

## **FDA Webinar- Technical Considerations for Additive Manufactured Medical Devices**

**Moderator: Irene Aihie**  
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**Coordinator:** welcome and thank you for standing by. At this time all lines are in a listen-only mode until the question and answer portion. At that time if you'd like to ask a question you may do so by pressing Star then 1 and recording your first and last name. Today's call is being recorded. If you have any objections you may disconnect at this time. I would now like to introduce your host for today Eileen Aihie. You may begin.

**Irene Aihie:** Hello and welcome to today's FDA Webinar. I am Irene Aihie of CDRH's Office of Communication and Education. On December 5, 2017 the FDA issued the final guidance on technical considerations for additive manufactured medical devices. Additive Manufacturing, AM, is a broad category of manufacturing encompassing three dimensional printing is an emerging technology. As a result this leapfrog guidance is not intended to introduce new policy but rather outline the agency's current thinking about the technical aspects associated with AM processes.

The guidance also provides manufacturers with recommendations for device design, manufacturing, and testing consideration for use when developing devices that include at least one adequately manufactured component or

adequately fabricated step. Today Matthew Di Prima and members of the Additive Manufacturing Working Group here at CDRH will present an overview of the final guidance document. Following the presentation we will open lines for your questions related to information provided during the presentation. Additionally there are other centers subject matter experts here with us today to assist with the Q&A portion of our Webinar. Now I give you Matthew.

Matthew Di Prima: Thank you Irene and on behalf of the CDRH Additive Manufacturing Working Group I would like to welcome everyone to the Webinar. For your convenience our Web site is going to be listed at the bottom of most of the slides. So a brief disclaimer if we happen to mention a commercial product or their sources or their use that will not be construed as an implied or actual endorsement of such products.

In the room for today's Webinar from the Office of Science and Engineering Laboratories there is myself Matthew Di Prima as well as James Coburn. From the Office of Compliance we did have a substitution and we have Jennifer Kelly in the room. From the Office of Device Evaluation we have Joel Anderson and we'll have (David Wong). And from the Office of In Vitro Diagnostics and Radiological Health we have (Nucien Karachi).

So a brief overview of the FDA's guidance documents, these are documents that represent FDA's current thinking on a topic. They do not create or confer any rights on or for any person. They're also not legally binding to the FDA or the public. Also it's very important to note that you are allowed to use alternative approaches if the approach satisfies the requirements of the applicable statute or regulation.

So for this guidance it was originally based off of input from a 2014 workshop held at the FDA. We were then able to take that information and release a draft guidance in May 2016. We were then able to issue the final guidance last month. And between the draft and final guidance we received over - we received 294 comments from 29 commenters and we've been able to discuss the guidance in a number of forms and through different stakeholder interactions between scientific and industry meetings as well as with various standards committees.

So the - there are three significant changes from the draft to the final guidance based on those comments. So the first was we added a brief section. That's going to be section B4 on cyber security and personal - personally identifiable information. This solely points to existing guidance and does not represent any new guidance or policy. We also updated the labeling section, that is Section 7. It's now consistent with other guidance documents and we clarified the labeling concerns to only apply to patient matched devices. The third change was we replaced most instances of the word cleaning with the phrase removing manufacturing material residue in what was then called the Cleaning and Sterilization Section. That is Section 6B.

This change was made to harmonize the language, my apologies, to harmonize the language with the regulatory language found in CFR 820.3. It does not refer to the removing of biological soil and it does not reflect a change in the technical considerations listed in the document. Another point worth clarifying is for patient match devices. And when we're referring to patient match devices we're not referring to custom devices. And for custom devices and the interplay with patient matching we recommend seeing the custom device exemption guidance specifically Section 5.E.

Patient match devices are treated as a specified design envelope instead of discrete sizes and this envelope will require validation and when appropriate substantial equivalence needs to be shown for the worst case or cases. Also it's - this guidance addresses patient matching in conjunction with added manufacturing and does not seek to address all technical concerns with patient matched devices. The guidance objectives, this guidance broadly addresses the technical considerations for the use of additive manufacturing medical devices. It identifies important aspects of AM technologies and workflows as well as providing a framework for evaluating AM processes.

It should be noted that not all technical considerations apply to every AM technology material or device. For example the polymer specific characterizations do not apply to metallic devices and considerations for powder bed technologies do not apply to stereolithography technologies. It's very important that sponsors should apply individual considerations based on their specific situation. This guidance supplements existing device specific guidance is our tests by identifying the AM specific concerns and aids in determining the worst-case positions. Additionally this guidance can be used as a resource for the device portion of combination products and for stakeholders who are new to using AM in manufacturing medical devices.

Now the scope of this guidance there are two main sections of the guidance. The first is design and manufacturing consideration. This section provides the technical considerations that should be addressed as part of the existing quality systems requirement. Now quality system requirements are determined by the existing regulatory classification and additive manufacture does not change that at all.

The second part is a device testing consideration. This section describes what AMs specific information should be included in a premarket submission.

Much like quality systems requirements the type of premarket submission is determined by the regulatory classification and this guidance does not seek to change that. So out of scope of this guidance and today's Webinar regulatory policy this guidance does not address point of care or hospital printing. It also does not seek to address any device specific regulations. It also does not cover the direct printing of cells or tissues. And any specific device or policy question should be addressed through the existing premarket submission process.

So to provide a little bit of background and clarity we've included the flowchart from the guidance. The design and manufacturing consideration section of the guidance will follow this flowchart. And it's worth explaining that for this guidance we include the support structure and design implementation as part of workflow and not the design process.

Now James Coburn will now describe a hypothetical and just excuse me. We're having some minor technical difficulties. There we go. James Coburn now will describe a hypothetical example to assist with the understanding of the technical considerations.

James Coburn: Thanks very much Matthew. So throughout this presentation we'll use this hypothetical example device to show how the guidance can be used in a specific case. This example is a patient matched cranial repair device so something that would fit over a defect in the person's skull and it is a patient specific device made with a patient specific anatomical imaging as well as patient specific surgical guides. We'll be using powder bed fusion process for titanium 6aluminum 4vanadium which is common in these kinds of devices. The examples we placed in a blue box on the side of each slide that I will describe after the main body of the slide is completed. Now back to Matthew.

Matthew Di Prima: Thank you James. So for the first section which was the design and manufacturing consideration device design. Additive manufacturing technologies have different design considerations both in what they allow and the constraints based on specific technologies. Additionally while the patient matching process is easier compared to traditional methods and manufacturing there are many different approaches that can be performed to achieve patient matching.

So the technical consideration called for in the guidance is to describe the additive manufacturing technology being used as well as providing a process flowchart. In terms of patient matching the guidance asks that the patient matched features be described as well as a design envelope being provided for those patient matched features.

James Coburn: In our cranial device example we use a brief description of the process using that flowchart that Matthew showed short earlier including the fact it's powder bed fusion, that there are patient matching examples in it, the software used and then the post processing steps all throughout. For the patient portion of it the design envelope is described. And that encompasses the entire range of shapes that can be made from this cranial device, the curve of the plate to mesh the skull contours and then limits on how thick, thin and the kinds of angles that can be used that are part of our validated design envelope.

Matthew Di Prima: All right the next stage is software workflow. So software workflow is critical to additive manufacturing device design and the production. This includes style conversions and translations from digital designed file formats to a printable form. And often especially in patient matched processing these workflows include a human in the loop. And the concern is that the workflow could lead to errors in either design, software translation or human error. So the technical considerations is to analyze the workflow for their effects on the

additive manufacturing processes. And we're really looking for clearly described analysis to understand what these potential risks are and how they're being controlled and specifically we're looking to understand how any variation in that workflow could affect the final product.

James Coburn: In our cranial device example there are several aspects here. The patient is imaged and that imaging is done with a protocol determined to give a consistent and accurate result across a population of patients that the device is indicated for. The users who do the patient matching or the segmentation process go through a training program which includes that segmentation of a specific data set where the true values are known. So it's a comparison data set. And they're evaluated for accuracy and repeatability.

And lastly we know that the printer has a higher resolution than that of the patient scans and the features that will be built. So during the entire validation event the repeatability and accuracy of the user is evaluated to not affect the device quality. And the resolution and segmentation are better than the clinically relevant dimensions.

Matthew Di Prima: For material controls in additive manufacturing unlike most traditional methods the final material is produced in situ which makes the quality and consistency of the starting material very important to the performance of the final product. Now each technology, process and even intended use may have different material requirements. And on top of that material reuse based on the additive technology venues can also affect the final part. So the technical consideration is to ensure that the starting material and any mixture of reused materials is applicable will yield the appropriate physical and chemical properties needed for proper device performance.

James Coburn: This cranial device is made of a TI-64 alloy as described earlier. And the material - the final material meets ASTM at 2924 for its chemical requirements. And the parts meet the mechanical requirements as well when tested. The raw material powder is created in a particle size distribution which is tightly controlled and to a validated range that we know can create the parts consistently. As Matthew just described powder is reused multiple times in this case. And that protocol was attested to look at the chemical characteristics of the powder over many reuses. And five reuses was determined to be similar to the virgin powder and with no differences in the chemical or mechanical properties. And that was selected for the maximum number of powder uses. A description of the material characteristics, validation testing and results would be included with the submission.

Matthew Di Prima: Post processing as shown in the flowchart there are significant post processing steps that can occur after the part is built. And these post processing steps can affect device performance as well as any critical material properties. So the guidance asks that the post processing steps be described and any steps that could have a detrimental effect on final device performance be identified and mitigation be described.

James Coburn: For a cranial device the post processing steps are fairly standard. You can see them listed here in the blue box. Now they include the removal of the residue powder, supports final rather renewing of the device and then final machining and final cleaning and sterilization. These are evaluated and included in the submission.

Matthew Di Prima: All right, for process validation and acceptance so additive manufacturing technologies have a number of parameters that can be controlled or in some cases not controlled and device quality can be affected by these. Additionally there's generally less experience in creating controlled as manufacturing

processes compared to the traditional techniques. So this guidance asks for an evaluation as to how each step of data manufacturing process workflow can affect the following steps. This is so we can understand sort of the validation risks needed at each in our step. And additionally the added manufacturing procedures may differ from other manufacturing techniques in terms of what is needed for process monitoring through validation triggers as well as acceptance testing criteria.

James Coburn: In this example we have a fairly simple shape but the device was made in a worst-case scenario to make an extreme cranial curvature representing that worst-case. It also was tested with a large build load and with a machine variance to see how the process could cope with the machine variance. These data were collected and the coupons were assessed to see if that was a way we could use to test for revalidation triggers and the infrared camera was used to monitor the bed to look at performance during the build itself. Lastly testing for mechanical testing at the end of a sample of any build was an acceptance criteria for the system.

Matthew Di Prima: All right so that concludes the design and manufacturing considerations and we are now moving to device testing considerations. Performance testing, so this is really focused on establishing what is going to be the worst-case condition based off of the technology used for the device. And we're specifically or the guidance specifically calls out orientation as well as field location but is open to any other parameters that can be found to be affecting the worst-case consideration. So these again, these factors again call - we're calling out orientational location should be factored into the worst-case consideration for testing of the final product. And the validation testing we just discussed as part of the design and manufacturing consideration can be levered (unintelligible) with the effective orientation and build location.

James Coburn: During the validation process for the screen out device example we ran into the fact that the corners of the build space had significantly poor mechanical performance than the rest of the build space. And we noticed that parts made in a variety of orientations had no significant change in mechanical properties. As a result the margin of the corners was - - there was a margin made around the corners so that no builds were made in that area. And a single part orientation that facilitated support placement was chosen because there was no adverse effect of changing the orientation otherwise.

Matthew Di Prima: All right for material characterization so not only did we mention that the final material is created in situ but there is often a change in the material as the part of the AM technology whether that's the melting and sometimes loss of lighter elements into metals or and when you're using polymers a fundamental chemical reaction changing that starting material. So the technical concern is to understand if the (adaman) process creates any new material risks. So specifically the guidance calls out to understand the effect the printing process has on your material and the specifics will vary based on material and the technology being used. Again and there are additional considerations for resorbable or other active materials but the overarching concern with resorbable materials is that the additive manufacturing technology and processing doesn't change that resorption or degradation profile.

James Coburn: In our example case the material characterization follows again the standard ASTM F2924. And as we described earlier the virgin powder, the maximum number of reused powder and the finished parts were all tested to conform to those material properties. The next section or slides will be described by Joel Anderson from the Office of Device Evaluation.

Joel Anderson: Thank you James. I'll be taking over for the next few slides. For the removal of manufacturing residue this is needed for device cleaning to be followed by

sterilization if using devices labeled as sterile as manufacturing residues refer to any byproduct or impurity on the final finished device that is not there by intent or design. So for additive manufacturing we generally require that these residues be removed which could include removal of excess powders or supports for overhangs.

So this is challenged by complex geometries allowed by additive manufacturing and you need to ensure that you're providing sufficient cleaning and sterilization. Therefore we recommend for technical considerations that you describe your manufacturing residue removal process and then validate the results. This can include accounting for the worst-case geometries of your devices such as the greatest porosity, blind holes and largest surface area. And you should also consider how you are placing your test samples for any cleaning or sterilization validation which may even include destructive testing if necessary. All this is to show that the unnecessary residues have been removed and that they do not adversely affect device quality and performance.

James Coburn: In our cranial example rather cranial device example during our manufacturing residue removal process the parts are removed from the powder bed, residual powder is removed by a blasting and cleaning steps. Then final machining is also done in that section. That process is validated on a worst-case part. In this case we do not have a veracity or blind hole and it is then machined to a final size. So there is little risk of powder residue however is still validated in that worst-case part. And it is in a cleaning cycle that is similar to the ones that are used with non-additively manufactured devices that have a similar complexity. And finally the sterilization is a more standard gamma radiation.

Joel Anderson: For this slide the biocompatibility of additively manufactured devices remains the same as we've been doing for all other medical devices. We recommend that you please continue to show your final finished devices are safe and biocompatible to specific manufacturing method used. This involves continuing to follow this series of ISO-10993 standards for biocompatibility. So for additively manufactured devices you may also need to account for the use of any photo initiators or other toxic substances included in your printing process especially if using any new materials with unknown long-term effects. For more details on this topic you can refer to FDA's recent guidance document entitled the Use of International Standard ISO-10993 part one. And now I'll turn it back over to James and Matthew to finish out the presentation.

James Coburn: Thanks very much Joel. For the cranial example the material TI-64 has a long clinical history in similar applications. However the - an appropriate risk assessment for this type of tissue surrounding the device is done and cytotoxicity or other testing that may be necessary because of the risk assessment would be included as well.

Matthew Di Prima: Okay on to the last section. And this is the additional labeling considerations. So the overarching concern here is that patient match devices are not always easily identified by clinicians especially in instances where there are multiple revisions or I should say design revisions of a patient match device. So the guidance asks that patient match devices be labeled with a patient identifier to ensure that the proper patient is receiving the right patient match device and anatomical location or identifier is included especially in cases where multiple and anatomies are being printed as well as the design iteration be used to produce the device. So this will ensure that the surgeon is in fact implanting the proper version. Now it's very important to note that these are considered a safety consideration and do not intersect with or alter the existing unique device identifier requirements.

James Coburn: For our cranial device example it follows exactly those recommendations. Each device includes a tag that is printed with it or on it rather that includes the patient identifier, the part of the anatomy which in this case is cranial and the designation of the design version so that the piece can be uniquely - can be identified excuse me, as that patient's device with that version of the design. The surgical guides that would go with it are also tagged appropriately with the match.

Matthew Di Prima: Thank you and with that we are open for questions.

Coordinator: At this time if you would like to ask a question you may do so by pressing Star then 1 and recording your first and last name. To withdraw your question you may press Star then 2. Again to ask a question please press Star then 1, unmute your phone and record your first and last name. One moment for the first question please.

Matthew Di Prima: While questions are queuing up the most common question we get with additive manufacturing is how custom devices and the patient match devices are different. Again we had the slides where we recommend that people with those concerns go to the custom device exemption guidance and look at the example in Section 5.E which clearly describes the difference between custom devices and patient matched devices.

Coordinator: Again if you'd like to ask a question via the phone please press Star then 1 and record your first and last name. One moment please.

Nooshin Kiarashi: Another one of the questions that keeps coming up is concerning the application of this guidance document to 3-D printed patient's specific anatomic models. We'd just like to clarify that really the scope of this

guidance does not include anatomic models that are 3-D printed in our patient specific. However we do realize that they are a very important development currently and we are engaged in advancing our regulatory thinking and policy in that field. If you do have questions we refer you to our Web site where we posted the Web cast and transcript from our recent joint meeting with the Radiological Society of North America in the summer of 2017 where we went through our current thinking and policy as it pertains to 3-D printed anatomic models.

Coordinator: We do have a question on the phone. It comes from (Oscar Quintana). Your line is open.

(Oscar Quintana): I was wondering if there is any acceptance criteria for validation of powder, residual powder removal stuff from (four) structures?

Matthew Di Prima: Okay this is Matthew Di Prima from OSEL. So to clarify your question is if there's an acceptance criteria for the validation of the manufacturing material and removal process?

(Oscar Quintana): Yes.

Joel Anderson: Hi. This is Joel Anderson from the Office of Device Evaluation. There's not any set criteria because that's going to be affected by the specific device, the location that the device is being used, the extended duration, the indications for use. So we recommend that you describe your removal process for any powders account for your worst case in regards to how much you were recycling that powder. So you can show that the virgin material in - on the - you would define how often you were recycling it and you'd account for the worst case in regards to that.

And then that you've shown comparison most likely to another similar device for that same intended use and application. It's kind of a good starting place depending on exactly what you were - are submitting to FDA but pretty much get to the same conditions you would want for that device as you would if it wasn't actively manufactured and factor in those considerations. And as always you can reach out to a specific device branch for that specific product area and they can give you more details.

Irene Aihie: And we'll take our next question.

Coordinator: Next we have (Kim Sand). Your line is open.

(Kim Sand): Hi. I was just I guess wanting to get additional clarification regarding what needs to be included within a 510K or a premarket notification. Would the level of detail of the manufacturing processes validations and quality systems requirements be needed in a submission or would it go more into the device level consideration on materials, powder removal, biocompatibility, et cetera?

Matthew Di Prima: In the submissions we are asking for an overview of the AM technology as well as a general flowchart of the processing steps. We also ask for additional information on any steps that are identified to be especially high variability or would substantially affect the performance of the device. Then we are also asking to understand the risks that the AM technology has in terms of the material performance. We're looking to understand the manufacturing conditions that would affect the worst-case device testing consideration. So that's going to be the potentially build location, build orientation as well as then the manufacturing material residue removal. The level of detail is going to depend on the specific application as well as, you know, the specific concerns with that technology. There - it's very important though that we -

there is a separation between the QSR requirements and the premarket requirement.

Joel Anderson: Hi. Yes this is Joel Anderson as well just to add onto that. We're not asking for the full level you would add to the QSR requirements. We're only looking for the manufacturing process that could impact the upfront safety and effectiveness of the device. Those tend to be typically the manufacturing could affect biocompatibility and material or device performance. And we look at it as how you've accounted for it across runs and also build locations and orientation in the printer. Those are examples of information we would look for but you would describe your specific process and how it would affect any of the premarket information we would look for that specific device type and indication for use.

(Kim Sands): Okay. Thank you for your response. I did have one follow-up question if you don't mind?

Irene Aihie: Sure go ahead.

(Kim Sands): So within that you mentioned build location, (build path), et cetera. Is that something that needs to be described within the premarket submission itself if it is a potential for affecting safety and efficacy?

James Coburn: What needs to be described is how you mitigate that concern. If you're validation testing shows that for your process there is no effect of placement in the build space you just say that and then you don't have to worry about that as a worst-case considered - consideration. Per the example we gave where we noted that for the cranial repair device the corners of the build space resulted in a diminished mechanical property you can either state in the submission that you're not going to use those regions to build the device or

you use devices built in that worst-case position for your performance testing to show that devices even made in those corners meet the requirements you have.

Joel Anderson: Hi again. This is Joel so just to add on. And it's also going to be dependent on how you're designing your additively manufacturing process. For example we've had companies only print in one orientation and one build location. Therefore there was - they just had to show that it was consistent across run, production runs. But if you're doing multiple devices on a build plate at once or if you have different locations as Matthew was saying in the corners we would account for that or different people oriented it in different ways with multiple directions on the plate. So it's going to be dependent after you described your manufacturing of the process which properties or other conditions of your device could be affected. So if you simplify it then that could limit the amount of considerations that you would need to factor in.

(Kim Sands): Okay thank you.

Coordinator: Next we have (Nadia Chavez). Your line is open.

(Nadia Chavez): Hello please. I would want to know if there is any regulatory consideration that we have to consider when you recycle or reuse the parts of the device? Apart from the one you mentioned the Result 10993 is there any other law or regulatory consideration that we should be aware of?

Joel Anderson: Can you clarify your question? Are you talking about reuse of the powders or leftover powders between production runs?

(Nadia Chavez): I'm talking about the re-use of the (unintelligible) powder.

Irene Aihie: I'm sorry. Can you repeat your question? We're having a difficult time hearing you?

(Nadia Chavez): Oh sure. I will note if when you talk about reuse or recycling is that (unintelligible) is low or (unintelligible) does it have to be (unintelligible)?

Joel Anderson: Hi. Yes this is Joel. So you would look at what they could potentially affect, manufacturing could affect biocompatibility device performance. There is no specific regulatory requirements we have to the powder of use. We're just going to ask how - what you're proposing affects the safety and effectiveness of the device. So we just - we typically look at the worst-case consideration. So if you're recycling your powders five times as we gave in the cranial repair device example you would show biocompatibility for a powder that has been recycled five times also accounting for the device performance testing typical of that device. So that's a hypothetical example but you'll need to factor it into the specific devices indications for use you're working with.

(Nadia Chavez): Thank you.

Irene Aihie: We'll take our next question.

Coordinator: Next we have (Mark Kline). Your line is open.

(Mark Kline): Hello. For Class 1 devices that are 510K exempt if the indications for use remains identical to a currently cleared product - or not cleared product but an indication as described in the FDA codes for a Class 1 device and the only difference is the manufacturing process, i.e., AM versus traditional manufacturing methods is that change in and of itself enough to require a 510K submission for a Class 1 510K exempt device again per the descriptions in the FDA codes?

Joel Anderson: Hi. This is Joel Anderson. The short answer is it's going to depend. We need to see the changes. We recommend you would come talk to that device specific branch for that area and we could have more clarification. And we would need to discuss that further.

(Mark Kline): Okay and then kind of a follow-up question for that, if the answer was yes you do need a 510K than the printer itself the 3-D printer does that then become an accessory to whatever device you're printing? And if the answer to that is yes what would be the requirement around the printer itself? In other words do you need full GMP quality system requirements for the printer manufacturing and testing and validation and so forth BTC?

Matthew Di Prima: Hi (Mark). This is Matthew Di Prima from the Office of Science and Engineering Laboratories. So that's going to fall back to the classic FDA question of it depends. And it's really going to depend on what the indication for use is, what the specific device is and a lot more sort of specific details. And again as Joel said like those questions would be best resolved with a specific branch or group that would be reviewing that product.

(Mark Kline): Okay thank you.

Coordinator: Next we have (Pamela Martin). Your line is open.

(Pamela Martin): Hi. My question is with regard to the additional labeling considerations where you talked about including a tag for each printed device. Specifically how are these tags included? Are they part of the device that the surgeon would break off or are they just included in the packaging?

James Coburn: So and - this is James Coburn. In this example we had a device that was - that had a tag on it but that is one way of doing it, not necessarily the only way of doing it. Many companies do it many different ways. It can be part of the normal labeling, it can be part of something on the device. It can be something part of something attached to the device. So we aren't prescribing how. But...

(Pamela Martin): Okay.

James Coburn: ...the diversion, the iteration, and the anatomy and the patient should be identified in a patient specific device that has gone through those kinds of iterations.

(Pamela Martin): Okay so if it's just appearing on the device label itself then that should be sufficient?

James Coburn: I think for this case -- and Joel can step in if he wants to elaborate -- again we're going to go with it depends on what the specific branch would take because every device is different but generally speaking those have to be present.

(Pamela Martin): Okay.

James Coburn: And I think that would be the main object.

(Pamela Martin): Okay. (Unintelligible) devices that...

Joel Anderson: Hi. Yes this is - I'm sorry go ahead.

(Pamela Martin): I was just thinking about devices that are too small to be laser marked or include that sort of tag. So...

Joel Anderson: Correct. So yes this is Joel speaking. We have I believe there's guidance out there for the UDI requirements and they do have space consideration. So a lot of it is device specific of what the device will physically allow. So we'd recommend that you would follow the requirements with you guys as applicable to your device and device size, I mean how it's accounted for. So I believe there are information of what to do to account for those type of cases. I don't know them offhand but that would be a good place to start. Also reach out to (DICE) who most likely will have more information on that topic.

(Pamela Martin): Okay I appreciate it. Thank you.

Coordinator: Next with (Keith Miller). Your line is open.

(Keith Miller): Hello. So my question is if you already have, a company already has a Class 2 device already cleared with the FDA that's additive and they just want to - they want - say I'm just going to give an example of this laser powder bed fusion and they want to change the 3-D printer company. So it's still going to be a major part of bed fusion but they'll make sure they do all the QSR activities and make sure the verification validation activities still meet the same standards of that device do you have to resubmit?

Joel Anderson: Hi. This is Joel Anderson speaking. We would - it would depend you would have to go through the recent FDA guidance deciding when to submit a 510K for existing device. You would walk it through the substantial equivalence flowchart. I believe there is accounting for manufacturing changes. So you would just document to where your device falls out on that flowchart if they would need a 510K versus documentation for your quality system record-keeping. And if you have specific questions or you think these are issues that could affect safety and effectiveness I would recommend you also reach out to

that device specific branch. But it would depend on where it goes through the FDA guidance in terms of deciding when to submit a 510K for an existing device.

(Keith Miller): Okay thank you.

Coordinator: Next we have (Emanuel Golati). Your line is open.

(Emanuel Golati): Yes hello. My question is mainly related to the interpretation of this where you're talking about the performance testing. You said in the slide that a performance testing can be executed or represent through the coupons and that's very, very interesting. I was wondering if due to the fact that there are any - each single 3-D printer device is unique if this approach on coupons and they can also be considered to demonstrate the repeatability of QRS (unintelligible) solution of the printer with regards to the dimensional part, dimensional validation let's say?

Matthew Di Prima: Thanks so much for your question. It's going to be one part it depends. Validation of the system is traditionally used - using coupons. And it's always going to depend on what your device is and what AM technology you're using as to whether or not you can substitute the coupon testing for the performance testing. But coupon testing will often let you understand if there are additional concerns and what the additional concerns are before you move directly to final device testing.

Joel Anderson: Hi. Yes, this is - oh sorry, just to add real quick for your follow up. We have also seen examples of hypothetical example where you do coupons to help determine your worst case for your device and then actually test those configurations for the worst case of your final finish so they can also be used in that manner as a consideration.

(Emanuel Golati): Okay thank you. Appreciate (unintelligible).

Coordinator: Next we have (Oscar Clintonic). Your line is open.

(Oscar Clintonic): Hi. I guess I have two question, the first question a follow-up is on for the (unintelligible) powder the 924 is there any specific toxicity concern from FDA perspective?

Joel Anderson: Hi. This is Joel speaking. So we would - we don't necessarily look at the raw material. We would look at it after it's gone through your final manufacturing process because we're going to look at your final device biocompatibility and toxicity. So we would consider how it went through your manufacturing process, how you set up that, any post-processing. So for the raw material itself we - it's - we're not going to focus and that'll be on the final finish device and how you've accounted and demonstrated that through your biocompatibility or any toxicity or tolerable intake considerations if you have any of those for your material.

(Oscar Clintonic): Thanks Joel. So particularly (A4) structure do you have any two (unintelligible) acceptance for particulates for the residual manufacturing powder? Do you have any recommend data known test methods a company can adopt?

Matthew Di Prima: So this is Matthew Di Prima. There are right now a number of different approaches that companies can use. We are working very closely with ASTM to try to consolidate some test methods. But there are - the end goal is to understand if there is any residual powder left in the final part and then to characterize any material that comes out of that final structure. So you can do it (grab metrically). We've seen a lot with ultrasonic cleaning. There are lots

of options. There are a couple of standards already that people have used. And I think James is a little bit familiar with the standards that currently exist.

James Coburn: Yes thanks Matthew. So the standards that we have looked at aren't usually made for the 3D printed kind of porous materials. They're made for just general porous materials and they can be adapted obviously to 3D printed devices. So the ASTM I'm just trying to get the number right because I always get it backwards.

The ASTM standard we have looked at internally as part of our research is F2459 and then which is a standard test method for extracting residue from metallic medical components and quantifying the (grab metric) analysis. That's what Matthew was talking about. And then there's also F2847 which is practice for reporting of those residues for single use implants. There are also some other standards like used for validating claim processes which is F - these are all ASTM, F3127 and there's another one for the ultrasonic techniques that Matthew was talking about which is G131. And I believe all these will be in the transcript afterwards so you don't have to write them down right now. But suffice to say there are number of different kinds of standards and what you use will vary greatly depending on what kind of device, what kind of geometry and what kind of features you have in that face. So...

(Oscar Clintonic): Thanks James.

James Coburn: ...hope that helps.

(Oscar Clintonic): Absolutely. So is there any like a FDA recognize a lab for those test the company might go to in general?

Joel Anderson: Hi. This is Joel speaking. So FDA will not endorse or recognize any labs over the other. We will just look at the reports that come in and the validity of the results. So we leave that up to your business decision of how to proceed.

(Oscar Clintonic): Okay but here from my (unintelligible) should be sure whole your - so appreciation your presentation talk about orientation and the location. My question would be what's a validation requirement? It's the same type of machine right but you had (model) machines. What is our validation requirement when we have a model machine to print a same product for the (matter) implants?

Matthew Di Prima: This is Matthew Di Prima. The over-arching concern is still the same. We are looking to understand what the worst-case manufacturing condition would be for your device. So if there are multiple machines you would already have to do the quality system validation for each machine. And that's straight out of the 820 regulation. So once you have that data you should be able to determine and demonstrate which AM system you're using would create the worst-case device. So it's really no different than having a single device. You just have - or a single AM system. You just have to run the same QSR requirements for all of them.

(Oscar Clintonic): Hello. One last question. In - if we want to sort of use S2934 for a specific product, ASTM3924 would you check on the oxygen content to sort of validate the, I would say the product regulatory-wise?

Matthew Di Prima: So that ASTM standard or specification does call out a maximum oxygen content and free to comply with that specification you would have to demonstrate that your material chemistry fit.

(Oscar Clintonic): Okay. Thank you.

Coordinator: At this time if you'd like to ask a question please press Star then 1 and record your first and last name. Again if you have a question please press Star then 1 and record your first and last name. Our next question comes from (Tracy Ann Dennis). Your line is open.

(Tracy Ann Davis): Hi My question is regarding revalidation. So I saw where you had were some examples that triggers or validation would include changing the spacing and orientation of your device. How will that impact us making custom builds on the slide, single builds and (unintelligible)?

Matthew Di Prima: This is Matthew. Can you repeat that question one more time please?

(Tracy Ann Davis): Okay so in the - there's a - the revalidation section it says some triggers that may impact a revalidation or may cause a revalidation there's a change in spacing or orientation of the device. One of the benefits of AM is that you get to mix parts on a build, you know, different part sizes, different types of parts. How would this revalidation now impact us being able to do that then that flexibility?

Matthew Di Prima: I think that question's going to require a little bit more of an answer than we have time for during this Webinar. You know, I am hearing that - okay yes. Actually so if you would please go ahead and email that question to (added) manufacturing at [fda.hhs.gov](mailto:fda.hhs.gov) we can get back to you with a more complete answer.

(Tracy Ann Davis): Okay thank you.

Irene Aihie: Operator do we have any additional question.

Coordinator: I'm showing no additional question.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation and transcript will be made available on the CDRH Learn Web page at [www.fda.gov/training/cdrhlearn](http://www.fda.gov/training/cdrhlearn) on Thursday January 18. If you have additional questions about today's presentation please use the contact information provided in the slide presentation.

As always we appreciate your feedback. Following the conclusion of today's live Webinar please complete a short 13 question survey about your FDA CDRH Webinar experience. This survey can be found at [www.fda.gov/cdrhwebinar](http://www.fda.gov/cdrhwebinar) immediately following the conclusion of today's live Webinar. Again thank you for participating and this concludes today's Webinar.

Coordinator: This concludes today's call. You may disconnect at this time.

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