medical packaging COMMUNITY

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This Q&A document was compiled from a live chat presentation in February 2016, moderated by Daphne Allen, Editor of *Pharmaceutical & Medical Packaging News*, and pertaining to Nicole Kaller's white paper "Medical Packaging Study - The Impact of Sterilization and Transportation Testing on the Microbial Barrier of Different Materials." Answering questions on behalf of the DuPont Medical and Pharmaceutical Protection Team were: Nicole Kaller, DuPont Packaging Engineer Tyvek® and author of the white paper, as well as her colleagues Thierry Wagner, Regulatory Affairs Director, and Jane Severin, Packaging Sciences and Customer Applications Leader.

We've reorganized the questions and answers to present them together in categories, and we have edited for clarity and consistency, while keeping the conversational tone of the exchanges.

Moderator

Hi everyone! Thanks so much for joining us for our chat today on Nicole Kaller's white paper "Medical Packaging Study - The Impact of Sterilization and Transportation Testing on the Microbial Barrier of Different Materials". I am Daphne Allen, Editor of Pharmaceutical & Medical Packaging News, and today I will be your moderator. We will start in 10 minutes at 10:00am – 11:00am EST | 7:00am - 8:00am PST | 3:00pm - 4:00pm GMT | 4:00pm - 5:00pm CET. (A quick housekeeping tip: please keep open the email confirmation with the link because you will need this link to re-enter the chat should you exit for any reason. If you browse other areas of the community before our chat you may lose connection to the chat so please click again on the e-mailed link.

Answering your questions shortly will be Nicole Kaller, DuPont Packaging Engineer Tyvek® and author of the white paper, as well as her colleagues Thierry Wagner, Regulatory Affairs Director, and Jane Severin, Packaging Sciences and Customer Applications Leader. To make the chat easier to read, I've asked Nicole, Thierry, and Jane to colorize and bold their typing. My responses will be bold and in black.

When do you need to test microbial barrier?

Moderator

Question: *For our first question I'd like start by asking, Should packaging materials or the packages themselves be tested for microbial barrier after heat sealing and sterilization processes?*

Nicole Kaller, DuPont

Answer: You have to ensure the integrity of your SBS through sterilization until the point of use, which means when it is opened by the nurse.

This can be achieved by testing package strength integrity and microbial barrier throughout the whole design validation process (before sterilization after sterilization after performance testing after stability testing).

Maintaining integrity is one of the key "shall" statements of ISO 11607.

Until the point of use and until expiry date.

Live Chat Participant

Reply: To add to this, various sterilization methods can affect the properties of the packaging. Post max-dose radiation testing is critical.

Nicole Kaller, DuPont

Reply: Fully agree.

Thierry Wagner, DuPont

Reply: Sometimes it is also double dose, if that is what is defined.

Live Chat Participant

Question: *If you are using DuPont Tyvek, which has known microbial barrier properties, would you recommend repeating microbial barrier testing after sealing, transportation, aging, etc.?* I would think only seal strength and integrity are needed to be demonstrated when microbial barrier is known.

Jane Severin, DuPont

Answer: It is recommended to repeat microbial barrier testing throughout the development process. The supplier data is important, but depending on the MDM risk assessment, additional testing may be required.

Live Chat Participant

Reply: We are testing after sterilization, transport simulation, and aging.

You are currently testing microbial barrier after sterilization, simulated transport, and aging?

Yes, that's the way we show that our products are still "sterile."

For those MDM participants on this chat, how often you do microbial barrier testing? During initial validation only or on-going? (lot to lot)

Initial validation.

Only during the initial validation of our packaging groups....one worst-case packaging per group.

Typically initial validation and, of course, after real-time aging time periods.

The test is performing MDS for us (external laboratory); they modified the DIN testing.

Hydrogen peroxide sterilization and microbial barrier

Live Chat Participant — **Question:** *Is hydrogen peroxide not the sterilization method which is most respecting package integrity?*

Question: *Do you have some information on hydrogen peroxide sterilization – on industrial scale, not hospital use?*

Thierry Wagner, DuPont — **Answer:** Yes, we will post a link.

http://www.dupont.com/content/dam/dupont/products-and-services/packaging-materials-and-solutions/medical-and-pharmaceutical-packaging-materials/documents/Effects_of_Sterilization_and_Accelerated_Aging_on_Microbial_Barrier_1073B_ASTM%20F2638.pdf

HPO hydrogen peroxide is included as one of the sterilization methods in the slide that I sent.

Should transportation simulation be performed after accelerated aging?

Live Chat Participant — **Question:** *Is it necessary to do transportation simulation at the end of accelerated aging? Or can it be done before the accelerated aging is completed?*

Karen Polkinghorne, DuPont — **Answer:** Transportation testing and accelerated age testing should be done as separate entities and not combined.

Live Chat Participant — **Reply:** Agree with Karen

Live Chat Participant — **Reply:** Your question "is it necessary to do transportation simulation at the end of accelerated aging? Or can it be done before the accelerated aging is completed?" - Karen beat me to the punch. You can get false negatives testing together.

Thierry Wagner, DuPont — **Answer:** This depends on your situation. You should review your distribution cycle. Some companies keep products in stock and ship up to the end of the shelf life; others ship immediately after production. Most test separately. I think it is good if you can keep it separate.

Live Chat Participant — **Question:** Thank you. *So if a package past the transportation simulation at year 0 it would still be considered acceptable for a package that had go through a 5 year accelerated aging test? We would not need to then test the packages that had been aged for 5 years to ensure they would pass a transportation simulation?*

Live Chat Participant — **Reply:** It is important that material property changes be understood before and after sterilization and aging when selecting materials for use. This data answers question of whether one needs to do distribution testing after aging stability as package can be shipped anytime in its shelf life. One can use physical property data of materials to demonstrate that testing before or after aging should be equivalent.

Jane Severin, DuPont — **Reply:** I agree with you, thanks.

Thierry Wagner, DuPont — **Reply:** Yes, I would agree.

Thierry Wagner, DuPont — **Reply:** But I do not know exactly your situation.

ASTM F1608 or ASTM F2638: What is an adequate microbial barrier?

Live Chat Participant — **Question:** *Are you using ASTM 1608 to determine microbial barrier acceptance?*

Nicole Kaller, DuPont — **Answer:** For the MPTP testing we used, ASTM F1608 and ASTM F2638 for sheet testing and only ASTM F2638 for protocol testing.

Live Chat Participant — **Question:** *Nicole, do you have an established acceptance criteria for F2638?*

Moderator — **Question:** *Nicole, in your interview you say that, "There is still some work to do to define what an "adequate barrier" is…" Can you explain what you mean?*

Nicole Kaller, DuPont — **Answer:** I think this is a similar question: Today, there is still no official definition of an adequate barrier in the market. The acceptance limit for microbial barrier performance generally depends on specific application requirements. Some may accept a +- 10% barrier change, some only +-1%, just to give an example.
The initial barrier performance of different materials can already be very different. Everything already starts with the selection of the appropriate material. ASTM F2638 is a very useful test to rank and qualify porous materials.

Live Chat Participant — **Question:** *Nicole, so what is the baseline for comparison of the % change? Is anyone using medical grade papers and not Tyvek?*

Nicole Kaller, DuPont — **Answer:** The baseline for each material is pre-sterilization; different packaging materials are used in the market dependent on the risk acceptance level.

Live Chat Participant — **Question:** *Is anyone using ASTM 2638 to qualify porous packaging material as an acceptable microbial barrier.*
I am looking into a physical test for validating the microbial barrier properties of medical grade porous packaging material. To date I have only found the ASTM 2638 method but do not know how to set the acceptance criteria. Any help to establish this?

Jane Severin, DuPont — **Answer:** F2638 is referenced in ISO 11607 and is an FDA recognized consensus standard. This method was utilized in the transition protocol for microbial barrier testing. At present the only laboratory that offers this test is Nelson Labs in Salt Lake City, UT. There are efforts underway to expand the offering of this method globally.

Live Chat Participant **Reply:** Yes we are currently using Nelson for testing but using the results to set an acceptance criteria still is a major questions/concern.

Do I need to repeat stability testing for a given package if I change from E-Beam to EtO sterilization?

Live Chat Participant **Question:** *We use Tyvek 2FS and try to change from e-beam sterilization at about 80kGy to EtO. Which tests would you repeat?*

Thierry Wagner, DuPont **Answer:** EtO is a different challenge than e-beam. There is a mechanical stress during EtO cycle. This needs to be tested, I am afraid. But there is a lot of reference information in the DuPont MPTP protocol reports.

Live Chat Participant **Question:** Thanks, Thierry. *What kind of mechanical stress do you expect in pouches that are filled only with a product that is a PE film with some adhesive?*

Thierry Wagner, DuPont **Answer:** It is really the stress when the pouch goes through the vacuum cycles in the sterilization chamber, and it is also the effect of EtO, which is different than e-beam.

Live Chat Participant **Question:** @Thierry: Yes, I agree, but that's why we have Tyvek. *So my question is, if we need to full cycles of aging and transportation, or if we can focus on the sterilization step only. Is there any known interaction between PE film of our product and EtO for example?*

Thierry Wagner, DuPont **Answer:** Stability testing needs to be done based on the sterilization process you are using, but you can leverage available stability data with EtO if you can show that there is no interaction between the packaging and the device.

Header bag sterilization validation issue

Live Chat Participant **Reply:** We were trying to qualify a new header bag constructed of film and Tyvek. Bio indicators were placed in the same place as for the regular revalidation of sterilization. The pouch will be fully capable to ensure sterilization of the products inside with no questions. But they failed the effective sterilization cycle BI samples after 7 days had positive 5 & negative 5.

They failed the effective sterilization cycle. BI samples after 7 days had positive 5 & negative 5.

We think as it was a header bag with a film strip inside the Tyvek strip this may be a factor so we are going to qualify a new header bag without a film strip inside of the Tyvek.

Thierry Wagner, DuPont **Reply:** *A film strip? Did this close part of the Tyvek window?*

Live Chat Participant **Reply:** Yes I think it covered all the inside of the Tyvek; it has been evaluated in our Czeck facility.

Live Chat Participant **Reply:** Yes, it sounds like the film is occluding the Tyvek from exchanging gasses properly.

Standard is used for seal strength testing and how to define the minimum acceptance limit?

Live Chat Participant **Question:** *What is the standard number for peeling test?*

Live Chat Participant **Reply:** ASTM F88 is used for peel testing. There is no industry standard for minimum peel strength requirements; ultimately the end-user must define what is appropriate based on packaging structure, device, packing method, storage, transportation, end-user needs, etc.

Thierry Wagner, DuPont **Reply:** Agree!

Live Chat Participant **Reply:** We test factory seals with the goal of getting better than 20% over factory seals.

Live Chat Participant **Reply:** *What about the DIN 868-5 with 1.2 N/15 mm for pouches?*

Live Chat Participant **Reply:** *Isn´t it 1.5N?*

Live Chat Participant **Reply:** EN 868-5: Section 4.3.2 of EN 868-5 is referring out only for the Vendors Seals (min 6mm).

Thierry Wagner, DuPont **Reply:** The EN868-5 standard has a minimum for pouches used in hospitals. This is often used in the industry, but it really has to be reviewed given the particular situation the size of the package and all other aspects like transport sterilization...

Live Chat Participant **Reply:** 868-series is addressing seal strength values to health care facilities only -1.2 EO and 1.5 Steam, however, medical device Industry is free to choose whatever is adequate for packaging and product.

Live Chat Participant **Question:** *Is there any scientific paper or literature that could be used as a guidance on how to define the proper or minimum seal strength values of the packaging?*

Thierry Wagner, DuPont **Reply:** *Did you look ISO TS16775?*

Live Chat Participant **Reply:** Minimum seal strength needs to be that which will ensure integrity to point of use. It can be different for a light weight device than for a heavy device.

Live Chat Participant **Reply:** I agree that seals strength has to correlate with challenge, which means in most cases product weight, but

sometimes transportation challenge also. Not really a topic for deeper scientific approach, therefore no literature as far as I know.

Live Chat Participant **Question:** *If you have done a full sterilization validation including aging and transportation testing on the previous Tyvek, do you think it is sufficient to do only seal peel testing on the transition Tyvek?*

Nicole Kaller, DuPont **Reply:** You need to perform a risk assessment in the context of your change management process, taking into consideration all the data and guidelines we provided - you can contact me separately if you need more information on the MPTP.

Bubble leak testing as quality control, humidity control during testing

Live Chat Participant **Question:** *Do you know the bubble leak test? Do you know the immersion test which is carried out in a tight chamber filled with water in order to test the seal resistance?*

This is a routine test used by our operators to validate the integrity.

Nicole Kaller, DuPont **Answer:** Yes the bubble immersion test is a widely used integrity test for example post transport testing - in the study of my first white paper we have performed this one as well.

Live Chat Participant **Reply:** Testing on Tyvek® has to be done in a climate chamber with defined humidity.

Jane Severin, DuPont **Reply:** Tyvek(r) is not humidity sensitive so testing in a humidity controlled environment is not necessary.

Live Chat Participant **Reply:** But without humidity it turns yellow

Live Chat Participant **Reply:** Film with water based primers can be sensitive to humidity.

Live Chat Participant **Question:** *Does anyone make a basic off the shelf bubble leak set up?*

Live Chat Participant **Reply:** For a bubble leak tester I received from China and the quote is for €5250 I have went back out to them to make sure this tester fulfils the requirements of ASTM F2096.

Gamma sterilization – Why using porous packaging?

Live Chat Participant **Reply:** Paper becomes brittle after gamma....I think this study confirms that. I am not sure why one would use paper for gamma other than cost. One can use a non-porous package for gamma which was not in this study. Note that any decisions made on microbial testing would also apply to non-porous packages.

Nicole Kaller, DuPont **Reply:** Of course non-porous packaging can be used for Gamma - I know MDMs who take porous packaging as they want to stay flexible (Gamma or ETO if needed) and sometimes the product is generating odors which need to abate. Further pressure changes during air or other transport can play a role for integrity, porous packaging allows for pressure equalization.

Particle burden testing

Live Chat Participant **Question:** *How do you all handle the particle after transport simulation? Any acceptance Levels?*

Nicole Kaller, DuPont **Reply:** Which types of particles do you mean?

Live Chat Participant **Reply:** Loose particles inside the packaging.

Live Chat Participant **Question:** *Are there any acceptance levels for the size and the number of loose particles?*

Nicole Kaller, DuPont **Reply:** That means you are measuring the particle burden inside the package post transport - is this for validation only or as quality control?

Live Chat Participant **Reply:** For both. During the validation and during the routine control....

Live Chat Participant **Reply:** You need to look at your product use and develop your spec for particles.

Live Chat Participant **Reply:** TIR42 can be a starting point for particulate.

Live Chat Participant **Reply:** TAPPI chart is one way to go.

Live Chat Participant **Reply:** Thanks for the additional reference.

Live Chat Participant **Reply:** Are there any acceptance levels as the TAPPI Standard defined?

Live Chat Participant **Reply:** You have to define based on risk.

Live Chat Participant **Reply:** Particulate topic is something that I consider difficult, too. What is the method to measure, is it tape-lift method or more liquid particulate from washing the surfaces? Who has experience? I agree with IEST-STD CC 1246 but this does not give a clear message which level to keep.

Live Chat Participant **Reply:** *What testing is the community using for in process package test? A) Seal Strength B) Seal Integrity C) Both*

Live Chat Participant **Reply:** Both.

Live Chat Participant **Reply:** I recommend you go to SPMC website and get their "Standards and Test Methods" document. In general there are different methods for "Package Integrity" "Seal Integrity" and "Seal Strength" testing. They all have associated ASTM methods.

Which test methods can be used for package strength and integrity testing?

Live Chat Participant **Reply:** Process package testing must include seal strength testing and also visual inspection followed were prompted by suspect seals by dye penetration testing

Reply: The bubble leak testing is for whole package integrity testing and not just for seals thus the use of dye penetration testing on seals.

Nicole Kaller, DuPont **Reply:** That is true also the sensitivity is different - I think those two tests (dye, bubble) are complementary.

Live Chat Participant **Reply:** Process validations should include both visual inspection, seal strength, and whole package integrity as packages can be damaged during processing. If one plans to include burst testing as part of in-process testing instead of seal strength. I recommend doing both during process validation to correlate seal strength with burst test values.

Live Chat Participant **Reply:** I do not think it is a good idea to correlate the results from seal strength testing with those from a burst testing as the seal strength testing is only given results from a 15mm or 25.4mm strip while the burst testing will only give a reading at the weakest point in the package.

What about "Whole Package Testing"?

Live Chat Participant **Question:** Hello everybody. *Do you know any test method or ASTM to challenge the maintaining of the packaging sterility?*

Thierry Wagner, DuPont **Reply:** In ISO 11607 annex B there is a list of test methods for testing porous materials or do you mean whole package test methods?

Live Chat Participant **Reply:** @Thierry Thanks; I mean the whole package.

Thierry Wagner, DuPont **Answer:** The idea of a whole package test makes a lot of sense, but in reality they have been so far more research tools and not so practical for validation of packaging designs because of the difficulty to validate these tests. Maybe this will change one day, research is going on, let's see what the future brings, however validation of test methods is a critical and important requirement of ISO 11607, the basis of proper design and process validation.

Live Chat Participant **Reply:** Thanks for your answer.

Moderator **Question:** *Can you tell us more about whole package testing?*

Thierry Wagner, DuPont **Answer:** Regarding whole package testing: ISO11607 states that in the absence of applicable validated tests for the complete package microbial barrier performance requirements can be established by testing microbial barrier properties of materials and integrity of seals.

So far not possible to really validate these tests.

The concept that you test seals and porous materials separately is based on studies that were made over 20 years ago and still valid today. A key piece of literature are the MDDI articles "In Quest of Sterile Packaging" published in 1995.

Moderator **Question:** *Can ASTM F2638 be performed with whole packages?*

Jane Severin, DuPont **Answer:** At present the equipment used to test microbial barrier per ASTM F2638-12 is not able to perform microbial testing on whole packages. This is not to say that future generations of the equipment and method will not have this capability. *Does the community feel that there is a need for a reliable whole package test?*

Live Chat Participant **Reply:** Hi all: on the question of when to perform sterility testing I recommend reading the 'FDA guidance to industry - Container and Closure System Integrity Testing in Lieu of Sterility Testing' From section II INTRODUCTION page 2: For products labelled as sterile we consider sterility to be a stability characteristic. As a result, the stability protocol should include confirmation of continuing sterility throughout the product's shelf life or dating period. The minimum sterility testing generally performed as a component of the stability protocol for sterile products is at the initial time point (release) and final testing interval (i.e. expiration). Additional testing is often performed at appropriate intervals within this time period (e.g. annually). However […] sterility tests for the purpose of demonstrating continuing sterility have limitations with respect to the method's reliability accuracy and the conclusions that may be derived from the results. Because of the limitations […] sterility tests are not recommended as a component of a stability program for confirming the continued sterility throughout a product's shelf life or dating period. Alternative methods may be more reliable in confirming the integrity of the container and closure system as a component of the stability protocol for sterile products.

...Because of the limitations […] sterility tests are not recommended as a component of a stability program for confirming the continued sterility throughout a product's shelf life or dating period. Alternative methods may be more reliable in confirming the integrity of the container and closure system as a component of the stability protocol for sterile products.

How to select the right temperature for environmental conditioning prior to transport simulation?

Live Chat Participant — **Question:** Hello: *For Medical Device Products, is it normal standard practice to test the Packaging Distribution using a conditioning temperature of minus 20 degree Celsius?*

Thierry Wagner, DuPont — **Answer:** The environmental conditioning conditions can be done according to ASTM D4332. In the white paper study this has been partly adapted based on ASTM D4169, ISO 2233, and ISTA 2A as recommended by the independent accredited laboratory in order to reflect worldwide distribution worst case conditions - we went till -35 C.

Live Chat Participant — **Question:** *Is it normal standard to test a conditioning temperature of minus 20 degree Celsius?*

Live Chat Participant — **Reply:** One should do distribution testing after conditioning the packages per ASTM or ISO pre-conditioning standards unless environmental conditions seen by your products is known to differ. Note that all attempts to maintain conditions during drop/vibration should be made so that packages are cold or hot while they are dropped or vibrated as seen during shipping. This is stated in ASTM D-4169.

Sterility tests: Yes or No?

Live Chat Participant — **Reply:** ISO 11607 also says physical tests can also be used to demonstrate a sterile barrier and we have those test methods validated and they test the entire package. I understand the limitations of a test like bubble leak but I don't see what we gain by generated data as in the white paper from what DuPont has already provided us with their compliance packet. We all know Tyvek is a better barrier than paper....

Thierry Wagner, DuPont — **Reply:** The standard tells us that physical tests can be used ALONG with microbial barrier testing to establish the capability … to maintain sterility. The reason it is saying that is because microbial barrier testing used to be exclusively microbiological tests and available physical tests, like the bubble test, did not have the required sensitivity. But in fact F2638 is a physical test method. The overall concept is clear, you have to test your entire SBS, not only the seals. For porous materials you now have the choice between microbiological test methods or the physical test method F2638.

Live Chat Participant — **Reply:** Thierry Thanks for the background. So if I follow your position…By testing the seals with a method such as Dye penetration a sample of the Tyvek barrier by one of these microbial methods and demonstrating the film/tray is impermeable is a better entire package test than bubble leak testing because the limitations of that method.

Nicole Kaller, DuPont — **Reply:** That is a good approach. However the bubble test can still be done complementary as it is checking the whole package at the same time (while microbial barrier testing is checking a section of the porous web).

Revalidation needed post process parameter change?

Live Chat Participant — **Question:** If you change your parameters of forming process, do you always need revalidation or PPQ with transportation test?

Live Chat Participant — **Reply:** If you change your CPP's then you absolutely have to re-validate.

Live Chat Participant — **Reply:** One would only need to redo a distribution test after a process change if it cannot be shown that the process change does not make an equivalent or better package. This rationale should still be documented such as film thickness previously validated vs. after process change or seal strength before change vs after change.

What is an appropriate sample size?

Live Chat Participant — **Question:** *How does validation sample size enter into the discussions?*

Live Chat Participant — **Reply:** Sample size based upon risk analysis FMEA.

Nicole Kaller, DuPont — **Answer:** For the study we took 10 samples per condition and 30 per pouch type for microbial barrier. But in general the selection of the sample size is complex as it depends upon the level of risk severity and risk probability associated with the process/events. It will depend on what you are measuring – continuous or discrete data, standard deviations, confidence interval etc. there are specialized statistical tools and sample size calculators publically available to help with.

How to test the barrier of vented closures?

Live Chat Participant — **Question:** *Considering medical devices with sterile fluid path, is it possible to NOT claim the protective (non-porous) packaging as SBS but the device itself?*

Live Chat Participant — **Reply:** Yes for non-vented closures but what testing can be used to support microbial barrier properties for vented closures.

Live Chat Participant — **Reply:** Yes, tubing sets used in non-sterile field applications may use sterile barrier caps/closures to maintain "sterile fluid path" and products should be labeled as such. Validations must be done to qualify closures and then validate that closure.

Live Chat Participant — **Reply:** *Are you validating vented closures? If so what method are you using?*

Live Chat Participant **Reply:** Thank you very much. *Do you know what kind of testing could be used with vented path barrier? What is the test method to validate vented closures as SBS?*

Live Chat Participant **Reply:** Yes I would like to know what that method is too!

Live Chat Participant **Reply:** I have always let Sterilization Sciences address the qualification of closures as it was not considered a packaging qualification....sorry I can't help more than this.

Thierry Wagner, DuPont **Answer:** I think it all depends on the size of your vent you may need to cut a sample with some film around and then to customize for this it could be done with ASTM F2638 I believe.

Live Chat Participant **Reply:** In this case we consider a little cap with a Versapore membrane so it is not really possible to cut it and use ASTM F2638.

Live Chat Participant **Reply:** It depends on whether the vent is a porous plug or a tortuous path closure but I would think the aerosol test to entire closure is the way to go and then test the interior of the fluid path.

Thierry Wagner, DuPont **Reply:** I understand. I was thinking about a vented bag.

Live Chat Participant **Reply:** Many thanks.

Which testing should be done during process- and design validation?

Live Chat Participant **Question:** *If one has executed pouch integrity testing (bubble leak) at design verification then is it necessary to execute it at OQ/PQ?* Seal strength and dye leak are a given at OQ/PQ.

Nicole Kaller, DuPont **Answer:** I think it is again a risk and application based decision - but usually for sealing process validation, e.g., the dye test makes sense as it is concentrating on the seals.

Live Chat Participant **Reply:** I recommend bubble leak for both design verification and also process validation, as packages can be damaged during in-process handling or sharp edges on equipment during processing. I have seen recalls due to this so always recommend this be done and now see auditors asking for it during both design and process audits.

Nicole Kaller, DuPont **Reply:** Good point; and of course for design validation some testing on pre-sterilization packages is included as well as baseline.

and you may add visual inspection to the process- and design validation

Live Chat Participant **Reply:** Re bubble leak: Thank you. BTW re: edges etc. we do a line inspection checklist to check for sharp surface edges, protruding parts, hand held devices potential impacts, etc.

Has Transition Tyvek® been used for the study?

Moderator **Question:** *Were Tyvek transition materials used in the study?*

Nicole Kaller, DuPont **Answer:** @Daphne – No. Only Legacy Tyvek has been used for this study at that time. But the Transition Protocol testing has demonstrated that the Transition Tyvek is performing functionally equivalent to the Legacy Tyvek.

Gamma sterilization, design verification

Live Chat Participant **Question:** Gamma sterilization: *Do we have to do all tests with worst case (for instance if sterilization dose is 25 - 40 kGy then at least at 40 kGy) or are nominal conditions sufficient?* There are performance testing shelf life testing transportation testing...

Live Chat Participant **Reply:** Again, one should know what effects max dose sterilization has on material properties....It may be that the device inside can withstand two doses but that packaging may only take one dose which means device must be repackaged before second dose.

Live Chat Participant **Reply:** Design Verifications for pre-sterile packages depends on situation.....some companies may ship to external sterilization site, which means the packages get shipped non-sterile then ship to DC and customer sterile which means design verification is needed to be done sterile.

Nicole Kaller, DuPont **Answer:** Right - for sterile packaging, I think design verification needs to be done pre-sterilization post-sterilization post aging and post transport.

Product family considerations to leverage testing data

Moderator **Question:** *If a company has been using essentially the same porous material for years, does it need to conduct microbial barrier testing when using it for new packages and products?*

Thierry Wagner, DuPont **Answer:** @Daphne: ISO 11607 requires us to validate design, but there are many ways to leverage the testing by testing the worst case for example of a device family or of a packaging family. In this case it is possible to leverage previous performance testing. It is also possible to use previously documented stability data, when it is demonstrated that the product does not interact with the SBS over time.

@Daphne: If you go beyond what has been tested before you may need to retest.

Why selecting ASTM F2638

Moderator — **Question:** *Were round-robin tests done with ASTM F2638?*

Jane Severin, DuPont — **Answer:** The precision of this test method is based on intralaboratory studies conducted in 2004 for the single counter method. Additional studies conducted in 2006 for the dual counter method and an interlaboratory study conducted in 2012 for the single counter method. The results of the independent intralaboratory tests conducted demonstrate that the method is repeatable in either the single or dual counter configuration.

Moderator — **Question:** *Why select ASTM F2638 and not other microbial barrier tests?*

Jane Severin, DuPont — **Answer:** There are several differentiating factors for 2638 vs other microbial barrier tests currently available. For example when considering F1608, some key benefits of 2638 are the elimination of the need to maintain viable colonies of microorganisms, therefore no need to incubate and enumerate colony forming units. This is because 2638 utilizes polystyrene spheres vs live spores. Another key point of differentiation is that of flow rates and pressure differential. F2638 exposes the test sample to a range of flow rates considered to be representative of 'real world' while 1608 utilizes one define flow rate which is significantly higher than 2638 and is considered to be not representative on 'real world. A concern is that excessively high flow rates can cause 'impaction' which may lead to misleading microbial barrier results. 2638 is also a faster test and considered to be more reliable than other currently available methods.

Live Chat Participant — **Reply:** I totally agree to the pros of the 2638 method where I struggle is how to set the acceptance criteria.

Tyvek® Transition: Does microbial barrier need to be retested?

Moderator — **Question:** *DuPont reports that the transition Tyvek materials have demonstrated the same microbial barrier properties as legacy Tyvek. Should new microbial barrier tests be conducted if the MDM isn't making any changes other than using the new Tyvek?*

Thierry Wagner, DuPont — **Answer:** Regarding revalidation: Wagner T. and M.H. Scholla Sterile Barrier Systems: Managing Changes and Revalidations (http://www.ivtnetwork.com/article/sterile-barrier-systems-managing-changes-and-revalidation) Journal of Validation Technology 2013. 19(3).

@Daphne: It all depends on the risk assessment of the MDM but since we have designed transition Tyvek with properties as good or better than legacy Tyvek it should be possible to come up with a rational that there is no reason why the performance during sterilization and handling, distribution... should be worse. Performance was not retested in the MPTP protocol exactly for that reason.

How to select the sample area for ASTM F2638 microbial barrier testing?

Moderator — **Question:** *In the study, how did you select the sample area on the pouches?*

Nicole Kaller, DuPont — **Answer:** @Daphne For ASTM F 2638 the laboratory cut samples with ø 120 mm selecting the area with most creases means the area with most of the risks. The seal area had not to be included.

Live Chat Participant — **Reply:** Nicole - the idea being that the creases are a visual indicator that the area could be compromised?

Nicole Kaller, DuPont — **Reply:** True. Selecting the "visually" worst case area on the package for testing.

Closing

Live Chat Participant — **Reply:** Many good questions related to sterile barrier systems and packaging integrity and seal strength requirements. I am disconnecting. I would like to recommend following SPMC FAQ's website for additional information: http://faqs.sterilizationpackaging.org/directory

Moderator — This concludes our live chat event. Thank you for attending! If you have additional questions that you would like to pose please hop on over to the "Ask the DuPont Experts" Section of the Sponsor area. You may find the Sponsor area by clicking on its link located in the top nav bar of the community. These will be answered via e-mail. Also feel free to peruse the webinars and resources areas of the community. Be one of the first to read a new article on automation that was just recently posted to the resources area.

Questions not answered during the chat

Live Chat Participant — **Question:** *What are typical methods to measure moisture transfer across SB for EtO preconditioning?*

Live Chat Participant — **Answer:** Currently our only method is to seal a data logger inside of a pouch. We do not have an answer

Live Chat Participant — **Question:** *Is there any information on the thickness variation of current and new Tyvek 1073B standard deviation or range say?*

Nicole Kaller, DuPont — **Answer:** For MPTP information please visit our website www.areyouready.tyvek.com or contact our experts

Live Chat Participant — **Question:** *Can you tell me the extent of the work you completed for 'new Tyvek' using VHP?*

Nicole Kaller, DuPont — **Answer:** For MPTP information please visit our website www.areyouready.tyvek.com or contact our experts

Future studies

Moderator

Question: *Nicole, you have stated that "We are considering another study on potential sources of contamination and the performance of packages while exposed to these sources." Can you explain this more?*

Nicole Kaller, DuPont

Answer: This refers to a study of the effect, on a sterile barrier, various inputs such as climate, airborne contamination, surface contamination, pressure changes, and physical stresses may have. These inputs represent what a typical packaged medical device is exposed to during distribution but also during handling and storage at a healthcare facility. For example, particle contamination can compromise product sterility and/or functionality.