

NWX-FDA OC (US)

Moderator: Irene Aihie
February 12, 2016
2:00 pm ET

Coordinator: Welcome, and thank you for standing by. At this time all participants are in a listen only mode. At the end of today's presentation, we will conduct a question and answer session. Questions and answers will only be taken over phone line today.

If you would like to ask a question you may press star 1. Today's conference is being recorded, if you have any objections, you may disconnect at this time. I would now like to turn the meeting over to Miss Irene Aihie. You may begin.

Irene Aihie: Thank you. Hello, and welcome to today's FDA webinar. I am Irene Aihie of CDRH's at the Office of Communication and Education. Today's webinar will provide an overview of the FDA's current policy on color additives for medical devices.

It will also describe the FDA's approach to the evaluation of marketing applications for medical devices containing color additives. Your presenter is

Jennifer Goode a senior scientific reviewer from the Office of Device Evaluation.

With technical knowledge of biocompatibility test methodologies and who works as a standards liaison for the development of national and international bio co-compatibility standards.

Following the presentation, we will open the lines for your questions related to the current FDA policy. Joining us for the Q&A portion of today's webinar are Dr. Jonette Foy, Deputy Director for Engineering and Science Review and Angela Krueger, Associate Director for Guidance and Regulations. Both are from the office of Device Evaluation. Now, I give you Jennifer.

Jennifer Goode: Thank you very much to everyone who has joined us for the webinar today. We're going to be speaking about color additives and medical device review. The goals for the webinar today are to describe and clarify the current policy in the Office of Device Evaluation and the approach we are taking for the evaluation of marketing applications for medical devices that contain color additives.

We also are doing this to ensure a consistent approach is being applied to reviews for medical devices that contain color additives.

Today I'll be providing some background information, and some definitions and so that we're all on the same page. I'm going to talk to you about the general color additive approach we're taking in the Office of Medical Device Evaluation, when this approach should be used, the hierarchal risk base approach that has been developed, some Guiding Principles that help support the color additive approach and details regarding this approach including some examples. And I'll close with some next steps.

For background, it's important to remind the audience that Section 721 of the Food, Drug, and Cosmetic Act outlines listing and certification requirements for color additives for foods, drugs, devices, and cosmetics.

And in the act in Section 721a it states that a color additive to be used in a device is exempt from listing unless the color additive comes in direct contact with the body of man or other animals for a significant period of time.

We want to point out that ODE does not consider use of a color additive in or on a device to be in contact with the body for a significant period of time if the contact duration is 30 days or less. And there are several sections in the FD&C Act and in the regulations specific to color additives that are listed here.

So, I'm going to start with some definitions that we think are important to understand so that the color additive approach is more clear. The first definition that I want to share with you is from 201(t) of the FD&C Act. It defines a color additive as a dye, pigment, or other substance that is capable of imparting color.

For use in a medical device, the color additive can be capable of imparting color when it is added or applied to the human body. But it does not need to actually impart color to the body from its use in a device to be a color additive.

We will be talking today about US legally marketed devices in terms of how these can be used as a comparison device. And this can refer either to a predicate device or a reference device which has similar tissue contact. And when we talk about contact, we talk about type and duration of contact.

So, an example on this slide is one for a coronary balloon angioplasty device. And that can be compared to a delivery system such as for a superficial femoral artery stent. Because these devices both have the same type of contact, cardiovascular tissue and blood and they're used for less than 24 hours and this type and duration categorization is common to biocompatibility review. And you can see more about that in FDA's Guidance G95-1 or the ISO Standard 10993-1.

For biocompatibility evaluations we also have some definitions that we use in those types of assessments and it's important to understand what we mean by the terms direct contact, indirect contact, and transient contact.

For direct contact, a device or device component would come into physical contact with body tissue.

For indirect contact, the device or component would be - would have a fluid or gas passing through it and that fluid or gas would then come into physical contact with the body tissue. In this case the device or device component itself does not physically contact body tissue.

For transient contact, the device or component comes into very brief or transient contact with body tissue, usually for less than one minute and some examples are included on this slide.

We also want to go over, very briefly, a biocompatibility term called tolerable intake or TI. This is a dose in milligrams per kilograms per day, below which adverse systemic effects are not likely to occur. This dose is not intended to be protective for all adverse effects, so it would not be protective for hypersensitivity.

But it can be used in the color additive assessments and the approach that we use has been described in 10993-17 if you'd like more information on this approach.

So, our basic approach in the Office of Device Evaluation is based on G95-1 our FDA Guidance and ISO 10993-1 which is a general biocompatibility standard.

And if this information is available, it can be used for this approach. In addition, our approach is based on our current practice. This is intended to be risk based and least burdensome, as well as scientifically based.

And essentially leverages information already available, that is biocompatibility testing of a device in its final, finished form. In addition, this approach is intended to minimize the need for additional color additive information or extraction studies to look for color additive release where appropriate.

So, when should this approach be used? This approach is specific for marketing applications. So, this means 510ks, PMAs, de novo requests or HDEs. The follow up question, of course, would be what about IDEs? So, this approach is not required to initiate IDEs.

However, if there is toxicity risk identified for any chemicals used to manufacture a device, including any color additives, it may be necessary for us to ask for appropriate safety information prior to investigation in humans. But of course, a risk based approach would be used.

So, the approach that is developed in this document or in this webinar is a hierarchical, risk-based approach which uses type and duration of contact categories as outlined in ISO 10993-1 and G95-1. And, in particular, we want to share with you that different color additive information is needed for:

Devices or components with either no patient contact - and we have several slides in Section 1 of this presentation.

Devices with less than 24-hour contact in Section 2.

Devices with 24 hour to 30-day contact in Section 3 and

Devices with greater than 30-day contact in Section 4.

The first Guiding Principle is the current approach that's been discussed with our staff which is to determine whether color additive information is needed per Guiding Principles Number 7 and 8 that I'll talk about later.

And just so we're on the same page, Guiding Principle Number 7 is specific to the type of descriptive color additive information that might be needed. And Guiding Principle 8 is specific to risk assessment color additive information that might be needed.

And our first Guiding Principle says that the least burdensome, risk-based approach is to be used and the need for information in Guiding Principles 7 and 8 must be interpreted in the appropriate regulatory context, that is - compared to other similar marketed products.

Guiding Principle Number 2 points out that if you're marketing submission is for a new device or device where the identified US legally marketed comparison device is made by a different manufacturer, the concepts described in slides through Section 1-4 should be followed.

Guiding Principle Number 3 states that if you have made a device modification, the color additive evaluation should be focused only on the

device or component modifications, unless the change could affect other parts of the device that were not changed. And in this case the color additive information should be provided for the impacted portions of the device, only.

So an example is that if the tip of a catheter is changed then only color additive information for the tip would be needed, unless the change could affect other parts of the device that were not changed.

Guiding Principle 4 points out that when assessing device modifications, it's important to explain why the modification is not expected to affect color additive release.

The types of changes that might affect color additive release include material changes or design changes. However, you may have prior testing that may help with the assessment. So, biocompatibility testing using extracts may help you if you can show through visual observation that the color or turbidity has not changed or there are no particulates present.

You may also have performance testing for a particular type of device that could help you determine whether or not color additives might be likely to be released. And these include in vitro particulate or wear testing with colored particles or animal studies with colored fragments at explant.

So, some material changes that might affect color additive release include changes to formulation of the polymer matrix, a color additive amount, or a color additive type.

Design changes that might affect color additive release include changes to how the color additive is incorporated into the patient contacting portion of

the device such as being mixed into the polymer versus being stamped on the surface.

Guiding principle Number 5 points out that if the device change is not likely to affect release of color additives, per the available evidence, no color additive information per Guiding Principle 7 or Guiding Principle Number 8 is needed.

However, throughout this presentation we want to remind you that even if you don't need to provide color additive information, your marketing submission will still need to include a biological evaluation. And this biological evaluation should assess the device in its final, finished form in accordance with G95-1.

And it may include either testing on the device and/or a rationale for why testing was not performed.

Guiding Principle Number 6 points out that if the contact is with intact skin for up to 30 days no color additive information per Guiding Principle 7, Device Description, or Guiding Principle 8, Risk Assessment, is needed.

For other types of contact up to 30 days, color additive information may be needed and there are slides in Sections 2 and 3 that help to explain this in more detail. For contact greater than 30 days, regardless of the type of contact, color additive information is needed. And so, we have slides specific to this as well in Section 4.

Guiding Principle Number 7 says that if color additive is needed and we'll talk about this later in the presentation in what we call Sections 2-4.

The following information is what we are looking for:

- The first is the chemical name or chemical abstract service number.
- Purity information which could include CFR color listing, raw materials certificates of analysis, or raw material or final device testing for impurities.
- And an estimated or calculated maximum amounts of each color additive and weight per device. So, that's the set of color additive information that would be needed.

Or you may be able to identify a US legally marketed device with the same color additives, the same matrix material and the same processing.

We want to point out that sometimes there may be relevant material supplier master files that include the information that we've asked for in Guiding Principle 7 items 1-3.

For Guiding Principle 8 no additional color additive information will be needed if the color additive amount in the proposed device is less than or equal to a comparator device with same color additive, same type and duration of tissue contact, same matrix material, and similar intended use.

Or if the color additive or impurity amounts are less than tolerable intake derived for the color additives and impurities.

We want to point out that prior submissions can be used as comparators even if these prior submissions did not include color additive information.

Additional color additive risk assessment will be needed if the color amount is greater than the comparator device that has the same color additive, same type and duration of tissue contact, same matrix material, and similar intended use.

You would need to do more in terms of risk assessment if the color additive amount is the same or less than the comparator, but the conditions of device use are not comparable: so, if your tissue or body fluid interface or duration is different.

So, for this example, if you're comparing to a device that's in contact with the skin and your new device is an implant, those would be different conditions of device use and, therefore, it wouldn't be sufficient to not need more risk assessment information.

So, for Guiding Principle Number 8 I want to point out this red box on the bottom because I'm going to bring this back later on as a reminder of what these Guiding Principles are. And this is the decision flow. If your amount is greater than the TI or the amount in the device is unknown.

We're asking that you model or determine the expected release such as with elution testing. If the amount released is greater than a TI then you go to the right side of this box and the first thing you would do is a benefit risk assessment.

Then, if the benefit doesn't outweigh the risk, you might have to think about reducing the color additive amount in the device. If that can't be done, you might need to look at some in vivo fate testing. And then, if that doesn't help you to resolve this, perhaps you might need a color additive petition.

So, I'm going to give a little bit more on this Guiding Principle 8 risk assessment process in the next few slides. So, some examples of benefit risk assessment include:

- a life saving device used in patients with less than one-year life expectancy.

- The amount of the color additive used in the device is needed for proper placement or the color or

- impurity risks e.g., for cancer, don't outweigh the benefits.

And so these might be some examples where you could provide a benefit risk assessment and decide that you could stop.

When considering whether you or not you might need to reduce the color additive amount in the device, you might want to consider reducing the amount of the color additive to the same or below a US legally marketed device with the same duration and route of exposure.

Or you might want to reduce the exposure to a level corresponding to an acceptable risk in accordance with the risk assessment.

Some other possible options:

- in certain circumstances such as for colored absorbable devices; you may need to conduct some fate testing to see where the color goes and how long it lasts.

- And in some cases you may need to submit a color additive petition depending on further risk assessment, fate test outcomes, and discussions with CDRH.

The last Guiding Principle we want to talk about is if other color additive concerns are identified during the review process. Our review staff will be discussing with their management whether or not additional information or testing is needed.

In addition, if you have questions about the color additive information being requested, we encourage you to contact our review staff and management to discuss this.

So, now I'm going to go into the detailed color additive approach.

In Section 1 we're considering devices and components with no patient contact. And these could be either direct or indirect contact. For these devices you would not need biocompatibility information and you would also not need color additive information per Guiding Principles 7 and 8.

If your device or component has contact for less than 24 hours we call this Section 2. And there are a couple types of devices in this category. If the contact is less than one minute, what we're calling transient contact, and you've determined that the device might release color additive, we would expect you to perform a biological evaluation of the device in its final, finished form. And this might include some device testing and/or a rationale for why testing was not needed.

However, no color additive information would be needed per Guiding Principle 7 or Guiding Principle 8, unless performance testing that you would already do for this device type suggests colored material release.

And as a reminder this could be in vitro particulate release testing showing colored particles. This could be embolized or migrated colored material in an animal study. Or it could be wear testing demonstrating colored particulates.

If the contact for the device is greater than one minute, there are three tests that we are looking at: Cytotoxicity sensitization and irritation, what we're calling CSI tests. If these were performed on the device in its final, finished form with acceptable results and the extracts showed no change in color or turbidity and no visible particulates, then we would like you to perform your

biological evaluation for all other endpoints per G95-1. This could be testing and/or a rationale.

But no color additive information would be needed per Guiding Principle 7 and 8.

For the same contact duration, if the device could release color additive, but the CSI test cytotoxicity sensitization and irritation were not performed with acceptable results or they were performed with acceptable results, but the extracts showed a change in color or turbidity and/or there were visible particulates present, then we would want you to perform the other - an assessment of the other endpoints for biocompatibility.

And in addition, we would like color additive information and risk assessment information per Guiding Principle 7 and 8.

So, as a reminder, Guiding Principle 7 says that you would provide the chemical name or CAS number, purity information, and the maximum amount. Or you would identify a US marketed device with the same color additive, matrix, and processing.

If the color additive amount is less than or equal to the appropriate comparator or less than a TI, no color additive risk assessment information per Guiding Principle 8 is needed. If this is not true, then you would have to go to Guiding Principle 8 and look at the amount.

If it's greater than the TI or amount in the device is unknown, you would model. If the amount released is greater than the TI, you'd have to move into this hierarchical approach on the right.

The next section has to do with devices that are used 24 hours to 30 days,
Section 3.

In this particular assessment your CSI tests: cytotoxicity, sensitization, and irritation should be performed on the device in final, finished form with acceptable results and other tests identified by G95-1 should be performed on the device in final, finished form with acceptable results.

And your extracts should have no change in color or turbidity, or visible particulates. If all of these three are true, no color additive information would be needed. We want remind you that repeat use could result in being in this category, 24 hours to 30 days. An example is provided on this slide.

So, what's different between the last section: less than 24 hours use, and this section: 24 hours to 30-day use? It is the second bullet here in this square. So, you may have other endpoints that you need to assess for a less than 24-hour use device, but you're making your color additive determination just on your CSI testing.

For 24 hours to 30 days, you have to make your assessment based on all of the biocompatibility testing.

So, if you're - so these next few slides are going to go over some examples for how you can use this information to determine what you actually do need to provide further color additive information.

So, for example, if your cytotoxicity, sensitization, and irritation tests are not performed with acceptable results or some other of your G95-1 biocompatibility are not performed with acceptable results or all tests were performed with acceptable results, but the extracts had either a change in color

or turbidity or there are visible particulates, then you would have to address these issues in your biological evaluation and you would have to provide color additive information per Guiding Principle 7 and risk assessment information information per Guiding Principle 8.

So, I'm going to give some examples so that this is a little bit more clear. All of these examples will use a multi-day infusion catheter and will talk about when you need color additive information versus when you don't.

So, if your CSI tests: cytotoxicity, sensitization, irritation were performed on the device in final, finished form with acceptable results, the other G95-1 tests were performed on the device in final, finished form with acceptable results and the extracts for all the tests: there were no change in color or turbidity, and no visible particulates.

Then, you don't have to provide color additive information for the 24-hour to 30-day group.

In Example 2, we again have cytotoxicity and sensitization performed with acceptable results, but in this case irritation testing showed slight toxicity.

The other G95-1 tests were performed with acceptable results and there were no problems with the extracts. There were no changes in color or turbidity and there were no visible particulates.

Because of this irritation test showing slight toxicity, we would ask for color additive information per Guiding Principle 7 and risk assessment information per Guiding Principle 8.

In Example 3, we again have the multi-day infusion catheter, all of the CSI tests were performed with acceptable results. There was no genotoxicity testing on the device in its final, finished form provided, but the other G95-1 tests were performed with acceptable results.

And all the extracts were fine. However, because genotoxicity testing was not provided, this would bump you into a category where color additive information per Guiding Principle 7 and risk assessment information per Guiding Principle 8 would be needed.

I have two examples that have to do with particulates 4a and 4b. So in this particular case your CSI tests were performed, your other G95 tests were performed. They all had acceptable results. But in the extracts there were visible particulates present in at least one of the tests.

Because there were visible particulates present, this would put you into the category where color additive information per Guiding Principle 7 and risk assessment information per Guiding Principle 8 would be needed.

I said I had two examples on this because there might be a case where you have visible particulates present. But if you can provide information down here in the caveat to confirm that the source of the particulates is not from the leaching of color additives during biocompatibility extraction studies, for example, if you have images to document particulates are cutting artifacts that occur prior to extraction or chemical identification of particulates to show that these are not colors, and then you would not have to give us color additive information per Guiding Principle 7 or Guiding Principle 8.

So, just a reminder, Guiding Principle 7 is your descriptive information. Either the chemical, purity and the amount, or an identification of an appropriate

comparator with the same CA matrix. If you can show that the CA amount is less or equal to the appropriate comparator or less than a TI, you don't need to give any risk assessment information.

If you need to provide risk assessment information per Guiding Principle 8, you make a determination based on the amount in the device from modeling or elution testing. And if the amount is then greater than the TI, then you have to move into your benefit risk assessment and considerations for maybe further information.

In our last section, Section 4, this is for devices with greater than 30-day use. Again, we have to consider repeat use beyond 30 days for this. An example of a hemodialyzer is provided here. For these devices, we expect to see a biological evaluation of the device as well as color additive information per Guiding Principle 7, and risk assessment information per Guiding Principle Number 8.

And we went over this slide previously. It's the same information for Guiding Principle 7, and the same approach for Guiding Principle 8.

Some other considerations that we wanted to share with you are how to determine what the most appropriate test article for your biocompatibility testing.

And this is specific for devices where you might provide a range of devices with a range of colors. So, for example, if you have a device that you're going to be submitting in a single marketing application that could include different types and amounts of colors, such as contact lenses. A device sample incorporating all the colors could be used for biocompatibility testing.

Similarly, if you are providing a device in a range of shades of a particular color such as for colored dental composite resins, the device with the most color additives could be used for biocompatibility testing.

So, in summary, I just want to remind everybody that this color additives approach is based on G95-1 FDA's Biocompatibility Guidance, ISO 10993-1 a Biocompatibility Standard, and our current practice in ODE. It's intended to be risk-based, least burdensome, and scientifically based.

It's intended to leverage information that, likely, is already available for your device, that is, biocompatibility testing of the device itself. And if this approach is used, it can minimize the need for additional color additive information or extraction studies to look specifically for color additive release, where appropriate.

We wanted to share with you that we are planning a future draft Level 1 Guidance for color additives in medical devices to include a lot more issues associated with color additives for which we know that some additional discussion and direction would be helpful.

At this time, we are going to open the webinar up to questions. Do we have any questions in queue?

Coordinator: Yes, our first question is from (Tony), your line is open. All right I believe she disconnected. One moment please for the next question. Our next question is from (Arish), your line is open.

(Arish): Hi, my question was in regards to, how does this relate to items listed in Section 81.10. In regards to color additives for food, drugs, and cosmetics that may be used in medical device applications that have been removed from the

provisional listing. Are those acceptable, given that this level, this assessment's made and appropriate testing's done?

Coordinator: One moment please for our next question.

Jennifer Goode: So, I think you're speaking about delisted colors, is that correct?

(Arish): Right, for, so, channel black, for example, that may be used in low percentages in medical device components, like a catheter tip for example.

Jennifer Goode: So, we know that some banned or delisted colors have been used historically in some medical devices. And so, this approach considers that if release into the body is minimized, such as for short contact duration where there's minimal risk of release, we actually need to balance whether the risk to the patient is appropriately controlled. And so, we are saying in this approach that if you can show that you have short term use and you don't have any apparent release, we're not going to be asking you for color additive information.

And so, if those colors are used that would be acceptable. But if there is release then we would have to have more discussion about this. And specific issues associated with delisted or banned colors such as carbon black will be addressed in the draft Color Additive Guidance in more detail.

(Arish): Thank you, that helps.

Coordinator: Our next question is from (Sharon K. Smith) with (H&S Sharon Smith Pharms), your line is open.

(Sharon K. Smith): Should I go forward on my question and repeat it?

Coordinator: Yes ma'am go ahead.

(Sharon K. Smith): The question I had was that I heard in your presentation, the mention once of the issue of genotoxicity, I was trying to get further information on when you might specify the necessity of genotoxicity testing.

And also, I did not hear you mention, today, the element of immunotoxicity. When if in your regulations have you specified or indicated some requirement for immunotoxicity testing?

Jennifer Goode: Thank you for that question. So, our FDA Guidance for Medical Devices and Biocompatibility G95-1 and the ISO Standard ISO 10993-1 identifies when genotoxicity and immunotoxicity information would be needed. And this is based on different devices and their type and duration of contact.

So, we didn't go into detail in this presentation, but we refer you to those guidances and standards to see where your device might require that that endpoint be assessed. And for a color additive assessment, if you don't want to provide color additive information, we are saying that you actually need to do the testing on the device in the final, finished form.

If you don't think that testing is needed, then you can certainly provide a rationale to us, for that. But that would mean that you would also need to provide us with the color additive information. And that's true for both genotoxicity and immunotoxicity as well as other endpoints.

(Sharon K. Smith): Thank you.

Man: See if can turn it off.

Coordinator: Our next question is from (Michael Yorksoft) with (Arid Flight Sciences), your line is open.

(Michael Yorksoft): Yes, you know, our question actually was already asked about the delisted colorants, but as a follow up, do you have a timeline when the draft guidance should be released?

Jennifer Goode: Yes, we're beginning work on that. It's a priority for our center, but we don't tend to be very good at predicting those things. So, unfortunately, I can't give you a timeframe. I'm sorry.

(Michael Yorksoft): Thank you.

Coordinator: Our next question is form John Schaefer with CFI Medical.

John Schaefer: A couple of related questions. We make a number of devices in the general territory of surgical drapes and equipment covers. Generally speaking, most of these are KXXs since the August 2014 Guidance, these are exempt.

The general principle, as we understand it, is that when a device is exempt we're obviously not making a submission, but we should hold the information that would have gone into the submission in our DMR technical file for FDA's review if they should deem that to be necessary at a later date. Is that principle also applicable to colorants and to the discussion of today's webinar?

Angela Krueger: This is Angela Krueger. Yes, that's correct. I think you're referring to the Intent to Exempt Guidance document where the devices you described were included there. And so, at this time we're not enforcing the requirements for 510(k).

But similar to other devices which are exempt, we would expect for you to keep that information in your records should you be inspected or have to submit at a later date.

John Schaefer: Okay, and as a follow-up to that, a number of the devices that we make because of the nature of their use either have no direct patient contact or patient contact only with intact skin and only for a short period of time.

So they're either non-contact or short term contact. But some of the devices might have a kind of a transient contact that might occur when a surgeon touches, for instance, our non-patient contact equipment cover and then resumes surgery and makes patient contact in an invasive manor.

Is that kind of transient contact which might be longer than a minute in aggregate during a surgical procedure, but not much longer, is that kind of contact considered in the evaluation of transient versus short term?

Jennifer Goode: I think that you would be safe in assuming just about the contact intended for your product and that type of transient contact would not kick you into the need for color additive information for those products.

John Schaefer: Okay. All right, thank you.

Coordinator: Our next question is from (Marissa Lotum) with (Silestica), your line is open.

(Marissa Lotum): Hi, I have a question regarding the impurity testing you had discussed. If I'm receiving parts that have a color additive, just a plastic part from a supplier that has a color additive. Do I need to request impurity testing from them for every shipment or is it the one-time submission that we require?

Jennifer Goode: So, I think that you should be working with your parts suppliers to determine whether or not they're changing their color additives information that's coming to them.

We generally ask for information on a one-time basis to show us how you and your suppliers are working together to assure that the toxicity risks are minimized. But we do recognize that color additive suppliers may change things over time and it's important for you to be aware if a change is made by them.

And so, you would need to come up with some agreements with your supplier so that you're assured that what they're giving you is reasonably understood to be the same every time.

(Marissa Lotum): Okay.

Jennifer Goode: And meets the specifications.

(Marissa Lotum): Okay, thank you.

Coordinator: This is the operator. I would like to remind the participants if you would like ask a question, please press star 1. Please clearly record your first and last name as well as your company when prompted. Those pieces of information are required to ask your question. Our next question is from John Iannone with Toxikon, your line is open.

John Iannone: Hi, yes Jen, thank you very much for that presentation. I was wondering, you made a comment as to the pooling of multiple products that may have various different color additives present in the individual components.

Is there any direction that you would suggest in terms of the concentrations or ratios in order to minimize any potential dilution effects in reduction and concentration of an adverse chemical constituent?

Jennifer Goode: So, in the examples I provided, I actually wasn't talking about pooling of devices in an extraction sample for a biocompatibility test. I was talking about what sample is selected. And so, the two examples that were provided for you, one which was for contact lenses and one which was for dental devices: those groups tend to have worked with their device manufacturers over many years and have come to an agreement for how a biocompatibility test article can be fabricated to represent a range of devices in that product area. And so, those are usually a single device sample for the testing.

And they're fabricated so that they can cover the range of products that a manufacturer would like to include in a particular submission, either for a contact lens or for a dental device, where it's common to have ranges of colors.

John Iannone: Understood. So, if I am understanding correctly that agreement in the various different components that make up of that representative sample. The concentrations of various different components and materials in this master test article considered the concentrations and how those dilution affects may occur in terms of elution.

Jennifer Goode: I think the assumption for those products is that they will either select a product for the testing that has the highest amount of the color or they will manufacture a product for the testing that includes the range of available colors.

And I think that the more colors that you put into a product, you're likely to get more colors out during elution if any comes out at all. And so, we have been comfortable with that approach.

John Ianoone: Fair enough, thank you very much.

Coordinator: Our next question is from (Montina Heim) with (Elcon), your line is open.

(Montina Heim): Hi, this is Montina. You currently have very specific guidance for use of color additives in contact lenses in the FDA Guidance for Contact Lenses and also in the separate document for preparing color additives petitions for contact lenses, which is actually due for review this year. So my question is since you mentioned the new proposed guidance, would you be looking into merging these or would the Contact Lens Guidance remain separate? Thank you.

Dr. Jonette Foy: Hello, this is Dr. Jonette Foy from ODE. I think the intent with the draft guidance that Jen mentioned at the end for color additives that we would like to have go out would be more of a generic type of guidance document.

And then, just like with other areas when we have a very device-specific guidance document, you know, for a particular product area you would refer to that device specific guidance. But this would - the intent for what we were talking about would be a horizontal type guidance document.

(Montina Heim): Okay, thank you.

Coordinator: Our next question is from (Corishe) with (Edward Life Sciences), your line is open.

(Corishe): Hi, we had a question in regard to how do we handle assessing color additives that are proprietary information of our suppliers? In terms of clarity in regards to formulation and things like that.

Jennifer Goode: So, we have experience working color additives or components suppliers who want to maintain confidentiality of their information. And many of them are perfectly willing to provide that information to us. They may provide it in a master file, either through our Center for Devices or they may have an existing master file in the Center for Drugs.

And if the information we need is in either of those types of submissions, we can use that to support the marketing applications. And we have experience working with many different color suppliers who are willing to provide that information to us.

(Corishe): Thank you, that works.

Coordinator: Our next question is from Allison Komiyama with Acknowledge RS, your line is open.

Allison Komiyama: Hi Jen, great talk. This is really, really useful. My question is with regard to, you mentioned you could remove a colorant if it's above a level of a predicate device. You could take it out or reduce it to a level that's below your predicate device.

Would FDA want to see retesting on this or is sufficient to say okay we've removed it or we've taken the colorant completely out, you know, would they have to redo the biocompatibility testing?

Jennifer Goode: So, I think when you make a change you have to explain why you think that previous testing that you've done before is sufficient. And depending on how you make that change, you clearly might need to do a rationale and that could be sufficient and in some cases it might not be sufficient.

So you would need to think about how that change might impact your biocompatibility. And you also might need to think about how that change might impact your performance testing.

Allison Komiyama: Sure.

Jennifer Goode: We have experience with people removing color additives and providing a reasonable rationale and not having to do any biocompatibility or performance testing. But it's going to depend on the specifics of a particular case.

Allison Komiyama: Okay, thank you.

Coordinator: Our next question is from (Ted Heis) with (Cook Medical).

(Ted Heis): Hey, thanks for the great presentation Jen. I wanted to ask you about the TI piece of it and if you had any thoughts or if the guidance would address what options might be if there wasn't a TI available from the literature?

Jennifer Goode: I think that there will be some cases where there won't be a TI from the literature and different toxicology approaches would be reasonable. Such as, a threshold of toxicologic concern.

And depending on what the color or the impurity is that we're talking about that may or may not be supportable and we are planning to have more detail in the draft guidance for people to consider.

(Ted Heis): Great, thank you.

Coordinator: Next Question is from (Allison Ray) with (Cordis), your line is open.

(Allison Ray): Hi, I have a question about the CSI testing and the products being in the final, finished form. Would you consider that being sterilized product or can it just be complete and built devices?

Jennifer Goode: Because sterilization can impact how chemicals are released from a device, we would expect that if your device is intended to be use sterile, that the product that's used in the biocompatibility testing would also be sterile.

(Allison Ray): Okay, thank you for clarifying.

Coordinator: Our next question is from (Bob Duffy) with (Bob Duffy Associates), your line is open.

(Bob Duffy): You had mentioned that you had received information from multiple material suppliers in way of their master files. Is there a plan to have some kind of a listing as to what information you may have that we can refer to or should we always need to just go back to the manufacturer and try to figure it out that way?

Jennifer Goode: So, anything submitted to us whether it's through a device submission or a master file is proprietary to the person who submits it. So, we can't necessarily say, oh these different people have master files because that would be revealing proprietary information.

So, we do recommend that when you're working with your suppliers, you ask them whether or not they have information available. If they're not familiar with our master file program, we have information that can be shared with them. We are always very happy to work with the materials suppliers.

We find the master file to be a very convenient way to share information with them, so that we can maintain the confidentiality of their information, but also use it to support a medical device application from you or another company.

(Bob Duffy): Okay, well in the case that either you don't have the material supplier's master files or the supplier is not willing to release that information to us as a submitter.

Is biocompatibility testing, and of course, with the G95 and acceptable results using the complete, finished device its final form with all acceptable results. Would that be acceptable in lieu of the information per Guiding Principle 7 and 8.

Jennifer Goode: Unfortunately, it's not because testing on a final, finished device cannot necessarily tell you whether there is a risk for toxicity for some of the endpoints that we're concerned with for color additives.

So, you would need a certain amount to show a positive in some of these tests, but a lower amount could cause problems in a clinical application. And so, you can't just rely on testing to say you don't need to provide color additive information for any device.

So, what we've laid out here is how you can potentially use that for some devices. So that there will be fewer devices where color additive information might be needed.

(Bod Duffy): Okay, thank you.

Coordinator: Our next question is from (Debbie Conneman) with (Conneman Regulatory Solutions), your line is open.

(Debbie Conneman): Hi, my question has to do with, can a color additive that is listed as being a color additive for foods, drugs, and cosmetics, but it's not listed for devices, can it be used for devices? And if so, is there anything different that needs to be done other than what was talked about today?

Jennifer Goode: So, there are some listings that are specific to medical devices and those tend to have information that's most relevant to the safety of medical devices. There are some cases where those listings may not exist specific to medical devices, but there may be listings for other types of indications such as you've identified.

As long as there's an appropriate analysis of route to route extrapolation. Sometimes those other listings can be helpful. And so, we do encourage you to look for medical device listings.

What we're concerned with is identity and purity specifications. And if there's not something specific to your indication then, you can explain why you think these other listings might be helpful and we would consider that.

(Debbie Conneman): Okay, thank you.

Coordinator: Our next question is from (Mark Ontereiner) with (Group Torunal), your line is open.

(Mark Ontereiner): Yes, we manufacture many different devices that are Class 2 devices and that are used for less than 24 hours in the patient. And during our reviews at the Offices of Device Evaluation we noticed that our reviewer will usually ask if the colorant is listed under 21CFR73 or 74. And we were just curious, why does the reviewer ask that question?

Jennifer Goode: So in 21CFR73 and 74 are the listings for all of the different indications, medical devices, drugs, cosmetics, and foods. And so if your color is listed in one of those places, this may be a place that you can go to and look and see if your color meets one of those listings, that might be a very convenient way for you to answer the questions we're asking.

And so some material suppliers, some color additive suppliers will say “my color is certified to meet these identity and purity specifications” and if you can get that from your color supplier, it's a piece of paper and it's very fast for you. And so, we will sometimes point out to device manufacturers that this is a mechanism that may be helpful for you to quickly answer this question.

(Mark Ontereiner): Okay, instead of doing like extraction testing or some other testing?

Jennifer Goode: Yes, it's our experience that if device manufacturers can get certifications from their suppliers it's faster for them than if they actually have to do testing. And it costs less money so that's least burdensome for everyone.

(Mark Ontereiner): Okay, thank you very much.

Coordinator: Our next question is from (Kim Geisler) with (Beck & Dickinson), your line is open.

(Kim Geisler): Hi, yes thank you for taking my question. I have a question regarding changes to color additives and the decision as to when to submit a 510(k) for those changes.

So, if we look at the color additive change and perform some biocompatibility testing on that colorant and determine that there are no significant affects to safety or efficacy with that modified material, and assuming that does not affect the performance of the device or have any other impact on the safety or efficacy of the device, would that trigger, would that change due to the fact that we've still conducted some testing require a submission to the FDA to review that test data?

Jennifer Goode: So, are you talking about devices that are used for greater than 30 days or devices that are used for less than 30 days? And are - one more question, are you talking about maybe changing from a red color to a purple color?

(Kim Geisler): So, in our specific case we're talking about Class 2 devices which are in contact for less than 30 days and the color would be the same. So, we're really talking about a change to the formulation of that colorant.

Jennifer Goode: So, if you change anything about your device, including a color, and your device used is less than 30 days and you do a complete set of testing your - for biocompatibilities and you see no color change in your extract, you see no particulates in your extract.

And there are no adverse findings from any of that biocompatibility testing, you would not need to tell us about the color additive information and I'm not sure if would actually need to - if that were the only change you were making, I don't know that you'd need to submit a 510(k) for it.

But, and I'm looking at my colleagues to see if they agree with me. If that were really the only change I don't know that you'd need to submit a 510(k), but you should certainly keep that information in your device master record.

(Kim Geisler): Great, thank you for that clarification.

Coordinator: Our next question is form (Nancy TsoTsi), your line is open and please state your company.

(Nancy TsoTsi): Hi, I'm from the (Bemis Company). We provide plastic packaging for medical devices and I was wondering if the colorant information is required for the application to FDA? We get the question from our customers to provide to you with their submissions.

Jennifer Goode: So, are you talking about packaging that would go around a device in a box or are you talking about packaging like there's a liquid component that's in a vial and that's the package?

(Nancy TsoTsi): It would be like flexible packaging. It would be like a pouch that the product is put inside and then the pouch is sealed and then that's how it's stored on the shelf or however it might be before it's sterilized at the hospital, say. But it would be in contact with that device until it's used.

Jennifer Goode: So, we have had some discussions with packaging suppliers when they're making major changes to their packaging. We do ask companies to think about if their packing is changing, could that impact the device overall biocompatibility.

So, I think this particular question is very specific and we might want to follow up with you if you're willing to send me an email because I'm not

exactly sure why colleagues of mine might have asked you for that information and I think it might be that we might need a little bit more detail about what your specific situation is.

(Nancy TsoTsi): Oh, and this it's a little more general. It's my customers are asking me. I think they're presuming that you might need to review it when you review their submission.

Jennifer Goode: So, we do encourage our device manufacturers whenever a supplier is making a change that they think might impact biocompatibility that they be made aware of those changes so they can make a judgement on whether or not they think it would impact their overall device. But I don't know that we would necessarily ask them for that information.

(Nancy TsoTsi): Okay, thank you.

Coordinator: Our next question is from (Aaron Gee) with Fujifilm, your line is open.

(Aaron Gee): Good afternoon, thank you (unintelligible). My question would be if our device, suppose we two different kind of devices. Device A and Device B. Device A is kind of bronchi-contact device.

And Device B is an esophagus, a stomach-contact device. If we try to expand our IFU of a Class 1 device. Do we need, you know, from the bronchi and esophagus into stomach do we need to do the colorant test?

Jennifer Goode: I'm having a little trouble understanding your specific question. It sounds like you may have some devices in contact with the bronchi and some in contact with the stomach.

(Aaron Gee): Right.

Jennifer Goode: I don't know where the color is, if that's in the devices or if it's in...

(Aaron Gee): Yes.

Jennifer Goode: ...the IFU.

(Aaron Gee): Yes, I'm sorry, I didn't explain very well. Now a company decided to expand the Device A which contains a colorant from the bronchi to bronchi and esophagus and the stomach. In that case do we need to perform the colorant biocompatibility study?

Jennifer Goode: So, what I understand you to say is that you have a device that's in contact with one type of tissue and it may now be indicated for a tissue with a different type of contact that may be more acidic.

I think that what we're saying in terms of this particular policy is if you do biocompatibility testing and you don't see color coming out in those tests than you wouldn't necessarily have to provide further information on color.

However, if you do see color coming out than you would have to give us more color information depending on how much color you have in your device or comes out, you may have to do some elution testing.

An elution to test to show what comes out in the stomach environment might be different than an elution test to show what comes out in a bronchi application. And so that's the kind of issue that I would encourage you if you want very specific input, to contact me. And we can work with the review branches to see if we can give you some more detailed feedback.

(Aaron Gee): Thank you very much. A Second follow-up question would be, is there any difference if some colorant already used marketing cleared device and some colorants never used in marketing cleared device? When the FDA revealed the data, is any difference between the two colorants?

Jennifer Goode: So, I think that it's appropriate to say that if a company has used a color before and we found it to be acceptable that maybe an easier path to follow. I think that if a company chooses a new color and there's toxicity information in the literature that they can use to support that color, we're very willing to talk with you about that.

If there's no toxicity information in the literature for a particular color, it makes it very difficult for us to understand the potential risks to the patient and that might be a more difficult situation.

(Aaron Gee): Is that going to lead to NSE if we - a company, you know, decided to use a new colorant on their new device. There's no literature reference available?

Jennifer Goode: I think that that's a very good question to talk with your specific review group about. We can't say in webinar whether or not something's going to be SE or not, but that is something that you should definitely speak to your review group.

We have a Q-submission process that is very helpful for these types of discussions. We'd encourage you to use that, if you're not familiar with it and you want to send me an email I can send you a link to our guidance on that.

(Aaron Gee): Thank you very much, I appreciate it.

Coordinator: Our next question (Mr. Rollins) with (Nelson Labs). Please state your first name, your line is open.

(Thor Rolands): Yes, this is (Thor Rollins) from (Nelson Labs). Thanks Jen you did a great job. The question I have is for the Guiding Principle 8. You mentioned that we could use the TI to look at the compounds and then aim for a toxicological evaluation.

But I didn't see any reference to a toxicological exposure calculation afterwards. I just wanted to see if we were okay to evaluate those compounds using a TI or do we need to also include or consider the TE?

Jennifer Goode: So we do, we use the concept of a TI for the purposes of this particular training. We know there are a lot of more complex issues specific to risk assessments using these types of derived limits. Part of the color additive assessment is to try and understand exposure.

The first part of a risk assessment might be to estimate exposure and if we agree with that type of approach that would be reasonable. Sometimes we actually have some questions remaining. And we would ask for either modeling or some elution studies to support that if there are remaining questions.

(Thor Rolands): Okay, great. Thanks Jen.

Coordinator: Our next question is from (Stacy Alberto) of Boston Scientific, your line is open.

(Ellen Hood): Hello, I'm going to field this question, this is (Ellen Hood) from Boston Scientific. For parts that are in contact for greater than one minute and less

than 24 hours, does the submission need to state why a new color additive or a new use of a color additive is not released to support not providing color additive specific information, provided that supporting toxicity testing or data is included.

Jennifer Goode: So, if the biocompatibility test data is provided, then we would not ask you for the color additive information in GP7 or GP8.

(Ellen Hood): And, just to follow up on that, and there would not need to be included a statement for - is that presumed? Because there is no visible color change in the biocompatibility extract?

Jennifer Goode: So, there's no color change in the extract, there's no particles in the extract, and there's no toxicity findings in the biocompatibility testing.

(Ellen Hood): Right.

Jennifer Goode: Submit it. Any of those shows a flag then you would need to address what the color is and why you believe it's okay.

(Ellen Hood): Okay thank you.

Coordinator: Our next question is form (Betsiana Cortsanski) with DPU, your line is open.

(Betsiana Cortsanski): Hi, I have a question about surgical sutures. I think it was on the insert with the contacts, but for surgical sutures, the colorants are very well defined and for any new colorants we need to initiate the colorant petition. So this guidance would not have any impact on that, is that correct?

Jennifer Goode: That's correct.

(Betsiana Cortsanski): Okay, thank you.

Coordinator: Our next question is from Tamima Itami with Boston Scientific, your line is open.

Tamima Itami: Hi, thank you very much for the clarity of the presentation and all the work that went into it. I just wanted to ask, for clarification, on the comparator device in Guiding Principle 8 and I think the concept appears throughout the presentation. I just wanted to make sure that, that device is actually - can be any legally marketed device, not just the company's own device.

Jennifer Goode: So, this approach assumes you're comparing to your own device because it's very difficult for you to know what another manufacturer includes in their device.

Tamima Itami: Even through testing?

Jennifer Goode: It has not been our experience that you can show through testing that you have the same things as what might be in another device and so this particular approach is specific to comparing to your own device.

Tamima Itami: Okay, so that's good clarification and I think that in the final guidance document, maybe making that clear would be helpful. Because I think it could be interpreted and then I just wanted to ask until the guidance document is issued, is it okay for the industry to use the slides as initial guidance for submission?

Jennifer Goode: Absolutely.

Tamima Itani: All right, thank you.

Coordinator: Our next question is from (Sharon K. Smith) with (H&S Sharon Smith Pharms), your line is open.

(Sharon K. Smith): Yes, I didn't see mentioned beyond the CSI any particular statement in regard to carcinogenicity. It seems that the CSI was more particular to issues of cytotoxicity rather than carcinogenicity. Was there mention in that in the regulations somewhere, what the requirements were in regards to considering issues of the cancer causing nature of the colorant?

Jennifer Goode: So, for the purposes of this approach we're using the G95-1 and ISO 10993-1 approach and we're saying you don't need color additive information for devices used for less than 30 days, if particular criteria are met. For these devices carcinogenicity is not an issue.

For colors, carcinogenicity may be an issue and that is why we are asking for color additive information for devices used for greater than 30 days and those are the only devices according to G95-1 and ISO 10993-1 where carcinogenicity should be considered. And so, normally for medical devices we do not ask for carcinogenicity testing.

For this particular approach we're talking about biocompatibility testing, but it doesn't apply to carcinogenicity because that issue is not addressed unless a device is used for greater than 30 days. Does that help?

(Sharon K. Smith): Yes, thank you. The question I have in furtherance of that, is there an organized list of color additives that have been used and have already been found to be carcinogenic. Is there such a list organized? Would that be in a toxicological compilation or something of that nature?

So that we sort of have a starting point from which we already know it's cancer causing or cancer producing. Especially some of the mentions of the red dyes and such.

Jennifer Goode: So there are lists in the CFRs. Some of the colors are limited to the amount that can be used. Some have impurities that we know could potentially cause cancer and so those impurities are limited. And then there are some colors that are delisted because of the cancer causing potential.

And so, there's information on both the FDA website and the CDRH medical device website specific to color additives that identifies the various listings in the CFR where you can find that particular information.

Coordinator: Our next question is from Brenda Seidman with Seidman Consulting, your line is open.

Brenda Seidman: Hi, this is Brenda Seidman. To what extent have you been coordinating with the Center for Food Safety and Nutrition in your development of this policy, or have you?

Jennifer Goode: So this particular policy that we're presenting for this webinar is to explain ODE's current policy which has specifically to do with our medical device submissions and how to use biocompatibility in medical device submission.

We have worked with our lawyers to determine where we have the regulatory authority to define how to review devices for less than 30 days. And so, this approach is consistent with our current policy. Our lawyers have looked at this and where devices are used for more than 30 days for particular devices such as those mentioned earlier in the call such as sutures.

Those would be coordinated with CFSN with the color additive petitions. And so, we believe that we're sharing with community the approach that's appropriate for these products.

Brenda Seidman: So for specific devices sutures, and probably contact lenses you're anticipating coordinating with CFSN, but in terms of your general scientific approach, I'm not talking about the legal approach right now, but in terms of your scientific approach, have you been coordinating with CFSN?

Jennifer Goode: So, we coordinate with our sister centers on projects that are appropriate for us to talk with them on. We have been talking with them for many years about how to coordinate the review of products that may or may not require color additive petitions. It's a pretty common discussion that we have.

Brenda Seidman: Okay, thank you Jen.

Coordinator: Our next question is from (Casey) with (Merit), your line is open.

(Casey): Yes, I have a quick question on the evaluation of a pigment versus a dye because we know many of the pigments are inorganic in nature and inert. And they're supposedly entombed in the polymer matrix. And I think approach can vary that way versus say an organic dye that could leach.

Jennifer Goode: So, I didn't hear a question, I'm sorry.

((Crosstalk))

(Casey): Can you hear me now?

Jennifer Goode: Yes.

(Casey): Oh, okay. So, my question was how would your toxicological approach vary based on the differences between dyes and pigments? So, most of the pigments are inorganic and inert in nature and wouldn't present themselves as a leachable.

Jennifer Goode: So, the topics that we're discussing here are more general than that. I think that our experience has been that we generally ask for information based on whether a color additive is present or not and we don't currently have information to share regarding what to do if it's one type of color versus a different color.

These are some of the issues that are sometimes addressed in an application to us. If we're concerned about the amount of color that potentially exists in a device that may or may not come out. It's been our experience that sometimes chemicals when they're incorporated into medical devices don't actually act as one might think they would, ideally.

And so I think that when we release our draft color additive guidance, we'll think about how we might be able to present some information specific to this topic to help with people making submissions to us.

(Casey): Thank you.

Coordinator: Our next question is from (Dennis Burk) of I believe it's (DePuy Synthes), your line is open.

(Dennis Burk): Hello my question was related to transient, less than one minute, versus a little more than one minute situations. And it seemed that you were guiding

towards, you know, a less burdensome approach for contact less than one minute, but that wasn't really clear to me.

Perhaps based on the definition of performance testing, I'm trying to find the slide right now. It's Slides 31 and 32. For example, often times when somebody performs a biological evaluation, including for the transient contact category. They're going to do the CSI and perhaps in those CSI they will see turbidity or color change or something like that and yet that isn't mentioned on Slide 31 with transient.

But what is mentioned is particular release during performance testing. I don't know if CSI is considered to be performance testing or if you meant something else by performance testing. Can you clarify?

Jennifer Goode: So, for the transient less than one-minute contact we were thinking about other performance testing besides biocompatibility that you might already be doing for a product. And so, one of the things that we were thinking about was, for example, if you had a coating on a needle, and your needle: you wouldn't normally be thinking about colors being left behind. But if the coating were colored and could come off, we might ask you does the coating come off just through a normal review. And if it does, you might have to think about the colors.

If you're doing biocompatibility testing for your transient use device and you do see colors or particulates in that testing, we wouldn't necessarily ask you about that unless you provided that testing to us a part of your review. And then if we saw colors or particulates in that testing we would probably ask you why is that okay? And what are those colors and are there any concerns with them?

(Dennis Burk): Okay, so the guidance would be if you do see color or particulate come off in CSI for transient device please consider that under our biological evaluation in general, but that doesn't mean that we'd automatically need to go to GP7, GP8.

Jennifer Burk: Yes, I think we would probably want to talk with you about that if you saw that.

(Dennis Burk): Okay, thanks.

Coordinator: Our next question is from (Marcus Duffin) with (Node DK), your line is open.

(Marcus Duffin): Hello, can you guys, can anyone hear me?

Jennifer Goode: Yes.

(Marcus Duffin): Perfect, perfect. Well, yes I'm a little bit of a different scenario. My company is actually a semi-start up where we export our medical device specifically to foreign governments. And one of the reagents that's in our medical devices, it's non-FDA approved, but it's manufactured by an FDA-approved facility.

And I'm curious as to whether or not there may be any legal ramifications for them for adding color additives since the FDS sheet and their classification with the Health Department in Pennsylvania states that it's a clear solution. Would they have any legal repercussions for adding this if we're not selling it domestically?

Jennifer Goode: So, as a biocompatibility reviewer, I might not be the best person to answer this legal question, but I'd be very happy if you emailed me some more specifics of this case to try and figure out an answer for you. This is not something that comes up in my normal daily review. So, I apologize for that.

(Marcus Duffin): Most of the stuff I do does not come up in everyone's normal daily review. All right, what would be your email address again?

Jennifer Goode: So, it should be on the slide that's in front of you right now. I'm Jennifer Goode so in the middle there. Or you can give me a call.

(Marcus Duffin): Unfortunately, my JAVA is not working or allowing me to see the slideshow. So, I've been having to kind of just listen in.

Jennifer Goode: Okay, so its JENNIFER.GOOD@FDA.HHS.GOV.

(Marcus Duffin): Perfect, all right I'll go ahead and send you an email. Thank you.

Jennifer Goode: Yes.

Coordinator: Our last question is from (Charter Murray) with Fujifilm, your line is open.

(Charter Murray): Hello thank you for having this presentation, it's really helpful and taking my question. This is in regards with the Slide Number 32. Basically, about Class 2 devices which are in contact with more than one minute, but less than 24 hours.

We have been recently submitting a detailed CSI test which provide acceptable results as well as their elution extracts which do not provide any color or turbidity to the eluent and if there is a color or particulate observed, we provide a source of the particle as well as the nature or the chemical composition by the FTIR methods.

Although giving all this information, we have been repetitively asked for the color additive information per Guiding Principle 7 such as the CFR number, percentage purity, and also questions on the batch certification from suppliers. So we were wondering, why is that so?

Jennifer Goode: So we have recently retrained our staff so that they are more aware of the policy. We do sometimes have some turnover such that everybody's not always on the same page. I would encourage you to contact your review staff and ask them and their managers.

And ask them if your understanding based on these webinar slides of the current policy is correct and dialogue with them on this. And if they still believe that information is necessary and you want to ask them to involve me in some of the conversations so that we can figure out the resolution for you, I'm happy to help with that.

(Charter Murray): That sounds perfect, thank you so much.

Irene Aihie: Thank you, this is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation in transcript will be made available on the CDRH Learn webpage at www.fda.gov/training/edrhlearn by Friday, February 18th.

If you have additional questions about the use of color additives for medical devices, please use the contact information provided at the end of the slide presentation. As always, we appreciate your feedback. Again, thank you for participating and this concludes today's webinar.

Coordinator: Thank you for participating in today's conference. All lines may disconnect at this time.

END