CDRH Learn - Deficiency Writing for Third Party Reviewers: Examples

Slide 1
Hello! Welcome to the CDRH Learn module titled Deficiency Writing for Third Party Reviewers, Examples. I'm Helen Jiang at the FDA's Center for Devices and Radiological Health or CDRH.

Slide 2
As we know, practice makes perfect! In any area, using examples that apply concepts often helps us master the principles.

Slide 3
The deficiency writing program consists of two modules. First, we have the first module titled "Deficiency Writing for Third Party Reviewers," which goes over the theory of deficiency writing. I encourage you to watch that one first. This module is the second one in the series, where we'll go over examples and check your knowledge about writing deficiencies.

Slide 4
Here are the learning objectives for this module. First, we'll review the basic principles of deficiency writing in four-part harmony format that we covered in Module 1. Then, we'll identify aspects of four-part harmony in a well-written, complete example. And finally, we'll do a knowledge check where you get to identify missing parts in several incomplete deficiencies.

Slide 5
Before going into details, I'd like to make the following disclaimers. First, the deficiencies and examples listed intend to illustrate teaching principles only. Second, this presentation does not intend to imply, or establish any regulatory policy with any device-specific examples. Finally, please review applicable FDA laws, regulations and guidance for cross-cutting, or specific matters.

Slide 6
According to four-part harmony format, each deficiency should include the following four parts: First, a brief summary of what was provided in the submission; Second, what is missing or deficient; Third, why this information is needed; and fourth, what needs to be provided for reviewers to make the decision, including any potential alternatives.

Slide 7
The following example and all other examples are slightly modified from the examples in the Deficiency guidance document presented in Module 1. I'll present the full deficiency first, and then we'll go over each part of the four-part harmony in the full deficiency.

Slide 8
Now let's look at the full deficiency. As you can see, it's very long. To understand it fully, I'll read the full deficiency for you. "You have proposed that your powered muscle stimulator is intended to be used in the home environment by lay users. However, you have only included professional labeling intended for healthcare providers. The FDA recommends in our "Guidance on Medical Device Patient Labeling" that you provide patient labeling for your device since you intend for patients to operate the device.

Therefore, please submit patient labeling that explains your device and includes directions for use, study design and results, and any additional relevant information. Please use clear language and terms

understandable by the lay person. Please also include a glossary of all relevant medical terms and ensure that all appropriate contraindications, warnings, and precautions from the professional labeling are conceptually the same but are rewritten for understanding by the lay person".

Please note, the word "you" in the deficiencies presented in this video refers to the applicant or the sponsor.

Slide 9
Now let's take a look at the deficiency, one part at a time. Let's start with Part 1: what was provided. "You have proposed that your powered muscle stimulator is intended to be used in the home environment by lay users".

Slide 10
Next is Part 2 - what is deficient. "However, you have only included professional labeling intended for the healthcare providers".

Slide 11
Part 3 identifies why it is needed, by citing corresponding guidance or standard.
In this case, it says, "The FDA recommends, in our "Guidance on Medical Device Patient Labeling", that you provide patient labeling for your device, since you intend for lay persons to operate the device." Of note, please provide the web link right after the Guidance name, as we did not include it here for brevity.

Slide 12
And finally, Part 4 identifies what is needed. This slide shows the part of the full deficiency that explains this.

Slide 13
Putting all 4 parts back together in color, here is the full complete deficiency again. Part 1, what was provided, is in black. Part 2, what was deficient, is in red. Part 3, why additional information is needed, is in purple. Part 4, what is needed, is in green.

Slide 14
Now that we have seen a good example, let's do a knowledge check using other examples!

Slide 15
In the following slides, I'll provide 3 example incomplete deficiencies. We'll give you, the third party reviewer, a chance to think about the answer and then we'll provide the answer. Please read the sample deficiencies first and then look for the missing part. As you do this, think about why it is important to add the missing part.

Slide 16
Deficiency #1 reads as follows, "You did not identify fresh and frozen samples in the line data, nor did you stratify clinical performance by fresh and frozen status. To ensure we better understand the performance of your test under your proposed conditions of use identified in your draft labeling, please update the line data to indicate fresh and frozen status and stratify clinical performance by this parameter". What do you think is missing in this deficiency? When you read it, do you know what I am

talking about? Not really, right? Because part 1 "what was provided" is missing, so the context of this deficiency is not clear.

Slide 17
Here we listed all 4 parts of a complete deficiency with check boxes, and the part that is missing is unchecked and in red. So, for Deficiency #1, the answer is part 1 is missing.

Slide 18
After we add the missing Part 1, in bold and red, this became a more complete deficiency. "You provided line data for your prospective study for your in vitro test. From the dates listed in the line data for specimen collection and inoculation, it appears that both fresh and frozen samples were tested." Part 1 is very important because it reminds the sponsor of the context and lays the foundation for the next three parts of the deficiency.

Slide 19
Now let's look at another example, Deficiency #2. It says, "You referenced the currently FDA-recognized version of ISO 7886-1 in your submission for your hypodermic syringe and did not include a declaration of conformity.

You should demonstrate conformance to Clauses 6 and 7, or, demonstrate substantial equivalence SE otherwise, because your identified predicate device was determined to be SE through conformance to this ISO standard. Therefore, please provide the test results from these two tests, or provide a declaration of conformity to the methods and acceptance criteria identified in Clauses 6 and 7 of this ISO standard so that FDA may assess whether your performance data support the SE of your device to the predicate device". What is missing in this deficiency?

Slide 20
Part 2 is missing this time. So, when the sponsor reads it, they don't know what was wrong or deficient.

Slide 21
Let's see how we can improve this deficiency by adding in Part 2, what is deficient! "While you have submitted several tests under ISO 7886-1, you did not include a summary of your testing regarding limits for acidity or alkalinity or limits for extractable metals, Clauses 6 and 7." This is very important because it explains what the problem or our concern is, otherwise the sponsor may not know what was wrong and therefore may not be able to address it fully.

Slide 22
Finally, let's look at a more complicated example where a third party reviewer has more than one concern or deficiency under one category. The deficiency says, "You have provided the protocols and results from a cytotoxicity test using your device in its final finished form, as recommended by the FDA guidance document "Use of International Standard ISO 10993-1". However, we have identified the following inadequacies in your testing. A. The currently FDA-recognized standard ISO 10993-12 recommends the use of surface area to determine the amount of device included in the extract. Please provide information to demonstrate that the use of weight to determine extraction ratio has an equivalent or greater amount of test article as compared to the use of surface area. "

Section B is not included here for brevity. If you cannot provide an adequate rationale, FDA recommends that you complete new cytotoxicity testing using a sample preparation approach

consistent with the surface area recommendations in the currently FDA-recognized version of ISO 10993-12." What is missing from section A of this deficiency?

Slide 23
Part 3 is missing in this example section A, right? Basically, the third party reviewer did not explain why they ask for the new information or alternatively, ask for a new set of testing.

Slide 24
Let's add the missing Part 3 back in red and bold for section A. That is, "We are concerned that use of weight, instead of surface area, may result in a false negative finding from the study. That is, a negative finding may occur as a result of insufficient sample being present in the test system". This is very important, because the third party reviewer is expected to explain, or justify, the request for certain information that is definitely needed for the 510k review decision, and not just what is "nice to have". It also provides the general guiding principle so that the applicant can apply it to other similar issues.

Slide 25
Let's summarize the four key takeaways we have covered in this module. One, the FDA follows least burdensome principles and guidance. Two, writing clear deficiencies helps improve understanding and resolution of regulatory issues. Three, a well-written deficiency consists of four parts, and four, including all four parts allows complete understanding of the issues and expectations.

Slide 26
For more information, please visit the FDA third party review program at the link below, and if you have any questions about this training module, please contact the mailbox at the email listed on the slide.

Slide 27
Let's conclude this module with your call to action! First, fully understand the regulatory issues, and details of each submission. And second, apply the principles presented in this and the companion module when writing deficiencies and corresponding with sponsors.

Slide 28
We hope this presentation is helpful to you. Thank you for watching!

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