ISO 13485:2003 Voluntary Audit Report Submission Pilot Program

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Hi, my name is Kim Trautman. I'm the Associate Director for International Affairs in the office of the Center Director in the Center for Devices and Radiological Health. Today I'd like to talk to you about a new program that we're very excited about. It's the ISO 13485 Voluntary Audit Report Submission Pilot Program.

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The pilot program is being based on ISO 13485, which is an international standard entitled, "Medical Devices Quality-Management Systems Requirements for Regulatory Purposes." Now, ISO 13485 is a recognized standard and is utilized in the medical-device sector in many places around the world. It is very similar to US FDA's Quality-System Regulation that we promulgated back in 1996, and, in fact, we harmonized with the earlier versions of 13485 when we did those revisions to try to make sure that manufacturers have very, very similar quality-system requirements and didn't have conflicting requirements.

ISO 13485 is directly called out in the Canadian medical-device law, so Canada requires ISO 13485 for their medical-device certification. The European Union and Australia recognize ISO 13485 as a means of meeting regulatory requirements for conformity assessment. And Japan, very similar to FDA, harmonized its GMP regulation with ISO 13485.

Now, this is very advantageous for industry, such that they hopefully can have one set of requirements - a very common, harmonized set of requirements - to set up their quality-management system, and at least don't have conflicting requirements from different regulators.

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So why is FDA interested in ISO 13485 if we have our own quality-system regulation, or GMP regulation? Well, we're interested because the world is using 13485 and many management audits - many quality-management systems audits - are being performed by other regulators and third-party authorized auditing bodies. And in doing so, FDA wanted to explore how we could leverage off some of these other audits and utilize some of the trusted partners' work that were already out there, or auditing manufacturers.

Now, FDA goes and audits manufacturers, both domestically and internationally, but again, there's only a set number of auditors and manufacturers and so many audits that we can perform in a year. So how can we leverage off some of the other work being done by our regulatory partners? We're going to use ISO 13485 as a risk-based process for planning and using FDA resources and inspection resources wisely. We have more inspections clearly than we can perform, but 13485 inspections are going on as well as our own quality-system inspections, so if ISO 13485 audits are performed domestically and internationally, why can't we utilize each other's work and try to share some of this information?

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So the premise of the 13485 Voluntary Audit Report Submission Program was based on an amendment to the law, which is in Section 228 of the FDA Amendment, and it basically tells FDA that we can accept voluntary submissions of ISO reports for purposes of setting risk-based inspectional priorities: "The Secretary shall accept "voluntary submissions of the audit-assessment conformance "with the appropriate standards set by the International Organization for Standardization." And of course, as we just mentioned, FDA is utilizing ISO 13485.

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The manufacturer's submission will come to FDA, and the audit report will come most of the time from conformity-assessment bodies that are a part of the Global Harmonization Task Force.

Now the Global Harmonization Task Force was a group of regulators that combined back in 1992 and worked with regulated industry from five founding nations. The GHTF was founded with Australia, Canada, the European Union, Japan, and the United States. And since 1992 we have a history of being able to understand each other's regulatory systems and we have confidence in the fact of the information and the knowledge of each other's systems, so for this pilot program, we are going to be utilizing audits performed under those regulatory schemes.

Now, certain of those regulators, such as Canada, the European Union, have their own system of recognizing or designating third-parties to do their inspections, whereas Australia has their inspector that also does some inspections, just like FDA. And Japan has an inspectorate as well a third-party system, so there's a mix of who might be doing the inspections, but bottom line is, there's confidence among these regulators and therefore the pilot program is going to accept audit reports from this subset.

So why and how is FDA going to do this?
The bottom line is for FDA, if we have Company A that we have not been inspected - you know - FDA hasn't inspected it for maybe 5-7 years, and we have a Company B, and Company B hasn't been inspected for 5-7 years, so if we haven't been out there and we don't know the current state of the quality-management system for that manufacturer, how does FDA pick between which manufacturer to go inspect? Maybe it's the same classification of device. One of the things that we want to be able to utilize in this risk-based system is the fact that if one of those manufacturers has submitted an ISO 13485 audit report from one of these jurisdictions, then we will assess it.

And if the audit report looks good, then FDA has some assurance, has some knowledge that another regulator has been to this manufacturer, has found them to be acceptable, so then FDA can take their resources and go to Manufacturer B, which again we still have no information on.

So if we're sitting there with A and B, and we have some information, some assurances from A because they submitted an ISO 13485 audit report under this program, then FDA is going to rely upon those assurances and take our resources and go to Manufacturing B. So that's what we mean by…utilizing it in risk-based work-load planning.

Some details about the program is the fact that we need the information on the audits to be current. So originally in the draft-guidance document that was published a couple of years ago, we had suggested that the submission had to be within 60 days. Many of the comments were that 60 days was very difficult. Sometimes the manufacturers might not have the audit reports from their third-parties within 60 days. An additional comment said because the audit reports need to be submitted to the FDA in English, there needs to be some time for translation.

So FDA has settled on the fact that the submissions need to come into FDA 90 days from the last day of the inspection, or from the close of the inspection or the audit, so not when the manufacturer gets their audit report or anything else - but from the last day of the audit.
The manufacturer is going to be responsible for submitting the ISO 13485 report as the current one, as well as the law mandates the fact that they have to submit the preceding 2 years' worth of audits.

Again, this goes to the fact that when you take an assessment of non-conformities, it's very important to know what might be a repeat violation and what might not be, in order to determine the significance of the non-conformances.

So the law requires that 2 years of preceding audits also accompany the most current audit. Now the good thing is that FDA has developed a completely electronic system by which manufacturers can submit this information to FDA, and it will be submitted through the FDA e-Submitter system.

Many of the manufacturers hopefully are already familiar with e-Submitter if they are doing ENDR submissions, or if they also could be using e-Submitter for RAD-Health. Sometimes IBD manufacturers also have the opportunity of using e-Submitter. So hopefully this is a system that many manufacturers are comfortable with, but it also is something that is going to be utilized more and more by FDA, so we're utilizing this e-Submitter system for this pilot program.

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Are there specific requirements for the audit and the audit reports? Yes.
ISO 13485, the audit, must conform to the Global Harmonization Task Force study group for guidance documents. These guidance documents can be found on the GHTF website, and it's a simple address, www.ghtf.org, and you go to Study Group 4 and you look at final documents and you'll see this series of documents. And there are guidelines for regulatory auditing:
Part 1 is General Requirements,
Part 2 is Regulatory-Auditing Strategies, and
Part 3 is Regulatory Audit Reports.

Now these requirements are going to have to be discussed with the third party or with the auditor that will be performing the manufacturer's audit for them. And one of the additional requirements - now this is very important - is there is a recent Health Canada guidance document, GD 211, and that guidance document is for the content of quality-management system audit reports.

Now FDA worked very, very closely with Health Canada in developing this guidance document, and, in fact, we do have training on that guidance document on FDA's CDRH Learn website, if anybody's interested in learning more about that guidance document. Also, the manufacturers need to understand what's in that guidance document, as well as the auditors that are going to be performing the audits, for eligibility in this program. So it's going to be incumbent upon industry to understand these requirements that are really requirements for the auditor, whether that be the inspector from TGA, or the third-party CAMDICAS auditors for Health Canada, they will understand these requirements, but it will be very important that the manufacturer make sure that these requirements are met, because they are going to be requirements for the 13485 voluntary audit report submission program for FDA.

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So what are some of the other specifics that we need to look at?
I mentioned the fact that we have these documents that the auditors must follow in order to write the appropriate audit report that should be submitted. Now, how is FDA going to check up on that? FDA will require the manufacturer to make an attestation during the FDA electronic-submission process, and those arrangements do need to be discussed and confirmed with the regulatory third-party auditor prior to the audit, so that these guidance documents are understood and can be adhered to during the audit and while they're actually drafting the report, prior to that report being submitted to FDA.

FDA will reject audit reports if they are not following these guidances, so it is very important that these arrangements be made up front to best utilize the audit report and the program.

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Some additional details are that the ISO 13485 audit report can represent either a full quality-management system assessment or a surveillance audit. So whether it is comprehensive or a surveillance audit - either way, FDA is willing to utilize that audit report. Therefore, we hope to be able to utilize more of the audits that are going on in that particular year.

Now, one thing is that there can only be one report for one FDA FEI number associated with that audit. So it'll be very, very important that when you go through the e-Submitter system, that you understand that one report is going to be associated with that one FEI. And the e-Submitter system will prompt you for that specific FEI number of the site that is being audited.

The manufacturer must submit a copy of the most recent ISO 13485 certificate as well. It's very important for FDA to understand the scope of the ISO 13485 audit, and the certificate really is the best single piece of paper that will help FDA understand the scope of the certification, the scope of the quality-management system that's being assessed. Therefore, we'll understand the scope of the audit and how we can utilize those results best.

In addition, manufacturers can choose - now this is a choice, they don't have to - but they can choose to submit responses and communications between the auditor and the manufacturer regarding any corrections or corrected actions on non-conformances found during those audits. And that's completely optional, but clearly if manufacturers are doing this for their third-party system for the five regulators that we discussed - the four, plus FDA - it doesn't hurt toshow the positive steps that are being taken to correct non-conformances, but this is not mandatory.

Again, the manufacturer must provide this requested information through e-Submitter, and FDA will only be accepting these audit reports for this pilot program through the e-Submission process.

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Now what will CDRH and our Center for Biologics, who also has some medical-device products that they regulate, what will they be doing with these audit reports?

CDRH and CBER will notify the relevant district offices if it's domestic inspection, or a domestic establishment, or the Division of Foreign Field Investigations in our office of regional affairs, if it's for foreign establishments.

So what happens is that the report comes from e-Submitter, it goes through the gateway, which is an electronic gateway for FDA for security purposes. Then it comes into FDA into our center-tracking system. Once FDA - being CDRH and CBER - receives that, then an automatic notice will be going out to the district offices or to DFFI to notify them that a submission has come in. It will be asking the districts, as well as DFFI, to please hold off any inspections for 30 days. The reason being is we'd like to have 30 days to try to accomplish the review of that audit report.

Now there are some caveats. Clearly, the audits or inspections that FDA is going to do if there are any for-cause inspections, or any inspections for pre-approval, this program does not cover.

So when you read the guidance document that describes this program, you'll see the fact that this is just to take off a manufacturer from the routine workload plan for one year, if it's just a routine inspection. But for-cause inspections and PMA inspections are not affected by this program. They will proceed. But we like to notify the district. Again, we're trying to save them resources if we have information that we could utilize and say, "Please don't inspect this firm for 30 days while we review the submission to determine whether this was a successful audit or not a successful audit, according to FDA's criteria."

So that 30 days will be a buffer. And again, when we talked about the fact that an audit report needed to be submitted in 90 days, now we're talking about an additional 30 days. When a manufacturer gets a 1-year bye, so if the audit is successful, we will be taking that manufacturer off the routine workload plan for 1 year. It will be 1 year from that last day of the inspection. This is similar to how FDA counts all of our inspections. We always use the last day of the inspection as the date to count how long between inspections, so we're going to do the same thing with this program.

But you can see that if a manufacturer waits for 90 days, and then there's another 30 days for assessment, we're already at 120 days, so we're digging into the year by - or off the routine workload plan already, so we want to make the best benefit out of that year that the manufacturer can come off the routine workload plan.

So we have that 30 days and during that 30 days, FDA - being CDRH and CBER - will strive to make sure we do our best to utilize that time to review the audit reports and information that was submitted by the manufacturer.

And we'll be assessing those audits against Part 5 of our Compliance Program. Under Part 5 of the Compliance Program, it defines what Situation 1 and Situation 2 are. And again, the final guidance document on the pilot program goes into more detail as to the exact words for Situation 1 and 2. But bottom line is - Situation 1, which is where FDA has concerns, typically where the manufacturer has an audit that's classified as Situation 1, there's a potential for a warning letter or other regulatory action - is where there are major issues or major non-conformances that might lead to non-conforming product being issued or being placed onto the market.

Where in Situation 2, there is minimal probability that the quality-management system will actually be distributing non-conforming product. So FDA is going to be assessing the audit reports and utilizing that criteria already existing in Part 5 of the Compliance Program, which is also available to you on FDA's website.

Now FDA really, really understands that the majority of the manufacturers that are going to be interested in this program are clearly only going to submit audit reports that they believe are going to be classified or assessed as a Situation 2. And that's absolutely appropriate and normal, so we don't expect manufacturers, if they are major non-conformers, to necessarily utilize this program. But that's okay, because FDA feels like even if we get information on successful audits - and a successful audit does not mean that there's no non-conformances - it's just that the non-conformances are not determined to be significant or a major non-conformance.

That way, we can use at least some of the information and some of the audits that are already out there being performed, and the manufacturers can hopefully eliminate some disruption in their facility by having one less regulator in there for that year. So after the assessment of the audit reports, the current audit report as to whether it's Situation 1 or 2, and like I mentioned earlier, the previous audit reports are basically used to see if there's any repeat violations to help determine the severity or the significance of the current non-conformances.

After that, CDRH or CBER will notify the firm, and concurrently, the district office or DFFI, like I explained earlier, depending on where that establishment is located, whether that's domestic within the U.S., or whether that's a foreign establishment outside of the U.S. And so, concurrently, the manufacturer and the district office, or the manufacturer and DFFI, will receive the outcome information of that review.

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Now I need to say one thing about foreign inspections. Any manufacturer that might be submitting an audit report for a foreign establishment needs to understand that FDA does a lot of work to set up foreign inspections approximately 2 to 3 months ahead of time. If a manufacturer has already received a phone call from DFFI to set up an FDA inspection, it would be appropriate, if they know that they are going to submit one of these audit reports, to discuss that with the travel arranger from DFFI and talk to them, because if DFFI goes too far down the track of setting up the travel to include ticketing and travel arrangements, even if the manufacturer submits that audit report, if those arrangements have already been put into motion, and FDA has already basically made the travel arrangements, the foreign inspection may still have to proceed.

So for foreign establishments, it may require a bit more forethought and advanced planning, but that should not be a problem because most of the audits that are performed by third parties and some of the other regulators, have ample notification and planning, such that some of these planning issues can be resolved and discussed up-front.

Anyway, the outcome of the review should occur; we're trying to shoot for approximately 30 days from receipt of the submission.

Now the other issue is why this is a pilot program, and we are estimating it to be a pilot program for 2 years, is that we honestly have no idea how many audit reports manufacturers are going to submit to FDA under this program. If we look at some of the other programs that we had in the past, like our third-party program, like our Health Canada PMAP program, the participation from manufacturers has not been optimal or at the level that FDA had hoped. So we don't know whether this is going to be a program that has just a few audit reports submitted under it, or if we're going to receive a thousand reports.

Now clearly, when Congress gave us the authority or legislative change back that I read to you earlier, there were no additional resources that came with this program, so we really have to assess - and the pilot program will be to assess - how many audit reports submissions come in, how many people we have to do it, can we basically accomplish these assessments in our target that we set for ourselves in 30 days? Or are we going to be inundated with so many of these that we may need to either re-think the program, or try to see how additional resources can be re-allocated?

But this is our goal and this is why we're opening it up as a pilot. And we really, really hope that as many manufacturers who are interested can utilize this and test this system out and utilize it.

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So many people, when we have discussed this program in public meetings and in conferences, have been very, very interested about what ORA - our Office of Regional Affairs, our inspectorate arm of FDA - how are they involved, and specifically what are they going to be doing during this process?

So most of this information that I alluded to - so we have postponed the inspections, or we've asked the districts to postpone any routine, again – this is very important - just routine inspections for 30 days after we've received notification that the firm has made a submission under this program.

Like I mentioned, ORA has the option not to postpone if foreign travel had already been arranged and the foreign manufacturer did not make previous arrangements with ORA. And I want to remind everybody that again, this is only for routine inspections. For-cause inspections, and compliance follow-up inspections, and PMA pre-approval inspections, will proceed as normal.

ORA will receive a copy of the CDRH/CBER letter that electronically notifies them that the audit report has come in, and it's under review, and then they will also receive an automatic e-mail, the same one that the manufacturer gets, that will inform them of the outcome of the review. So ORA will then know after that, whether they should proceed with routine inspections for that manufacturer during that calendar year, or if they should remove that firm from their work plan for 1 year.

The review memo and supporting files will be stored in FDA's electronic database and therefore, it can be utilized as far as historical knowledge, and it will be assessed, or the system is set up so that if subsequent submissions under e-submitter go forward, the pilot program is successful and we go forward.

We hope that manufacturers will not have to constantly submit the 2 years of audit reports that they had already made those submissions previously. We're working very hard with our IT people to try to optimize the fact that, you know, some of that duplicative filing might not have to happen. So we are working on how to store that information so that hopefully, this program is successful, and we can use it in the future. And when the manufacturer uses it in subsequent years, some of that information will already be maintained in the IT system for them.

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So how confident is FDA in these ISO 13485 audit reports and results?
Many groups, such as advocacy groups and even some manufacturers, have expressed concern about FDA utilizing other regulatory bodies, and on the other side of the fence, many manufacturers and associations feel very, very confident that these reports are comparable and can be utilized by FDA.

With FDA ourselves, we have had experience with third-party accredited, auditing organizations, and I mentioned a few of these programs already. We do have our own accredited-persons program that was developed back in 1999 and 2000. There have been several, I don't know the exact number, but approximately 50-plus audits have been performed under the accredited-persons program.

We also have the Health Canada PMAP - Pilot Multi-purpose Audit Program - where we had 10-12 audits performed under that program, where third parties that were accredited, both under FDA's third-party program as well as Health Canada's CMDCAS program, performed single audits according to both Health Canada's and FDA's requirements, produced two different reports--one for FDA and one for Health Canada--and then we did an analysis of those reports. The information on the pilot program, and the summary and conclusions of that pilot program are also available on FDA's website, if you're interested.

And some very good information and experiences came out of that. And that experience led FDA and Health Canada to draft that GD 211 document that I had mentioned earlier in the telecast, and that's why we feel very, very confident that now, we are really striving and moving towards a true single audit.

And also, we're working currently on a very exciting program where we truly are not just taking the PMAP program and making it operational, but we are really working on a medical device single-audit program, where one inspection can be utilized by multiple regulators, and it doesn't have to be different. It can be one audit report, one set of information, and regulators can utilize that information. That's a new program under development, so I ask you to look forward to hearing more information about this.

We are also utilizing the new IMDRF, the International Medical Devices Regulators Forum, to help us to launch some of the activities under this program, and I refer you to look at the new IMDRF website for information in that regard, as well.

So FDA does have experience with how audit reports or perform, and again, like I mentioned, under the Global Harmonization Task Force, and now the new IMDRF, we have worked with regulatory partners, and we feel strongly that we can utilize the audit information in some of these reports, and we want to leverage off of other regulators' work, and we want to provide information to other regulators.

So again, globally, we optimize and minimize the disruptions to manufacturers and really try to help improve the public health in a more global, consolidated manner. FDA believes that ISO 13485 voluntary audit reports submitted under this program will again give us another degree of assurance. If, over the next couple of years, we have the opportunity to review these ISO 13485 audit reports, and we have more assurance, this is one more way that will help the fundamentals and the progress of moving toward a true medical device single-audit program.

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So some important points to remember as we wrap up:

Number 1, ISO 13485 is a voluntary audit submission report program.
It does not preclude FDA from conducting PMA pre-approval inspections, or for-cause or compliance follow-up inspections. If successful, it will be a 1-year pass, and that off the routine workload plan for 1 year will start from the date of the close of the ISO 13485 audit.

Also under discussion, but not decided yet, is how many consecutive years can a manufacturer or firm be allowed to use this program? At the conclusion of the pilot, we will assess many different data points, and we hope to be able to determine what would be the most - from a logistics resource perspective as well as a utilization perspective - how many consecutive times can a manufacturer utilize this program to take them off the FDA routine workload plan.

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So some final details…again, this is a voluntary program, but very, very important is that FDA intends to start this pilot program on June 5, 2012.

I ask you to look to FDA's webpage for the final guidance. Make sure that the final guidance is right there and you read it and understand it beyond just what we have mentioned here; that you also go to the CDRH Learn part of the website and look at the GD 211 guidance document on how audit reports are supposed to be written - and that training is available; that you coordinate with any third-party auditors that you utilize and that you also go to the e-submitter section of FDA's website.

In order to use the e-submitter program, there are some certain IT verification and security processes that are required, and some of those processes can take up to 4-6 weeks.

So even if you're watching this telecast earlier than June 5, I encourage you to use the time ahead to go ahead and start possibly setting up your e-Submitter system, if you're interested, if you haven't already done so for some other program like e-MDR or Rad Health, or some other FDA program that uses e-Submitter.

So we're very, very excited to launch this new program, and we hope that manufacturers take this opportunity. FDA is excited about learning more and using the experience to help further develop a medical device single-audit program, and we're also very excited to possibly use information that's already available, to help us leverage off of other inspections so that we can optimize the use of FDA resources and really put those resources to the high risk and to the places that really need the most attention.

So we look forward to starting this program on June 5, when the e-Submitter section and the IT section will be up and ready for you to utilize. And there will also be some information that will be coming out in future conferences and some Q&As.

So I thank you very much for your time, and I hope you are as excited about this program as I am, and that we utilize this program and learn from it together.
Thank you very much.