what should be the values for that.

So it's important that is followed because this actually -- N.1 extend makes it all foolproof that these reports will stay and not get exposed publicly. And the report needs to be published, also it makes sure that it goes to the right reviewer for review, so it's very important that

these values are maintained and set in your systems so that when you send these XMLs, and send it to the right headers.

We also have rules where it says that if you send something with an AS2 header or a routing ID but does not have an N.1.4 or N.2.R.3 values, then there will be a rejection. So -- and -- so for all messages -- for all messages received that are in the file, which is CDER and on the batch receiver and different ZZFDA. So if you had that as CDER or your N.1.4 was ZZFDA_PREMKT, then you're going to get a rejection.

And similarly, that if you had N.2.R.3 as CDER_IND, or CBER_IND, or IND_Exempt_BA/BE, then N.1.4 must be ZZFDA_PREMKT. If it was only ZZFDA, you will get a rejection.

So -- so, yes. So these rules are very important and you follow them so that we can appropriately have these, you know, set in our database, in our FAERS system, and that these reports are secure and not -- and also, remember, just to

note, that based on this setup, we have in our FAERS system, a concept of a published flag, which gets set based on this. So it probably sets it up to not publish.

So we are very -- because now that FAERS is going to start getting premarket safety reports, which it used to not before because everything was in CTD, so more and more -- it becomes more and more important that we take the right precautions and right controls in order to safeguard these ICSRs. Okay. Next slide, please.

Okay. Some other things that we had discussed was the regional extensions for IND, IND_Exempt_BA/BE, and postmarket safety reporting. We have plans for validation and implementation. We have the E2B validated. We will be posting that on the Electronic Submission web page as a link. And I'll let you know what the date is, it's on one of the slides. This validator will actually help you in testing your excimals [ph] before your submission.

We also last time talked about

regional-specific rejection and warning rules that we have. There has been some updates to those rules based on our industry testing, which I'll go over. We also talked about FDA OIDs in our regional extensions.

And also, the R2 to R3 forward compatibility. It's mostly applicable for postmarket safety reports, because premarket, we never had R2 standard. So this has not changed, still the same.

So -- so for forward compatibility -- and that is very -- also very important that we have also noticed, especially in our organization, when we are talking about R2 and R3, everybody is looking only at the ICHS BFC document, which is the backup forward compatibility. But BFC document will not talk anything about the regional data elements.

So it is all -- it is important that you also look at the regional data elements for that, look at the FDA's forward compatibility document which is also posted on the FAERS Electronic Submission page. So both documents are important to see. Next

slide, please.

All right. So just -- and I'm changing gears a little bit. I have got some questions I have received recently on ESG NextGen. And I know this is not part of -- this is not E2B, this is not E2B R.3 standard, but I just wanted to give a little information on where we are and -- and you know, what the status is.

So the ESG NextGen offers an application like an API assistance with tasks including initial and subsequent submissions. All of the ESGs NextGen are built using RESTful Standards for ease of integration. And the API standards for security enforcement to ensure data exchange is secure, data is secure.

So with ESG NextGen, the industry can use API to generate the API submission ID, create submission payload, and submit the payload to the FDA to process. The combination client ID and the secret key is a unique identifier that each industry partner will use to submit data to the FDA. The FDA will

publish more details in the future, but the draft specifications is here.

How this is going to have an impact on what you have today will also be communicated, which currently it's not, but we will definitely communicate that to you all as to what in fact -- will it have an impact on the way it's working today with our industry. Next.

And FDA will also disseminate this testing information in advance so industry partners can update their respective process to be prepared for the testing. So there will be a good amount of time that will be provided to do that testing. But as of now, this is what the status is, nothing has advanced much.

So as of now, you know, the status quo is whatever you were doing, continue with it. And when new updates come, you know, you definitely will get notified of those. All right.

All right. So next then we will talk about some of the comments and questions that were

asked in the previous meeting that we had on this April meeting in April. And I'll go over a few questions I think that will be important for you to understand. And we made these questions more an FAQ and posted up on our FAERS Electronic Submission page.

So going into some of the questions, so one question was that, yes, there has been change to the latest MedWatch. This is dealing with certain data elements that the MedWatch had. Like, for example, gender was a new data element, and there was one more data element that was added to the MedWatch form.

And the question was does R3 technical specification -- consider these new gender data elements. When we had published this R3 the first time, these data elements weren't there. But once the authorization happened, these data elements came in. And so let's go into the answer.

So FDA is considering updating the R3 to include the gender data. We still have to -- just

to add a new data element is just -- R3 is flexible, but it's not that easy. We have to work through the -- through the -- you know, the HO7 [ph], B3 model, so -- so right now, yes, we are looking into it, but currently, we are not going to be updating our technical spec to include this data element right away. But at some point, we will incorporate this, so we are considering updating for the future of the specification, but not right now.

All right. Another question, once 7-day or 15-day IND safety reports are submitted via either submission method, the ESG or the SRP, does the sponsor still need to submit in eCTD format or notify the FDA project manager? So once the IND safety reports are submitted electronically via the -- via SRP or the Gateway, submitters do not need to submit them in the eCTD format or notify FDA project manager.

Because once it has come, it comes into FAERS, the project managers -- the FDA project managers and the clinical reviewers will automatically

get notified based on that submission that has come into FAERS for those IND safety reports.

All right. For a small business sponsor that has an ESG account but does not have in-house XML capability, are they able to submit ICSRs through SRP? And the answer is, yes, they can submit using the Safety Reporting Portal. That's the whole reason why we have the Safety Reporting Portal. We have registered the Safety Reporting Portal. And once you are registered, you have an account, then you should be able to log in and submit safety reports through the Safety Reporting Portal.

All right. Next. So if we -- so if we are cross-reporting ICSRs, which IND number should be in the header? The IND for the study in which the event occurred or the IND for which we are submitting to? And the answer to that is sponsors should use the IND number under which the clinical trial where the event occurs is conducted as the primary IND number in the indicated E2B data field.

So when you have a cross-reporter,

that's what -- the primary IND number will be in the primary IND number field and the cross-referenced INDs will be the in cross-referenced IND fields. Given that these two fields are regional elements that the FDA has defined.

Can we upload an XML file in SRP instead of entering data manually? And the response is, no. Because if you have XML, then might as well use the Webtrader and submit the XML. Right? Because Webtrader is something which doesn't cost, and you can have an account, and you should be able to submit. In Webtrader, of course, you can only submit one file at a time. But with SRP, the whole purpose of SRP was that the data is to be entered in, which becomes structured, and then -- and then we get that data and put it into our FAERS system. So -- so no, SRP, you have to manually enter all the data. If you already an XML, then you can use the Webtrader to submit.

All right. So is there any work being done to sync the required fields between FAERS, VAERS, and MedWatch? And the answer is, yes. FAERS has

harmonized the data elements between these to the extent possible. We have tried as much as possible to -- to make sure that the required fields are in sync.

But with the VAERS data elements, there are some additional VAERS elements that we don't have. We will -- we do have plans to work on making sure that the FAERS and the VAERS structure or the technical specification is combined into one harmonized specification. We have not done that yet. We want to get our affairs started. When we work with VAERS, we will work that through.

But to an extent, we have tried to make sure that core values, the data element properties that is being used between FAERS and VAERS are the same.

All right. Please confirm if FDA.C.1.7.1 must be set to a value of six, which is 7-day when submitting follow-up information to an unexpected fatal or life-threatening adverse event study for a clinical trial. And the answer is, yes, that is correct. This is a very straightforward

answer. Okay. Next question.

Okay. Regarding the Medicinal Product Name as Reported, presumably, it would be preferred to use the coded product description and local tradename from the company's product library rather than the verbatim medicinal product name as reported; is that correct? And the answer is, please refer to the FDA Regional Implementation Guide that we have talked about in the Section 4.2.5.3, Data Element G.k.2.2, it stands for medicinal product name as reported by the primary source.

So what would FDA prefer? FDA would prefer to receive the United States Local Medicinal Product Name, which would be the same name submitted in the structured product labeling format as a standard format for the exchange of drug listing.

So this also supports auto-coding of the submitted safety reports. This is something we really encourage all the companies, that when you are submitting the -- the suspect product name, especially with a primary suspect product that you have, please,

please, please use the name that you're registered with through SPL. Because that's the name that is -- in also in our product dictionary. So when a report comes in, it auto auto codes and we don't have to stop to report for manual intervention. So it's very important that those names are the same.

All right. Next -- another question is regarding the data element FDA.G.k.13.r. That is FDA Specialized Product Category, for combination products, would this be entered for any combination product ICSR or just malfunction or 5-day? Also, would this be provided as -- provided in addition to FDA Procode? The response is, yes. I missed the why, sorry. Yes. The FDA Specialized Product Category for combination product is applicable for all ICSRs for combination products.

So if you have a product report, yes, that special category is useful. And just not only for malfunctions, but -- but any combination product. It just gives us additional information about that combination product. So it has different

categories, and depending upon the category, you can provide that information in the FDA.G.k.13.r.

All right. Could you please confirm that when cross-reporting IND -- okay.

Cross-reporting IND Safety Reports to FAERs, sponsor needs to only submit one report to the primary IND and provide a list of all of the affected INDs? All right. And the answer is, yes, that is correct. Sponsors should use the Data Element FDA C.5.5a. It stands for IND number where AE occurred, to report the IND number under which the clinical trial where the event occurred. And sponsors should also use the indicated repeatable Data Element, which is FDA.C.5.r6, IND number for cross-reported IND to submit individually other relevant INDs.

So if you also have -- you can report all the cross-reported INDs, you don't have any kind of -- any kind of criteria to say only reporting these ones and not that one. So if you had cross-reported INDs for that primary IND, then just put all the cross-reported INDs in that Data Element

FDA.C.5.r6. Okay. Next.

Okay. Is the mechanism to validate E2B(R3) available only to the WebTrader account? Will anyone with a Gateway-to-Gateway connection be able to access the validator tool? And the response is, the E2B(R3) validator tool is independent of the submission mechanism. Okay. Submitters may validate XML files prior to submitting ICSRs to the agency. If rejected, submitters may adjust their XML generator and then submit the ICSR via WebTrader or the Gateway.

So WebTrader or Gateway is basically the -- basically, I consider them as more like the -- the postman who says the XML is the letter and the letter has been validated through the validator. So the validator is independent of that. And that will be available on FAERS Electronic Submission page. I think this month, we are planning to put that validator so that you can start accessing it.

All right. Next question. All right. Does the E2B validator show both soft

validation and hard validation? Suppose if we receive validation errors, does it mean it will fail the transmission of the case? All right. So the ETB validator shows both rejection and warning. Any rejection will send a negative acknowledgment to the submitter and the ICSR will not transmit to the FDA. I mean, not transmit. It's not the right language. I think the ICSRs will not be committed by FAERS, basically. I would say that. Because transmission, you have already transmitted, but now the transmission has a negative acknowledgment.

So I will change the answer to say it will not be committed by the FAERS database so you get a negative acknowledgment if there was a rejection.

Warnings? Yes, we will accept it. But again, the warnings are given just for that. And follow -- then you get a follow-up -- when you submit a follow-up, the idea would be to correct that warning and submit that to us. The warning is not going to -- not going to reject that submission.

All right. Next question. Can

premarket ICSRs be submitted via ESG database to database during the voluntary submission period? The answer is, yes. During the voluntary submission period, premarket ICSRs can be submitted via ESG in E2B(R3) format only. There is no R2 format for premarket ICSRs; okay? So just remember that premarket ICSRs, we don't accept any R2, it only has to be R3.

For postmarket, during the voluntary period, you can submit through R2. And as you're moving through R3, you transition over to R3. So keep in mind about the transition period that for your information you may want to have.

All right. Okay. A few more questions. What do you mean when saying a single batch must have the same sender? This is an interesting one. Can you please provide an example? Okay. So the response to that is, this applies to a Contract Research Organization, CRO, who are submitting reports for multiple sponsors or application holders. So when more than one ICSR is

sent in one batch, then all ICSRs must have the same Message Sender Identifier Information.

So which means that if you have company A and company B, two different companies, so in one batch when you are sending an ICSR, do not send ICSR where ICSR 1 is company A and ICSR 2 in the same batch is for company B.

So if you're sending, please send that all in one batch. So if you had ICSR 1, 5, 6, and 7 for company A, then put it in that one batch. And if ICSR 2, 8, 10, and 12 are for company B, then put it in a separate batch. Don't mix them up. So that's what this particular question -- this particular response behind saying the single batch must have the same sender is talking about.

Then regarding sending literature attachments, many times we do not have the final literature document ready for -- ready at the time of submission due to various reasons, maybe translation is required. When we would send the final literature attachment, would this be sent as an amendment? The

answer is, please send the final literature attachment as a follow-up ICSR.

For more information about reporting follow-up, we all know where to look for. But it can be submitted later. Once you have, you can submit that, and then it can be sent as an amendment or it can be sent as a follow-up with an attachment.

Can we still submit FDA codes for devices or IMDRF codes only? The answer is that you can submit either the FDA codes or the IMDRF codes for the device, problem codes. So I believe that's about in FAERS. When it comes to the postmarket combination reports.

Okay. All right. So with that, there weren't too many questions, but I wanted to address these questions because we didn't have time the last time and we wanted to make sure that what would be a good answer we have for you to answer.

So with that, we will go into the next topic, which is implementation plan and progress. Where is FDA with the implementation of

E2B(R3)? Okay. All right. So this is just one slide, there are a lot of things here. I had presented this slide the last time also. There were a lot of things that had not started. Right now, we are at a state where a lot of things are completed or in progress.

So we published the Regional Specifications. So this is the Regional Spec, which is all the documentation, so we produced them as a package because it has got, I think, three or four documents. And this was published initially in April 2022. And then we had it published updated in August and September. I think I missed one. There was one also updated in October of 2023.

So if you go to the FAERS Electronic Submission web page, the document which was last published in October of 2023 was the Code and the Regional Elements and the Excel Spreadsheet of all the data elements. There was some updates that were done. All updates are documented in the -- the change history. So you will see what has been updated.

So this has to do with all the Published Regional Specs. Again, as I said, I will repeat, please also look into the follow-up compatibility. If you miss that, you may face an issue because in the follow-up compatibility, there are some data points that in R2, FDA would consider them as -- as numeric values. But when it came to R3, that same data field has become -- and so that is FDA's rule for follow-up compatibility and is documented in that. Okay.

There are some data elements in the follow-up compatibility which has original data points. When it was an R2, each had its own tag, but now it has become repeatable. So -- in R3. So please keep an eye on the follow-up compatibility of the Regional Elements.

Then we come into tool enhancements. So enhancing both our intake and analytic tool to include regional extensions. This work has already been done. The main theme here is why this is in progress because -- because of this R3

implementation.

We also have to make sure that some of our downstream systems are able to accommodate the R3 model. Because the downstream systems we have in our data mining tools, and so on and so forth, and that they are able to accommodate this. So that's where we have -- that's why we have in progress. But the first bullet is completed. Because the first bullet is completed, we were able to complete all other areas that we have.

So we have the ESG setup. That is completed in preproduction environment. That's the reason we were able to do industry testing. And -- and the setup completed for inbound and outbound folders. And of course, we have also completed our production environment setup for the routing IDs. We have not notified, but internally, we have completed that and we are ready.

So once we publish on our Electronic Submission web page about that we are ready, you know, whatever is in the technical specification for the

routing IDs and production, it becomes applicable.

If you were to test with FDA, and when you are ready, we are open to test. With FDA, our preproduction environment will be open. Only that we have to use the preproduction routing ID. With the routing ID, we have to use the word TST as a prefix, I believe. No, post-fix. I think post-fix. We use the word TST. So everything stays the same, but you have a post-fix of TST. So you can test with us, you can -- my recommendation would be to try with the E2B validator first, making sure that XML file is good, and then you can submit that.

Testing through the Gateway will actually tell you your acknowledgment files. That's what you may want to -- you would like to test.

From the FDA's perspective, system testing is completed, all issues have been identified and fixed. And for industry -- we did some industry testing with eight companies, tested both premarket and postmarket ICSRs through the Gateway. Two-phase testing was completed. Tested E2B validator. And

testing completed with a few issues that were identified, and of course, corrected.

We also tried to test large files, small files, and so on and so forth. And that is something that I would recommend also for you all to do. Have a big batch, have a -- you know, what do you say? A file with a large attachment. And those are some of the tips we will talk about in the future slides that I have.

And then finally, public communication, that is also in progress and it's ongoing. We have done some public communication. For example, today, I am presenting to you on what we have done so far, our readiness, and so forth. We are preparing, as I said, an FAQ for the technical specification, onboarding, and any inquiries.

So all these questions that we answered today, some of these will be put onto the FAQ. And as we are getting questions from companies, we have been getting individual questions from sponsors, so we are documenting them. They will come into an FAQ. And we

will, of course, communicate the go-live date and we'll tell you in the future slides. I have a slide on the FDA's readiness, which will tell you the go-live date of things.

So with this implementation plan and progress, this is where we are. Most likely, all this will be complete by the end of this year. And most likely, we will be done with all these activities by the end of this year. So -- but these are some of the steps that we have followed. And -- yeah. And I really appreciate all of the companies who actually tested with us. And I think we had a good testing. Because these companies were ready with the Regional Elements, also. Which was most important because everybody is probably ready with the Core Regional Elements, but we had to get it with the code, as well as the FDA's Regional Elements.

So yeah -- so I think we are in a good state here with the implementation plan and progress.

All right. Now, on to -- now, that we

had this presentation today until we give you a date and we force that on the Electronic Submission -- our FAERS Electronic Submission web page, please continue to submit ICSRs in eCTD format and postmarket ICSRs need to be in E2B(R2) format until we notify that date.

So just don't start submitting the premarket -- premarket ICSRs -- I have a typo there. Okay. It should be premarket. Premarket ICSRs need to be R3 format right away. But just let us give you the date, and then after that.

Now, again, as I said, when we give the date, from that point, you have two years of one and two repeated before you become already -- and the compliance date is put for submission of the ICSRs in R3 format.

All right. Okay. Based on my presentation, we might have the -- I may continue with the next topic because based on the presentation and the timing, we are running fast.

All right. External and internal

testing update. So how did we do? This might help you also in testing with the FDA, as to what we did with our industry partners when we did our testing. So it might help you when you're doing testing with us.

So let's go over -- so first thing, this was some of the internal testing that we did that, again, might help you in doing your internal testing. So multiple scenario testing was conducted. We had a whole bunch of different types of scenarios. We took premarket. We said, okay, let's do premarket safety reports. Okay. IND safety reports.

Also, have a separate testing for aggregate safety reports. And also have a testing for safety reports with cross-referenced INDs. So let's do all this in the premarket safety reports. We also have the IND_Exempt BA/BE safety reports.

We also have done it like if it was the same IND number but for different CDER and and CBER, making sure that N.1.4 and N.2.R.3 are appropriately

set. So we did that testing also.

And then we also -- then going into postmarket, making sure that we have, you know, the safety reports including combination products, attachments, postmarket study reports. And then there will be two reports that will be submitted. Looking at all the different rules that has been defined, the Business Rules of Data Checks. They have been testing all of those where -- as part of our list.

Then we wanted to -- we also tested for both positive and negative acknowledgments. So we are expecting that this file will give me a negative acknowledgment, and did I get it? Or this file is going to give me a positive acknowledgment and did I get it?

So all this type of testing was done internally. Yes, it did take us some time preparing our test files and so on and so forth. You could actually some of our XML files that we have posted, and that could be a baseline, and then you can manipulate those files to do your testing. You know,

and all -- of course, you'll have to do your testing once you generate XML from that file -- those external instances may not be useful, but useful to compare.

But you'll have to generate from your system, get to the validator, see what failed, go back to your system, do that fix, generate again, back to the validator. If everything is good. then you know that you have worked it out. All right. Next slide.

So the external testing we conducted in two phases. So phase 1 testing was that you submit those ICRs along with the regional extension. Of course, to start with those testing, companies first went to the validator. We gave them access to this validator. They went and walked back through. All those seven-eight companies that worked with us, they really liked the validators. It actually gave them -- because they were able to prepare a lot of things ahead of time before the submission and getting the acknowledgment. So the validator was really useful.

And in that validator -- once they did their submissions, they also used the different types

of criteria's that we had done during our internal testing. Submitting premarket and postmarket. We did that sometime in July with 7 companies as participants. We received over 169 XMLs from 4 companies, 3 in postmarket, which was a good number to start with. And with that, we then identified issues.

And our finding during our phase 1 testing was external connection URLUs need to be validated. We had some issues with the URL, I think we got it fixed. And now, when we publish it, I think it should be all okay.

Then we also have the ESG Routing ID and AS2 Header changed to receive industry file, use the TST prefix. I think we used just the prefix TST. I think that was the one that for testing, we had to do that. And that's what you're going to do when you test with us.

Our dosage unit not accepting UCUM codes, so that was something we had identified to get fixed in phase 1 testing. Updating the rejection and

warning tag for non-aggregate reports. So there was some XML tags related to that that had to be fixed. Country code EU was not getting accepted, which was fixed. The IND numbers were aversive in that code. Currently, only six IND numbers were getting accepted, that was fixed after phase 1. They basically accept -- that field is, I think, ten characters -- ten numbers long. So as long as you have the right number, we will accept it.

Then the ability to download the list of warnings and rejections shown in E2B validator tool to Excel. That was something that was a change request for the validator. We were unable to finish through that. We have kept it now backlogged. At some point, we will work through it. But it shows you the list of all the warnings and rejections. This was some additional request to download that list. So that was kind of a few things that we found in phase 1 testing. Next slide.

Some recommendations we got from phase 1 testing was in a FAERS test environment

availability. The FDA's ESG Gateway and FAERS testing environment will remain open for use. You can continue to submit (R3) files for internal testing and development efforts.

Data setup in FAERS. Now, this is something that you will have to work with us, especially for IND safety reports. You will have to let us know on -- which INDs or cross-reported INDs you are reporting on. We do have our FAERS dictionary where we have got all our INDs.

But if you -- before you start testing, if you notice this to us, then what happens is you will not get a rejection. Because if the IND numbers don't match, then you will get a rejection. So it'll be good to notify us or the organization which IND numbers you are going to be reporting on and the cross-referenced IND numbers too.

Communication. If you have any questions or need further clarification, please do not hesitate to reach us out for our test. And for this -- when you reach out for E2B(R3) testing, please put

in the subject line E2B(R3) Testing that helps us to triage which question or which inquiry is for what. Because we also have so many other types of inquiries through the FAERSESUB. So that will help us.

If you need -- if needed, we are available to set up a one-on-one for any further discussion and clarification.

And then, of course, after the phase 1 testing, we finally addressed our retesting in phase 2. We did that. But the first four bullets are something that is applicable to all of you. We're not part of investor testing, but when you start your testing, the first four bullets are applicable to you all, and you can really -- we can collaborate to make sure that you are fully set and ready for submitting, you know, ICSRs in R3 format. Next slide.

All right. In phase 2 testing, so we retest the issues reported and we did some performance testing. So use the same -- you know, we use the same Routing IDs and AS2 Headers, but we did some rigorous

testing to submit files -- batch files with multiple ICSRs, attachments, and all R3 supported format, you know, large size files. And there was one also recommendation for the E2B Validator. We also incorporated that and went in to test that too. Okay.

So this is also important that you may want to do some rigorous testing of large files. I think our technical-specific problem will tell what is a max size that we can take, but -- but I would recommend that you also -- that you do that. There are situations that happen where some company may later realize that there was a whole bunch of ICSRs which are nonexpedited, but they were identified late, and they weren't all submitted in a big batch. Yes, you can submit, but we need to make sure that these batches are not so large.

And also, we know that R3 XML files of large six is really -- makes it really bigger than R2. So we want to make sure that you're getting your acknowledgements on time. I think we have a 24-

hour -- I believe 24 to 48-hour turnaround to get your acknowledgments. Small size files, I think you will probably get it in two hours, within two hours. But large size files, it may be more. So please do test that. All right. Next slide.

Okay. So all the issues we resolved from phase 1 testing, and the reason I am telling you this is because this has got updated in the implementation -- FDA's regional implementation package. So the big spreadsheet actually has these changes.

So updated rejection R2 and D.2 warnings. So this one became from a rejection to a warning. Changed the existing rejection to a warning. And the condition was if the type of report is a report from study, and the IND number where AE occurred is provided, and the identification number of the report linked to this is populated. That means you're talking about an aggregate report. And your patient identified must have the value of aggregate.

So this is what used to be a rejection,

we made it into a warning, so the file won't get rejected, we'll just give you a warning.

Another one is system must allow submission of IND numbers with less than six digits. So we had a situation where the IND number was ten digits, so now we just said, let's go to six digit and five digit. We have the IND number as ten numeric. As long as the IND number is a valid IND number. Okay. It could be a five-digit, it could be a six-digit, it could be more, it could be a seven-digit, but it has to have a valid IND number. So that is when you will get a rejection. So that's the rule that was put in for this.

Looking at the length, that was -- of course, if you give me an 11 numeric data value, yes, it's going to get rejected. But anything 10 and below, but it has to be a valid number, and we will accept it. Next slide.

Okay. So postmarket study report logic. So that I want to mention it because it's very important. We submit two reports. So when it comes

to the premarket, so you will have to have your Batch Receiver Identifier, that's ZZFDA_PREMKT, which I mentioned earlier. The N.2.r.3, that should be CDER_IND or CBER_IND. And then type of report is 2 report from study type where the reaction was observed is 1, which is clinical trials.

This is for the postmarket report. Now, with these values, this report will not get posted publicly. Because the public -- the published flag will be automatically set to know.

Now, for the postmarket side, you will say the Batch Receiver Identifier is ZZFDA, so I know this is coming from the postmarket route, but on a postmarket study. And how do I know? Because the type of report is 2, which is report from study; okay? And observe type is 1. And the good advantage of this, setting them up this way, this report also won't get published publicly.

So all postmarket study reports will not get published publicly. But it will go to the right reviewer, who is supposed to review this

report.

We have not talked about yet should we make it into one report or not as most of the -- all of the regulators are getting us two reports, so we have also -- we are doing it in these two reports. But they probably, at some point, we may all discuss together to see if this could be just one report submitted to FDA.

But as of now, it's two reports. And these are the values that need to be used to define those two reports for the postmarket study. Okay. Next slide.

Okay. Remedial Action Initiated tag value. So the earlier system was providing warning for Remedial Action when a malfunction is true and local criteria is 4, which is 5-day. System will now generate a warning if Remedial Action is not provided; right? And malfunction is true and local report is 5, which is 30-day. So this one, I think, should be probably 4 -- 4-5 day report. Because then you are saying there's a Remedial Action because it was

immediately taken. So 5-day -- no. 5-day, 30-day is fine, because that's a malfunction report.

So in this case, the -- it will just provide a warning and there's no rejection in this. Next -- next. Okay.

There were some defects and issues. I talked about UCUM codes not accepted, this is now going to be accepted. Date of death, null flavor not accepted. This will get accepted, especially when the report is a premarket report. And when I say premarket report, one thing that I keep in mind is I translate that into N.1.4 equal to ZZFDA_PREMKT and N.2.R.3 is CDER_IND or CBER_IND. And you know, if it's an IND, then IND with adverse code is -- so that's kind of things I keep in mind when I talk about the premarket report.

So in this case, if it is a premarket report and there was -- if result in death is true, then the death date is required. But if you don't have the death date, you can submit a null flavor. But this will only happen with the premarket

report.

EU country code not accepted. This will now start accepting, so not a problem, we have fixed it. And the system will start accepting it.

Okay. E2B Validator UI changes. So the validator only had one change. We added an indicator called severity to indicate if the XML file has any warning or rejection. So this was something that was not there. Because it will tell you what the error is, but it will tell you it was a warning error or a rejection error. So we now are displaying that on the validator. So those are changes with the validator. Next slide, please.

Okay. During the testing, we had some frequently asked questions. When will FDA start accepting ICSRs in ETB(R3) format? So from this slide onwards, you will start getting the hints of when FDA is starting to accept in E2B(R3) format. As we go through this presentation to the end, you'll probably get some hints and all of that.

So during the voluntary period, you may

begin -- begin submitting both pre and postmarket in R3 format. So we anticipate that companies may begin to accept postmarket format in January 2024. And we hope to have the final Guidance for Industry in March of 2024 for the IND safety reports. And will begin accepting ICSRs at that time.

You may ask, hey, I thought you said the pre and post are going at the same time, but here, they say January and March. And the reason is that you also have to understand that for the premarket or the IND safety reports, we have been getting PDFs of MedWatch.

So we have a big change management that we have to do within our organization to move our clinical reviewer from looking at a MedWatch to looking at this digitized ICSR. So that's why we need some more time for the -- for the premarket one. Post-market one, I would review. It's already getting R3, so they already are used to and accustomed to looking at the ICSR in a particular format. So that's -- that makes it more easier.

Will I be able to submit R3 files for both pre and post-prior to the mandatory reporting start date? Yes. During the two-year voluntary period, you will be able to submit both pre and postmarket reports.

Can a company choose to submit postmarket reports in R3 format and paper for premarket prior to the compliance date? Yes. The company can choose to submit postmarket safety reports in R3 format and premarket safety reports using the eCTD format. Okay.

So it's very important in eCTD format, not paper, prior to the compliance date. All right. And as I said, that is a two-year voluntary period. So if the -- yeah. I'll go into the slide and that'll show you what the voluntary period is going to be and when the compliance date is going to be.

When will the E2B(R3) Validator tool be available? So here is a date. So I'm trying to make it available by -- starting November 20th. I believe

that's a Monday. And I just got the okay from our security team that URL can be posted publicly.

So we will post that on the Electronic Submission web page and I will have my office -- our communication team will get that for us and they will make sure. And as soon as they are -- I think people who are subscribed to the page will automatically get a notification. But starting November 20th, we will have that E2B Validator available.

And then, of course, we'll an FAQ which we will post on the same FAERS Electronic Submission page. Okay. All right. Next slide. All right.

So today, I wanted to also discuss with you about the E2B Validator, what it is, and how you can use it.

So FDA will provide this E2B Validator, as I said, November 20th, you'll have it, to facilitate the validation of E2B(R3) XML files from your safety database during your pilot testing phase. So once you generate from your safety database, the XML file, you can come here, browse, and

test it.

And so this validator will provide a web-based interface and it will enable to select the E2B XML file and validate. And it also provides you a status of the results that are displayed to the user.

So I'm going to give you a live demo of the validator. And in doing that, we will first click on that link here, which then opens up the validator. All right. So I hope everybody can see the validator. And in this validator, as you see at the top, it says what it is. It validates, just not the code. ICHS Elements, it validates also against the Regional Technical Specification. FDA's Regional Technical. So it has all of that.

And then -- so you can either paste -- copy and paste a file or you can browse. The one important thing about this here is that when you browse an XML file or you paste an XML file and that shows up in the big box at the bottom under XML source, we don't store this anywhere in our database

or in our location. It's just in that session. You want to close that, it's gone; okay? So just to let you know that when you're testing.

Now, what you could do is if you copy, you can copy and paste. Or if you have an XML file, we'll click on browse. When you click on browse, you can pick one file, open and it's going to give us a positive acknowledgment. We open that. And then you see here the XML shows up here; right? And that XML file can show up here. So if you scroll down in the small scroll bar, and you see that XML, and that XML file is here; okay?

Now, what we will do is you can do -- next, is to click on the validate button. And -- and you see that validation status that shows up at the bottom, it says validate XML file, that means your file is a valid file; right? Now, you know what? Let's say in this particular file, can we scroll up in the file? Yes. Scroll up all the way up. Let's see. So in this file, let's say we go and change a value in this file itself. If you scroll

slightly down a little bit. Okay. Hold there. And let's say in this we update -- we just changed some value. Let's say extension is CDER. So -- no. Scroll a little more down. A little more. Some more. A little more down. Okay. Availability time value.

All right. So let's go to the row that says availability time value code 2.22 and add a zero after the number four. Okay. Now, hit unvalidate. Now, you see there is a problem with the latest receive date.

So from -- from an industry perspective, you can also manipulate this file to see what you can do; okay? This is something which also helped us that, okay, we fixed this, I saw what the issue is, I fixed it right in this file, and then take a copy of this file, and then I know what things have to be fixed. So if you go back and remove the zero again, that will be that zero. Yes. And hit unvalidate. You will see that it will say it's a valid file.

All right. So now, let's clear this, and let's find a file which has got some issues and click on that. It will give you a negative acknowledgment. All right. And here is the XML file that we have. Same thing. And we will click on validate now. So if you click on validate, it says it's an invalid XML. And it tells you the issue.

Now, here is where the severity is. It tells you -- it says rejection auto warning. So -- and it gives you the validation detail message, so you know what the issue is, and you can accordingly go and fix the data there, and fix the issue there. And then begin validate, and if everything is good, that means you're ready to submit that to the FDA.

So this validator, at least for all the companies that we tested with, our partners, they -- they really liked it. They said, you know, it really helps us in prechecking things before things are submitted. This also helps the FDA, because then everybody who wants to test, test, test, you know, you would like to -- we would want them to test here first

before they do. Because our hope is that if everything is good here, then when you submit the XML through the Gateway, you should get your appropriate acknowledgments.

And in that case, the hope is that you will get a positive acknowledgment. So it is important that you perform all your testing here and then get into submitting to the Gateway.

So with that, this is the validator. We go back into our slides. All right. So we talked about the validator, what it does, how it checks, the interface, and it displays you the results right there. All right. Next slide. Okay.

So I think I'm almost there on time. It's what? 10:15. 14. We wanted to take a 15-minute break and come back at 10:35. So I guess, we can give a 20-minute break and come back at 10:35. So we'll take a break. Yeah. My throat has started hurting now. But we'll take a break and come back at 10:35 and continue with some other updates on

FDA's readiness, and preparedness, and go into the Q&A. All right. So, thank you. And we'll see you in about 20 minutes.

(Off the record.)

MR. DE: Okay. So we are back and we will continue with some other topics that we have planned for today. And the next topic in the agenda is the regional extension updates.

So since we had the last meeting, there has been some updates to the regional extensions and we will go over some of those updates. All right.

So there was some -- going into this, there are some good number of items here. One is that we corrected the OID value in XPath for data elements listed here. There were some void value which were incorrect, we realized that, we have fixed that. We corrected the XPath for specifically the element FDA because that's a regional element. We identified it was an issue, so we corrected it.

Then we also had a date element, which was FDA.G.k.10a.r, we changed that to remove the .r,

so that field is not repeatable. We had a few questions on that if it's repeatable or not repeatable. So it's not repeatable. We updated the Rejection and Warning Rules tabs to shorten the error description.

The error descriptions that you saw in the validator tool is the same error description that you will see in the acknowledgment file, just an FYI. It is basically the same error description data that is coming from the same place. And our E2B Validator and actual check that happens is actually looking at the same place. So if tomorrow we have an update to a data check, it will automatically be applicable to both the validator and the actual submission. So it is -- it is that -- important that, you know, to know that the error messages will be same as the error message that -- that you saw in the validator. So that XML file -- the acknowledgment file will have the same message.

XML file also will have a message which kind of divides that same -- one of the warning

messages versus one of the rejections messages. So you will be able to very clearly identify.

All right. A few things that we changed. Device problem codes. So as long as we -- we added a warning rule with an error ID W0008, provide valid FDA or IMDRF device problem code.

So message sender identifier N.2.r.3. N.2.r.3 provided is not the same for all reports and does not match the Batch Sender Identifier. This is a situation where you had -- where I explained about in a batch you have senders from different companies. So the same batch should have the same sender.

Added rejection rule with error ID, R0101. This is a report nullification or amendment. That this is only -- this is -- you cannot do a nullification or an amendment for an initial report. An amendment or nullification always is for -- for a noninitial report. You had a follow-up, to that follow-up, you had the initial report submitted, and then to that you do an

amendment. That's okay. But I need to have that reported into my database to say that that was an amendment or nullification. So that's the rule.

IND number of cross-reported IND. IND number for cross-reported IND must be a valid number registered with the FDA. So whatever the numbers that you are providing, they must be valid IND numbers as registered with the FDA, because that will be checked. Just because this is a cross-report IND, we'll give you a warning, but definitely, we will be checking it. Next slide.

Okay. Remedial Action Initiated. Remedial Action Initiated is required if malfunction is true and Local Criteria Report Type is 4. So I think I had a typo in that previous slide. It should be a 4 5-day report. So warning error said 30-day, it should be a 5-day. So that was a fix that was done. So the actual spreadsheet where the rejection and error rules are, they are corrected.

Okay. Business rule generated an error

and rejected the ICSR. That was original and updated one was Error ID R0028, that reduced to warning, and added additional criteria for the data element D.1.

So this is the one when I was talking on the aggregate report, it says the Identification Number of the report, which is linked to this report, and the IND Number where AE occurred is populated, then the patient name ID must have the value of aggregate. Of course, this is part of IND report and IND aggregate. So this will give you a warning instead of a rejection.

Okay. Then we have another one, which is the Medicinal Product Name as reported by the primary source. So this is where we had -- we have a rule where -- that when we try -- if an Medicinal Product Name is matched, it does not match the registered product name for the application number reported. Then it gives you a warning.

And what we did was we updated that to say that the error description was updated to now say that G.k.2.2, the product number, does not match the

registered product name for the application number reported. So whatever the application number is reporting and the registered product name, they kind of have to match to each other; okay?

Now, this was a warning given by -- because yes, if it does not match, okay, we will give you a warning. But please ignore this message for comparator study product. Because in that case, you may not have the right combination match. So -- but otherwise, it's a warning that's given, so saying that if your application number is so and so, then it didn't match with the right product name, that gives you a warning so that you can actually correct and fix your product and submit. Okay.

So -- but with comparator product -- study product, I mean, that was not possible, you may not know, and in such case, so you can ignore this message for comparator study product. Next.

All right. For error ID R0065, now, what is this error? This error says that error description, that F.r.3.1 must be provided when

F.r.3.2 and F.r.3.4 is -- 3.4 is not provided. So this is for test results. So basically, what we are saying here is we changed the error description to shorten it. Because again, when it comes to the acknowledgment file, we don't want it too big. So -- because acknowledgment, the description has specific bend [ph] on what we can put it. I think it's 2,000. So trying to fit within that.

So we just want to give one simple error message saying that at least one of the test results, F.r.3.2 and 3.4 must contain a value when F.r.2.2b is provided. So basically, that's the message that's going to come for any of those three data points that is listed on the first three rows.

The fourth one is error type of the reaction event. So this is where original error ID is R0066, so it's a rejection. Only check for message -- only check for N.2.r.3, which is CEDR_IND or CBER_IND, but not CDER_IND_EXEMPT_BA_BE. So also check for that because -- because whenever we see the IND -- IND and BA_BE, it is also premarket report and the value must

be 1 clinical trial because that's what the study is.

So the value must be 1 when you have the value of -- when you have N.2.r.3 as CEDR_IND, or CBER_IND, or CEDR_IND_EXEMPT_BA_BE, and that type of report is 2. So the -- we are missing the CDER_IND_EXEMPT_BA_BE, so that was corrected. Next slide.

All right. Going into some of the characterization of drug role. So G.k.1 must be provided with Observation Code Value of 1, 3, or 4 when N.2.r.3 CDER. That means it's a postmarket study report -- or postmarket report, then you at least must have 1, 3, or 4. So that is -- that is the rule that this one says.

The next rule that we corrected/updated was added rejection rule with error ID RO104. So the rejection rule was if type of report is 2, the message receiver is CDER, the batch receiver is ZZFDA, then the observation code value of 1, 2, or 3 for study type where reaction/events were occurred. So this was the rule that we had to add. So because it's CDER and

ZZFDA, so it's a postmarket.

But when it comes to an ID report, you could have a value of 1, which is clinical trial. Or if you have -- if you have a report which is from a PSP program, this program, then you may have a value of 2 or 3. Okay. So for the -- for C.5.4, so that's why we had to make sure that we allow them.

Added rejection rule with error ID RO105. So this is IND number where AE occurred must be valid number registered with the FDA. So this rule wasn't there, so that's a new rule that we added.

Next one was the same thing, 106 is for the pre-ANDA number for IND_EXEMPT_BA_BE, it must be registered with the FDA.

And then the last one is that there was an update. The original rule said RO103 error ID, if type of report is 1, it's a spontaneous report, and message receiver is CDER, observation code value of 2 and 3 for the study type. This was a rule and what we are saying that this cannot happen because 1 is a spontaneous report. So if it is a spontaneous report,

then you cannot have a study type where reactions/events were observed because it's a spontaneous report. It was a PSP program, then your type of report would have been become 2, which is report from study, and then -- and then C.5.4 would have been 2 or a 3.

So that's what the updated rule is. A spontaneous report cannot have -- must not be provided with a C.5.4. Okay. Next.

All right. Now, comes all the exciting slides. Probably everybody is -- excuse me. I'm waiting for it. So as you see, the changes are not too many, there are business rules changes. No new element was added. No new data attributes have changed. Maybe a few expired were fixed, not many. So -- so with all that, we posted in October of 2023 all updated business rules and so on with that document, which call is the Report and Regional Element Business Rules. And you will be able to see all of them there.

All right. So with that, we have the

next topic, which is FDA readiness. All right. So what is our path forward? How are going to go? So our proposed timelines to implementation.

All right. First one. All right. January 2024, we communicate -- we will communicate via the FAERS Electronic Submission page notifying the FAERS system is ready to accept postmarket safety reports using E2B(R3) standard. So in January, we'll be ready. And I also explained why we will go in January with postmarket first and then premarket. It's because of the change management process that we have to accommodate.

That's where the voluntary period starts. When I say voluntary period starts, the voluntary period for E2B(R3) submission of postmarket safety reports. Okay. If you're not ready with submitting postmarket safety reports in E2B(R3) standard, then you continue to submit that in E2B(R2) standard until you're ready with R3. All right.

So that is why that is a voluntary period for the R3 standard. Okay. When it comes to

postmarket.

So that's -- we're targeting January 2024. What's the exact date in January? I don't know that yet. But we will be updating through the FAERS Electronic Submission web page the exact date because it all has to happen at the right time. But definitely happening in January.

All right. Next. All right. Comes March 2024. What do we do in March 2024? So we anticipate a publication of the final guidance, along with an FR notice. Okay. Concurrent to the publication of this guidance, FDA will begin to accept premarket ICSRs in E2B(R3) format to FAERS. It will also -- the safety reporting portal also will be ready during that time. Because they all have to go at the same time.

So the day the guidance is published with the notice, the same day we have the website, that tells you that you can submit an R3 and at the same time the Safety Reporting Portal is also ready for companies to submit. Companies who want to submit

through the Safety Reporting Portal because maybe they are not ready with E2B(R3). Please, right after that, start your registration so that you can get registered. But once you have moved to the Gateway, then we will have the similar account in that -- in Safety Reporting Portal. The Safety Reporting Portal cannot be a backup plan.

Because -- because submitting through Safety Reporting Portal and then submitting through the Gateway, it disrupts the -- the reports, the same report coming from two different places. We have seen sometimes it creates two separate cases through the system, and so on. And so we just want one method of reporting and backup reporting. And refer to the FAERS Electronic Submission web page for the updates.

So this is when the premarket we anticipate to start. What date in March? Again, we will be posting that. We don't have an exact date, as we are going through our change management process. Okay. Next point.

All right. So once we have in March,

then from that point in March to February 2026, about two years, will be the voluntary period. So again, when we start in March 2024, that's when the voluntary period starts of submitting ICSRs and E2B -- using ETB(R3) standard.

Of course, if you're not ready, you continue to submit in eCTD. But once you are ready and you're moved, during that voluntary period, you do not revert back to the latest methods. So once you've done the ETB(R3), you continue with the ETB(R3). And our hope is that once you have converted everything, you converted both post and premarket ETB(R3), and everything is coming through that.

As you know, there is big advantages in moving everything to R3 just because then you don't have to go through regulatory affairs, you don't have to, you know, send 1572 cover letter, and so on and so forth. You don't have to sub with more people. ICSRs or cross-reference INDs. And there's a lot of advantages that you have. So the March to February will be that voluntary period.

And then finally, March 2026, companies then must submit premarket and postmarket ICSRs electronically to FAERS in the ETB(R3) format or SRP, whichever they have chosen.

So this is the proposed timeline to implementation. We are targeting these timelines. And as the time comes, we will start seeing updates happening on the FAERS and Electronic Submission web page, which then also will trigger all other notifications that need to happen. So keep an eye on that. And I have been getting a lot of questions about when we believe it will be ready.

Please make sure that just being ready for FDA includes taking into account all the FDA's regional extensions; okay?

So this also kind of is something that you may have to work with your vendors of your safety databases, because any safety database that you use may probably today do the regional requirements for other regulators who have already mandated. It will do the code ICH elements, but may not do that in FDA's

regional elements. And we need to make sure that they also do the FDA's regional elements. So -- and they are tested, and so on, and so forth.

So you can start working on this. These are timelines so we're telling you when FDA will be able -- you know, when FDA says it's ready in January and March, does not mean you have to submit in January and March. You know, you have two -- two years of voluntary period to prepare yourself, develop, test -- get ready, test with us, so on and so forth, and then have the process to move through.

So, yeah. So that is very important. Because also, remember, I think -- we don't have this problem, but from an industry perspective, you have one global database. You submit to different agencies around the world. They have different rules; right? And now, you are introducing FDA with its own -- with its own rule.

So, yeah. You have more effort to report because of the -- of the regional extensions that different regions have. So again, be cautious,

but -- but these are the dates that we are anticipating that we will go live with FAERS. All right. Next slide.

Okay. Submitter preparedness. So with submitter preparedness, there are a few things that as a submitter you can start. And these are, again, suggestions that we are providing, nothing is mandatory here. But let's go into the slides on some of the preparedness items that you can have.

So first and foremost, make sure you have downloaded the guidance and the technical specification documents posted on the FAERS Electronic Submission web page. All right. So you have to make sure that -- all the documents that you have, you have downloaded all of the documents. Just downloading the ICH documents won't work, you have to download the regional ones also. Okay.

All right. Review the regional extensions very carefully. So it's very important that you review the regional extensions. What it says, what it is, you know, there's a whole section

for combination products, there's a section for IND safety reports, and so on and so forth.

Then prepare your safety database accounting for the regional extensions. So this is also very important, that your safety database should account for the regional extensions that we have. This is where you probably will work with your vendors. If you have a vendor -- if you have in-house and you like to work with your in-house, you know, intergrader or contractor to -- to get these regional elements in there.

Account for regional forward compatibility. And I specifically say that again and again because I just have seen very recently that, yeah, we are R3 ready, we have translated from R2 to R3, they did that, forgot the regional elements to translate and do a forward compatibility of the regional elements. So please keep in mind on the regional elements. Ask us questions if you have any doubts.

Generate the XML files and test them

using the E2B Validator. So once your XML comes out of this database, then send to be validated. We provided the link. The link will be provided on the FAERS Electronic Submission page. And as I said, by development, you will have -- you will see on the FAERS Electronic Submission page, a link which you can click which can open up E2B and FDA to be validated.

Okay. Correct any issues identified by the validator. That means you've corrected that, gone back to your database, you fixed them, and so on. And again, some of these things here you are to work probably with your vendor or your in-house contractors.

Then perform the Gateway setup. Now, for postmarket, you already have a setup. But for the premarket ones, you only have to do a setup of your Gateway so that you're in the right parameters. The routing ID or AS2 Header is set. In a preproduction environment, by the way.

Then you test your XML files. Sample XML files that has cleared the FDA E2B Validator via

the preproduction Gateway. So now you've tested the XML files, you've fixed everything, begin your tester, everything looks good, your Gateway is set up. Now, you submit the files, and you should be getting the acknowledgements back. Okay. And most likely, you should get a positive acknowledgment.

Now, there may be instances where you may get a negative acknowledgment, especially if your routing ID is not equal -- not in line with the batch, the receiver, or message receiver, then you may get a negative acknowledgment. That test, we cannot do through the E2B Validator, because as you know, the Gateway IDs are not available for the E2B Validator. So we will not be doing test on that. But that is a rule when you actually submit through the Gateway.

Then you are -- next is once everything looks good in the preproduction environment, then you go into your production environment to set up things, and you set up based on the technical specification. And you have set up your Gateway setup

for in the production environment.

All right. So these are some of the tips that we could think of to give you. I'm sure you will have exhaustive validation plans, and so on, and so forth. But some of the things that we could help you, we just list it down here. Next slide.

Okay. When you send files to the preproduction environment or preproduction Gateway, you can test the following. You could test the premarket safety report.

Now, when you test a premarket safety report, making sure that the IND number has to be the right IND number. So if you can let us know that this is the IND number, then we can say, this is in our dictionary, it's all good.

During the industry testing, we just created some dummy ID numbers so that they can be tested. But in the preproduction, we can test with the appropriate IND numbers. You can test it and it will begin -- we created dummy INDs. But if you feel that, you know, you want to get some dummy ID numbers,

we can always do that.

Also, including IND aggregate safety reports and cross-referenced IDs. The postmarket side, test the postmarket report. But one thing I will also suggest, create a mega file that has got all the data elements in there. Lots of help. And including combination production and safety reports. Combination productions are also tested. And safety reports with attachments. Large-size safety reports. Batch submissions of safety reports.

And please make sure you test for both positive and negative acknowledgments. So you send a bad file and you are -- what are you expecting that the header should be when getting that in the acknowledgment? And same with the positive acknowledgement. So these are some of the things that are tips, and tricks, and suggestions that we reviewed in testing the -- in doing your testing with the agency.

So with that, I think I'm going to be

early. So there are a few case scenarios that I kind of presented here so that it gives you some ideas of -- on how you could prepare your XML.

So the first one is premarket report on an IND or IND_EXEMPT_BA_BE. So if you had that, then your batch sender identifier must be the ZZFDA_PREMKT. So the batch is of the premarket batch. The message within that batch, you're saying it's a CDER_IND or a CBER_IND or IND_EXEMPT. Okay. It can't be all, it has to be either one.

All right. Then the report type is 2 because it's a premarket report from study. Study type where adverse event is observed is 1, which is clinical trial for premarket. And then if it was an IND, then the IND number where adverse event occurred. You put the IND number, which will become mandatory now because it's a premarket, on the Pre-ANDA number where the adverse event occurred.

So the Pre-ANDA number has become mandatory, depending on what your reporting in the

message receiver identifier is. Okay. So that is the first scenario on premarket report on IND and IND_EXEMPT.

Now, if you have a solicited report or reports from Organized Data Collection Systems. So in such case, we ask to consider them like a study report but they are like on the postmarket product.

So in such case, you will be sending that report to the postmarket site. Based on the routing ID and the -- the routing ID, you would send it to the postmarket site. But within the XML, your batch sender has to be ZZFDA. The message receiver is CDER. The report type is 2 report from study. And the study type where the reaction event was observed is 2 individual patient use or 3 other type of studies.

All right. So that is what -- currently what we have, these values. And that is what you will use. So this will tell us that these are not fully for clinical trials, but they are for other type of studies that we have. Next slide, next

scenario.

Number three. So this is premarket aggregate report. So this is where you're aggregating all the -- all the ICSRs and submitting on. So this will have the batch. You will submit it to the premarket site, the routing ID. The batch sender identifier within the XML should say ZZFDA_PREMKT. Message receiver identifier would be CDER_IND or CBER_IND.

Aggregate reports, I think do not apply for IND_EXEMPT_BA_BE. Then the type of report is 2 report from study. Study type is 1 clinical trial IND number. The IND number on which where AE occurred. You have the patient name, you put it as the aggregate because it's multiple patients or -- since this is an individual report but an aggregate, so we can put the patient in front of the aggregate, and then the list of all the sender case report ID on which you're doing the allegation.

And that -- those cases should be reported under the data field C.1.10.r. Okay. So

this would be for the premarket aggregate reports.

Let's see. Scenario number four. Premarket report with cross-referenced IDs. So in such case, you have ZZFDA, again, you're submitting through the routing ID of premarket. You will have ZZFDA_PREMKT. Message receiver identifier is CDER or CBER_IND. Type of report from study, it's a clinical trial. The IND number where AE occurred and all the other cross-reported INDs in our regional data element are IND number of cross-reported INDs. So that's -- .r, that means a repeatable. So on the cross-report, INDs can be reported there. Okay.

The next scenario is postmarket study reports. You submit two reports, one on the IND. And two, on the NDA or BLA. In this case, I just gave the NDA or BLA just as an example. So show what report number one and report number two look like.

So if you look at report number one, you have -- it is on the IND. So in such case, of course, you will be sending the report through the routing ID for routing -- routing ID on the premarket

side. Batch sender identifier, again, ZZFDA_PREMKT. CDER or CBER_IND for message receiver identifier. Type of report, 2 report from study. The observed, clinical trial, study type where the reaction was observed is 1, clinical trial. And then IND number where the AE occurred is the IND number.

When it comes to the postmarket side, the report number two that you submit, so that's ZZFDA, CDER, 2 report from study, 1 clinical trial. And then on that report, the two other fields we recommend that -- two or three. One of the fields we recommend that when you put the Medicinal Product Name, along with that, put the job authorization number of the NDA number. Don't put the IND number there. Because IND number, you have already put in the previous report. So put the drug authorization number, so we know that it's a study report, but it's against that -- that marketed product with that IND number.

And every time -- another suggestion that we would like to give you is, every time you have

a product, and if it is your product and you know that is your product, which of course, always doesn't happen, please supply the submitter application number also along with it -- along with the product number. If it has an NDA, BLA, or an ANDA, if you know it is yours, then please do submit that.

Many times, we don't get that. Of course, we understand, many times you will not know that it is truly your product or not because you just know the active ingredient. You may not know it, but if you know it is yours, then please do submit that identification number in the postmarket report.

Okay. All right. So with all the scenarios, we come to basically the last slide that we have. Now, before I go to the last slide, please note that this entire session that I'm doing today is being recorded, and the recording will be available on that meeting page of FDA in about two weeks. So you will have the entire video recording with the slides and the agenda, everything available publicly in about two weeks.

So right now, on that meeting page, you have the previous sessions I have had before, all the recordings. Today's recording, it takes us about two weeks after we have gone through it, reviewed it, and then publish it. Okay. So just letting you all know.

So as a summary, we will recap our previous public meeting. So you saw all these questions. And as I said, the slides, the questions, the answers, this recording today, all will be published, so you will have all the questions and answers. Many of those questions and answers will go get into an FAQ. So my team will be working on an FAQ, which will be published by the -- January when we publish -- when we say that FDA is ready for postmarket in R3.

We will also -- of course, as I said, everything will be there. And the validator also will be made available by November 20th. So a lot of things will be published in about two weeks. Okay. So we had the recap.

Next, we discussed the implementation plan and progress showing the activities completed and ones that are in progress. You saw that. A lot of things have been completed.

Next, we talked about conducting external and internal testing that we did. And as the reason, as I said, I mentioned about all this because maybe some tips and bullet points may interest you to say, hey, okay, we need to do this kind of testing with FDA to be very sure with our testing. So that was the reason we -- I mentioned all about our internal and external testing.

Okay. Next, issues that were identified were fixed, implemented, and retested. I told you, they all have been updated in the technical specification. Not the PDF document, but the big Excel spreadsheet. Many of the updates, as you see, will go into that big spreadsheet of the code and regional elements, just because that is a document I can update and don't have to go through an elaborate clearance.

If I go and update the PDF document that was posted, that -- every time I go through an elaborate clearance, so we just wanted to make sure that the spreadsheet is the one that we get updated most often. And PDF, actually, I think it has got a lot of words and a lot of paragraphs of explanation, but they all point eventually to that spreadsheet of all the data evidence. All right.

Next slide -- or I'm sorry, next bullet. Update to regional extensions are posted in (v 1.5). So this was posted on October 2023. So you will have a version 1.5.

Okay. Next, we discussed the FDA readiness with some plan dates. So I hope all this anxiety that you all have of when, when, when, when is FDA going to go live, we now have some tentative dates. And we believe that these dates will be attained, and we will be able to complete this. So -- so, yes, those are the dates that we have.

Hopefully, then you can work around with your vendors, work around with your releasors,

work around with your testing, and all of that. Because as we all know, that we also have to work around with our vendors, with different releasors, with their releasors, with our releasors, and so on and so forth. So everything had to be worked around to make sure that it was successfully done.

Next bullet point. So update on FDA Electronic Submission web page, as I said, a lot of this information that we have all talked about will go into the FAERS Electronic Submission web page. We will be updating with the E2B Validator. You know, the FAERS Electronic Submission web page will also point to the meeting page where you will have all of this information available. And finally, the FAERS Electronic Submission web page.

At some point, we'll get revamped. Because we're going to make one page a main page, and from there, there will be two links. One going to E2B(R2) and (R3). So that once the time comes that we are reconditioning R2, the link to the

R2 page will be gone, and it will be only R3. Okay. So you will probably see a revamp page in January of the FAERS Electronic Submission page.

Okay. Next, we communicated what submitters can do to prepare themselves. So these are all some, you know, suggestions. And hopefully, that will help you in testing with us.

And next bullet point. And we recommend some scenarios to test. We gave you some scenarios, we listed some scenarios. You know, please do test them, that will be great. We will want you to all have positive acknowledgments and files getting into FAERS.

If a file does not get into FAERS, that means you have a negative acknowledgment. And please do make sure that you've got the acknowledgment. Sometimes the acknowledgement is a little delayed, but should come. If the acknowledgment does not come, then you will contact us. But you should get an acknowledgment.

So that kind of keeps the loop closed,

to say that you submitted something and you got an acknowledgment. So that loop is closed. And make sure that you have -- because a negative, of course, you have to resubmit correct -- with the corrections and all of that.

All right. Next bullet point. Okay. So this is basically my last slide. And this slide is basically talking about all the differences that we have, where what is. All the links to everything.

Of course, the dates may change when we publish something, but the links will still be the same because it will have the latest and the greatest document of the information there.

Once we publish things like the rough guidance becomes a final guidance, and that will become a final guidance, anything that is to do with -- with the -- with any kind of binding items and all of that, so they will all be published. And so -- so, yeah. So this page -- this link. Keep a bookmark on this. If you just put a bookmark on the first link

that you have, all of these are under that. So you will be able to go find all the documents under the main web page.

So with that, today, I know I finished early. But my throat has started hurting. But we will take a -- probably a ten-minute break and then start with some questions and answers that we can answer. We will probably -- instead of noon, we'll probably end this by around 11:45. 15 minutes earlier.

But basically, a ten-minute break so that I can go over some of the questions and answers, and then come back at 11:30 to answer some of the questions that we have got through the question-and-answer window on Zoom.

All right. So with that, thank you. And I will see you at 11:30. Thank you.

(Off the record.)

MR. DE: So welcome back again. We're going to have a 15-minute session for answering the questions. And I will be answering whatever I can

answer in the 15 minutes and then the meeting will be definitely posted. Because some of the questions and answers, we have to go back and walk through that. Some dealing with compliance things, we have to work through some clearances. And we will definitely then post those questions for you.

Okay. So there is a question about if you're a small academic entity and if you need to submit a premarket ICSR via SRP, then you all have all other documents. Yes, the other documents are to be submitted. The ICSRs are only to be submitted by SRP if you're a small entity. If you don't use a Gateway process, or a Gateway system, or a Gateway setup, then just submit -- you will use the SRP to submit those ICSRs.

So there could be other documents, and you know, risk management plan, change with the protocol and all of that, so those still need to be submitted through the ACTD. And same also applies for other sponsors that those type of documents you will submit to ACTD. If it's ICSRs, you can use the

Gateway to submit to FAERS.

Okay. All right. Next question. So if you have something -- if something, you know, was sent as expedited incorrectly, but it was non-expedited, do we need to collect it immediately or wait for the next significant follow-up and send a downgrade then?

So I mean, if you have identified that it is an issue, then you should immediately notify that to us by submitting it so we can follow up to say that this was a nonexpedited report, we can correctly submit it as an expedited report.

But we will also recommend that you put down a sentence in the narrative stating that this was incorrectly submitted, and so we have corrected it. Because just changing an expedited to a non-expedited, you know, sometimes we may be wondering what happened here. Why did an expedite suddenly become a nonexpedited; right? So giving a little bit of a line or so in the narrative will really help us to know that.

Then we have another question that -- so if you only have an AS2 account, where and how can I find and use E2B Validator? As I said, that it is to account for an E2B Validator there with each other. The E2B Validator is as simple as you have a bookmark on your browser. You just go to your browser, click on the bookmark, the screen that you saw will come up. You test everything. It has nothing to do with the Gateway; okay? It's totally independent.

So -- all right. Let's see. So when does FDA finally begin accepting adverse event under the new regulation? I wouldn't say it's a new regulation, it's a new standard that is under the Electronic Submission. So I gave you the timelines. So postmarket, we will start in January and premarket will start in March.

How long will there be acceptance on R2? As I said, it will be two years of voluntary period.

And let me see. Any other

questions? Okay. How do attachments work? Yes, attachment is part of the XML. It's not separate, so it's part of the XML.

So the ICH needs to be -- the implementation guide will tell you how attachments are to be embedded with that XML and sub. And specifically, our technical team should be also able to set that up for you. But yes, it is part of the XML. And like R2, they are supposed to be separate. R3, it's all embedded.

Okay. So E2B(R3) Gateway will be launched or initially testing and productive use by end of this year 2023. So we said that if by the end of this year 2023, we will have our system all set up ready and everything to be done.

So we -- our actual launch -- so when we said it's the end of this year, that's our double end up work, our testing, everything so we can say we are ready to launch. And we will give it a few days and then our launch date, as I said, will be January.

And how do you know about the launch date? The FAERS Electronic Submission web page will notify you that and say, hey, FDA -- it will probably say something like, FDA is now ready to submit R3 to accept postmarket safety reports in ICH E2B(R3) format, along with the regional data elements, and so on, and so forth. So that is what those dates will say.

How would solicited ICSRs be sent? ZZFDA_PREMKT or -- as I said, it will all be ZZFDA. And I gave some examples, some scenarios in some of the slides. So when you go back and look at the slides, you will be able to see those scenarios.

What are the size limitations of the batch? The batch, I think, is 100 GB. And each ICSR, I think what we are saying is -- wherever there is a -- the ICSR submission size is less than 100 megabytes. So -- so the entire big size of the entire batch could be up to 100 GB. So that's what FDA can accept through the Gateway.

Okay. So there's another question,

what would be the impact of having multiple warnings on a -- for ICSRs? Again, warnings are something that we have brought for our sponsors to go back and please look at it and see if they can correct it and send it to us in a future follow-up.

I mean, if you don't correct it, of course, nothing is going to get rejected, but I think it's a good idea that -- to have better data quality, both from our side and our side, and so that we can do better review and for better public health assessments that we do. You know, good data is important.

And so we will suggest and recommend that you correct the warnings and send it to us, but if you don't send it, you know, it's just going to stay the same, nothing is going to happen. But of course, rejections definitely will be rejection.

Okay. Then -- yes. Can you please confirm if the validator will be available post the mandatory data -- validator will be available throughout. I mean, it will be on the Electronic Submission web page. And we are not going to get that

down. It's going to be available throughout. Because in future, let's say we find there is some data points that are an issue, and we are constantly seeing that we may have a change in data rules.

Of course, we will notify that way ahead of time, but we will update the validator to make sure that that is checked. So the validator is -- will be available and that you can also check that for those changes in the validator.

Okay. The messages that shows up in the validator is the same messages that will show up in the acknowledgment. So there is a question that -- will the messages be the same? Yes, the messages will be the same in both the validator and the actual acknowledgment.

How long will the transition from R2 to R3 be? So again, as we said, it's approximately a two-year transition period. That means that two years is a voluntary period. Which means -- what is the voluntary period? It means that if you have not moved over to R3 during that two-period -- two-year period,

fine. But right after the two-period is over, we are expecting an R3. We will not accept any R2 submission. So that is the voluntary period.

That means, if you're ready, please go ahead and start submitting in R3. That's the two-year one repeated. So it could be -- you can consider yourself as a two-year transition period. The sooner you do, the better it is.

So a question is, can you elaborate on the report and case nullification? Are the requirements same for both pre and postmarket? And how about spontaneous report in pre and post -- yes. I mean case nullification is case nullification. That's -- that's if the case was -- was -- should not be -- probably is not your case, somebody else's case, somebody -- another company case and you wanted to move it from your database and you have submitted it accidentally, then yes, we'll nullify that report and then that nullification will come to us and we will nullify. We'll get it nullified.

But if you had a change, saying, I did not want to submit this version of the report, I wanted to -- then in that case, that we cannot nullify because it's always a case nullification, not a report nullification.

So you may want to submit just a follow-up to correct any kind of information or an amendment to correct any kind of information. So -- so, yes. So it is what a case nullification is, to nullify an entire report.

Where is the report? Everything is available at the webinar. So what is available in the webinar is -- so let's click on the first link. It says accessible at. So this is the -- whenever I say FAERS Electronic Submission web page, this is the page. This is the page in which the E2B Validator link also will be available.

Okay. Now, on this page, let's go to the bottom of the page. And there are different resources for you. In the resources for you, the third one, which is a public meeting, if you click on

that, it takes you to the meeting page. This is where all the previous meetings are put; right? So the last meeting that happened was -- so and so. The last meeting's information is also provided with the recording and everything, the agenda, and everything.

So now you see under November 4th -- April 4th, you have the agenda, you have the presentation slides, it also has the recording down at the bottom. Same way -- yeah. I think they have the live recording for April 4th. Same way for November 7th, today. You only have the agenda. You will have the presentation slides and we'll convert in PDF. And the live recordings will also show up here.

So this is where you can see the entire thing. If anyone has missed anything or anyone have -- if colleagues have missed anything, they can all go in here and look at it.

Okay. All right. Maybe we can take one more question. Maybe two more questions. Okay. So this is a question about the

population of the local criteria report type, which is the 5-day, 7-day, 15-day, all that kind of thing.

So the question is, my understanding is the sponsor should report fatal life-threatening ICSR within seven days of initial receipt of the information. This ISCR would reflect the 7-day report, which is 46. Can we as a sponsor continue to send follow-up for this scenario as a 7-day report? And the answer is, yes, you can continue to submit that as a 7-day report. It's basically follow-up information on the 7-day report that should be submitted.

Are there communications going on with safety database senders? Yes, there are communications going on. But in my personal view, is I don't know how communication is going -- should be going on to an extent that it's going on right now. I would think that with all our specifications submitted and all that, you know, they will be connecting with us. And what can you ask? Because I do understand that things have changed. It was not those days when

we implemented E2B(R2). Now, most of the companies have their own -- they have exports. So they have vendors. So if the vendors have updated their systems and they provide that release to all their customers, then all the customers are now E2B(R3) ready.

But -- so I don't know at what -- they do send us questions, we do answer them. But I still feel that it's probably not enough. Or maybe they are -- their exports now, with looking at the specifications, that our specifications are so good and so well-organized that it's very clear to everyone. But yes, we do get some sometimes, we get questions from these vendors.

But I would, again, suggest that, you know, work with your vendors, talk to them, and you know, the better connected we are, I think the better smooth implementation will happen. We really do not want any glitch happening. We do not want -- because it's good for both of us. Because you won't be asking us too many questions on this and we are spending too much time on the specifications again. So the sooner

we can do this, the better it is. And work with your vendors, talk to your vendors, and -- and they can also talk to us.

Another thing that we give the vendors, we told the vendors that they can have actual access to the WebTrader on the preproduction environment, which we used to never give the vendors. We actually gave the vendors this and I only probably know one, maybe two vendors, who have taken an account on the WebTrader, because they all wanted to test this. So -- so encourage your vendors to get access to the WebTrader and preproduction so they can test before the releases come to you.

All right. One last question. During the voluntary period, can a particular company submit some reports in E2B(R2) and some E2B(R3) format? It's a very tricky question. It's -- if you're submitting on the same ICSRs and there's a problem, if you have the same safety report ID; right? Because the case has come as an E2B(R2), you submit on that.

And now, you're submitting an R3 on

that. And if you go back to an R2, then there's a problem. Yes, some can continue to be R2, then you have some continue to R3. But I -- the way I see it is if you move to R3, you probably will have moved to R3 for all the reports.

But yes, there is a choice that you can go -- as I said, you can start with postmarket to do R2, and then move to premarket in R3; right? Or you could have postmarket going to R3 first, and then going to premarket in R3; right?

So it's up to you. So all the postmarket reports have come in as R2, as you are submitting today, but you are focused on premarket first and then postmarket.

So, yes, then that is possible. But it's important that once you submit a report in R3 format, you cannot go back to an R2 format for that report; okay?

So -- so for all the comments, and questions, slides, they all will be posted. So don't worry, we will post -- we may post even the

presentation slides first and then the recording. So we may have -- I think we should be able to post the presentation slides hopefully by this week, you know? So you will have all of that. So don't worry about that, you will get everything.

So with that, I end my presentation, I end my talk. Thank you so much for your time and for your effort. We want to be collaborative. We want to work together. Better communication -- you know, communicate better, and so that we make this as a success with E2B(R3) submissions to the FDA.

And we really look forward for your cooperation and your help. And -- and to even make this as a success for all of us from your sponsors' perspective, as well as from the agency's perspective.

So thank you. If you have any further questions, please do send the questions through the docket. Or you can send the questions to the EPrompt mailbox that we have, Eprompt@fda.hhs.gov. And we will make sure that we will try to answer those

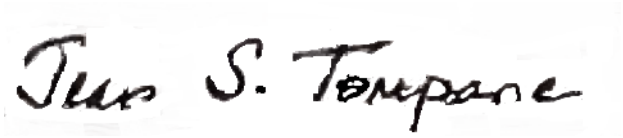
questions. And of course, also these questions and answers will get into an FAQ.

So, thank you. And have a wonderful day and a wonderful week. Bye-bye.

(Whereupon, the meeting concluded at 11:51 a.m.)

CERTIFICATE

I, JEAN TOMPANE, the officer before whom the foregoing proceedings were taken, do hereby certify that any witness(es) in the foregoing proceedings, prior to testifying, were duly sworn; that the proceedings were recorded by me and thereafter reduced to typewriting by a qualified transcriptionist; that said digital audio recording of said proceedings are a true and accurate record to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.



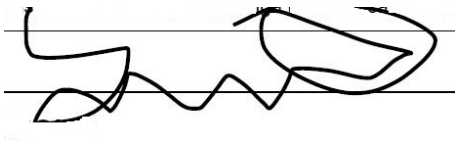
JEAN TOMPANE

Notary Public in and for the

State of Maryland

CERTIFICATE OF TRANSCRIBER

I, SAMANTHA TAMBURRINO, do hereby certify that this transcript was prepared from the digital audio recording of the foregoing proceeding, that said transcript is a true and accurate record of the proceedings to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.



SAMANTHA TAMBURRINO