

# FDA CASE STUDY



A new company considers pathways for marketing a low-to-moderate risk device

## USING THE *DE NOVO* PROCESS TO CLASSIFY AND BRING TO MARKET AN INNOVATIVE, LOW-TO-MODERATE RISK DEVICE

THIS FICTIONALIZED CASE STUDY IS THE FOURTH IN AN EDUCATIONAL SERIES PUBLISHED BY THE U.S. FOOD AND DRUG ADMINISTRATION.

### Improving Quality of Life

“Laup. Laup... Earth to Stacia Laup! Can you hear me?”

Startled, Dr. Laup swiveled in her chair to level a look of irritation at her business partner, Dr. Regie Cahn.

“What is it Cahn? I know you could see I was in the middle of an important experiment.”

“You’re always in the middle of an important experiment,” Cahn retorted. “If I let you, you’d never leave the lab. Be grateful your body hasn’t fused with that chair.”

This was a common conversation at CranialCare, LLC. Laup and Cahn had started the business with the mission of developing a device-based treatment approach that could improve the quality of life of patients living with Parkinson’s disease (PD) (See [Exhibit 1](#)).

A biomedical engineer specializing in magnetic and electrical

stimulation, Laup was especially driven after going through the PD journey with her father, who had passed away a few years earlier. Her dream of finding a better approach to helping people who suffer from PD was fully supported by Cahn, a regulatory specialist with a Ph.D. in regulatory science and an MBA degree. He might annoy her at times, but Laup knew Cahn was the best partner she could have gone into business with to get her experiments out of the lab and into the marketplace where they could do the most good for people living with PD. She reminded herself of this as she turned away from her work to face her exasperated colleague.

“Sorry, Regie. What can I do for you?”

Relaxing now that his colleague was engaged, Cahn responded, “We need to discuss the intended use of the DailyStim.”

### A Novel, Low-to-Moderate Risk Device to Treat Tremors in PD

DailyStim, a portable, hand-held, AC-powered medical device, was CranialCare’s first invention.

Intended to serve as a prescription treatment device, DailyStim was created to be used as an adjunctive therapy to reduce the severity and frequency of tremors in adult advanced PD patients. Through the use of daily Transcranial Magnetic Stimulation (TMS), the device delivers externally directed brief duration, rapidly alternating, or pulsed, magnetic fields to induce electric currents in specific regions of the brain and lowers the severity and frequency of PD tremors.

Cahn and Laup had just begun discussing plans to get the DailyStim on to the market, but Laup was having trouble understanding the first steps in the regulatory process they needed to take.

“Regie, our research shows we don’t have to convince anyone of the need for a new approach to treat PD,” she responded. “Even celebrities are advocating better treatment options to improve the quality of life of PD sufferers. I know we are going to be successful!”

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## EXHIBIT 1. PARKINSON'S DISEASE

Many have been touched by the lives of family members, friends, or celebrities<sup>1,2</sup> who have PD. According to the National Parkinson's Foundation, 50,000-60,000 new cases of PD are diagnosed each year in the United States, adding to the 1 million people who currently have PD.<sup>3</sup>

The disease was first described in 1817 by James Parkinson, a British doctor who published a paper on what he referred to as "the shaking palsy."<sup>4</sup> PD is characterized by four main symptoms<sup>5</sup>:

- tremor, or trembling in hands, arms, legs, jaw, or head
- rigidity, or stiffness of the limbs and trunk
- bradykinesia, or slowness of movement
- postural instability, or impaired balance

### Footnotes:

<sup>1</sup>The Michael J Fox Foundation for Parkinson's Research

<sup>2</sup>Muhammed Ali Parkinson Center

<sup>3</sup>National Parkinson's Foundation

<sup>4</sup>NIH Senior Health: Parkinson's Disease

People with PD also experience non-motor (non-movement) symptoms including mental and behavioral changes, sleep problems, depression, memory difficulties, and fatigue. There is no cure for PD, but treatments, mostly drugs, have evolved over time to help control the symptoms.<sup>6</sup> For many, PD medication works very well initially, but over time, side effects may develop and/or medication may become ineffective.<sup>7</sup> Side effects from medications can have a big impact on a person's life and must be kept under control, along with the symptoms of PD. When the symptoms are well-controlled by medication, those situations are referred to as "on times." Times when symptoms are non-responsive to medication are referred to as "off times." As their PD progresses, some patients may find that a dose of medication doesn't work as long as it used to. This is called "wearing off." The effects of "wearing off" can happen quickly, and patients may experience sudden changes between being "on" and "off."<sup>8</sup>

<sup>5</sup>NIH Senior Health: Parkinson's Disease

<sup>6</sup>Mayo Clinic: Parkinson's Disease

<sup>7</sup>Parkinson's UK

<sup>8</sup>Parkinson's UK

"I understand that the need is there," Cahn responded patiently, "but one of the most critical things we have to do now is to specifically define the **intended use** of our device so that we can identify and follow the appropriate FDA regulations to legally market the DailyStim in the U.S. How we define the intended use of our product will make a big difference in the regulatory hurdles we'll have to surmount before and after we obtain FDA authorization to go to market. Some of these **regulatory pathways** may involve using larger quantities of resources

and money, while others may require less resources and different clinical data requirements."

"Okay...so what are these regulatory pathways, Dr. Marketing and Regulatory Affairs Expert? Do you have a roadmap for commercializing our product?"

"Very funny, but at least you're paying attention." Cahn sat down next to Laup and placed his laptop and a folder on the table. "Like I said, the first thing we'll need to do is clearly define our product's

intended use. Our next step would be to determine which **device classification** FDA would apply to DailyStim. An easy way to do this is to find out if there are any similar products currently cleared for marketing by FDA that may serve as **predicate devices**.<sup>9</sup> If we can

<sup>9</sup>How to Find and Effectively Use Predicate Devices.

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm134571.htm>

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demonstrate **substantial equivalence (SE)** to a predicate, we could pursue **clearance** to market our device through a **Premarket Notification-510(k)**.”

“That’s great!” Laup responded excitedly. “All we have to do is find a predicate device...what is a ‘predicate device’ exactly?”

Cahn laughed. “According to **Section 513(i) of the FD&C Act** and **21 CFR Part 807.92(a)(3)**, a predicate device satisfies at least one of the following conditions:

1. It was legally marketed in the United States prior to May 28, 1976 (preamendments device), and it has not been significantly changed or modified since then, and FDA has not published a regulation requiring a **Premarket Approval (PMA)** application for it.
2. It has been classified or reclassified into Class I or II, or has been found exempt.
3. It has been found SE through the 510(k) process.

“And how similar does DailyStim have to be to the predicate in order for FDA to determine that DailyStim is SE?” Laup asked.

“If I remember **Section 513(i) of the FD&C Act** correctly, to be determined ‘substantially equivalent,’ DailyStim would need to

have the same **intended use** as the predicate device, and

1. The same technological characteristics as the predicate device

OR

2. (a) DailyStim can have **different technological characteristics**, but appropriate clinical or scientific data demonstrates that it is as safe and effective as the predicate device, and (b) does not raise different questions of safety and effectiveness than the predicate device for the same intended use.

“If you need more information, FDA has **guidance**<sup>10</sup> describing how to determine substantial equivalence that I could send you.”

“Thanks, that would be useful,” said Laup. “But my main question is this: doesn’t our business plan center on the fact that our device is novel? What happens if we, and by that I mean you of course, can’t find a predicate device DailyStim is SE to so that we can pursue the 510(k)?”

“Then we, and I do mean we, may need to submit a PMA application before going to market. The PMA

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<sup>10</sup>The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notification [510(k)]

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM284443.pdf#page=30>

application is usually reserved for high risk, **Class III devices** and is more labor intensive, but we might be required to submit one anyway if there is a similar device to DailyStim that received approval to go to market through a PMA.”

“But DailyStim is a low-to-moderate risk<sup>11</sup> device! Aren’t there any alternative regulatory pathways to market for low-to-moderate risk devices that don’t have predicates?” Laup asked with concern.

“Yes. We might pursue a process called the Evaluation of Automatic Class III Designation, or ***de novo* classification**.”<sup>12</sup>

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<sup>11</sup>Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and *De Novo* Classifications.

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM296379.pdf>

<sup>12</sup>*De novo* Classification: The Food and Drug Administration Modernization Act of 1997 (FDAMA) added the *de novo* classification option as an alternate pathway to classify novel devices of low to moderate risk that had automatically been placed in Class III after receiving a “not substantially equivalent” (NSE) determination in response to a premarket notification [510(k)] submission. Section 513(f)(2) of the FD&C Act was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA), on July 9, 2012, to allow any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence to request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act (i.e., via the *de novo* pathway) without first submitting a 510(k).

<http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm232269.htm>

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## Regulatory Pathways Available for Low-to-Moderate Risk Devices When No Predicate Exists

Cahn explained. “The *de novo* pathway allows a novel device like DailyStim that poses low or moderate risk to be classified into Class II or Class I even when no predicate device exists as long as<sup>13</sup>

1. **General controls** or general and **special controls** are sufficient to ensure a reasonable assurance of safety and effectiveness of the device, and
2. Any risks to health associated with use of the device can be mitigated through the appropriate application of general or general and special controls.

“The *de novo* process results in the creation of a new Class II or Class I classification regulation.”<sup>14</sup>

“Why didn’t you say so in the first place?” Laup asked relieved. “But I’ve gotten ahead of myself, so let me ask: have you looked into finding predicates that would allow us to pursue 510(k) clearance, or have you found any similar PMA-

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<sup>13</sup>*De Novo* Classification Process (Evaluation of Automatic Class III Designation): Issued August 14, 2014

[http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Guidance Documents/UCM273903.pdf](http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM273903.pdf)

(Note: A Draft Guidance is subject to change and is not for implementation.)

<sup>14</sup>*De Novo* Classification Process

approved devices that would require us to submit a PMA?”

“What do you think I’ve been doing while you’ve been puttering around this stinky old lab?” Cahn chuckled. “I searched the **FDA databases** and found **product codes** associated with TMS and treatment of tremors in PD, then used the codes to search the 510(k) and *de novo* databases for potential predicates among currently cleared devices. I found one product that has the exact same technology as DailyStim that went through the *de novo* pathway, but it has a different intended use. I also found a Class III PD treatment device that went through the PMA approval process, but it’s an implanted device with higher associated risk. I do know that we can explain all the known risks and benefits of DailyStim as well as how all known risks can be effectively mitigated and that the application of general and special controls are sufficient to ensure a reasonable assurance of safety and effectiveness of this device.” Cahn opened his laptop and turned the screen towards his partner. “I’ve summarized information about our device and the potential predicates in this table. (Table 1)

“As we compare the devices, let’s make sure we follow FDA’s logic for determining substantial equivalence by looking at intended use and technological characteristics. The intended use and technological characteristics are the two major attributes FDA uses to determine whether a proposed device can be

placed under an existing classification regulation via 510(k), or if it is so different that it requires creation of a new Class II or Class I classification regulation via *de novo*.” Cahn pulled a printout out of his folder and placed it in front of Laup. “I found a flow chart from a guidance document on the 510(k) program that will be very useful as we determine possible substantial equivalence of our device to a predicate.” (Figure 1)

“Could you explain these attributes to me a bit more so I can be sure I understand what we are looking for as we run through the flow chart?” Laup asked.

“Sure. The intended use of a device is the general purpose of the device or its function. This should not be confused with the indications for use, or IFU, which is the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient population for which the device is intended. By definition, the intended use of a device encompasses the IFU.

“The term ‘technological characteristics,’” Cahn continued, “refers to the mechanisms behind how a device operates. An example could be whether a device like ours uses magnetic stimulation or some other form of stimulation to treat tremors in PD.”

Cahn motioned to the comparison table on his laptop screen (Table 1).

“From a technological characteristics perspective, DailyStim is very similar

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TABLE 1: COMPARISON OF DAILYSTIM TO CERENA AND ACTIVA

Attributes	Cerena	Activa Parkinson's Control System	DailyStim
Manufacturer	eNeura Therapeutics	Medtronic, Inc	CranialCare LLC
Submission Number	K130556	P960009/S7	-
<i>De Novo</i> Number	DEN130022	-	-
Product Code	OKP	MHY	-
Classification	Class II	Class III	-
Intended Use	The acute treatment of pain associated with migraine headache with aura.	For bilateral stimulation of the internal globus pallidus or the subthalamic nucleus as an adjunctive therapy in reducing some of the symptoms of advanced, levodopa-responsive Parkinson's disease that are not adequately controlled with medication.	Adjunctive therapy to aid in reducing some of the symptoms of advanced levodopa-responsive Parkinson's disease that are not adequately controlled with medication.
Technological Characteristics	AC-powered device that delivers a brief pulse of magnetic energy to the back of the head to induce an electrical current in the occipital cortex.	Uses an implantable neurostimulator to deliver electrical stimulation to the internal globus pallidus (GPi) or subthalamic nucleus (STN) of the brain. The device consists of the following implanted components: a lead, a neurostimulator, and an extension that connects the lead to the neurostimulator. External components include a physician programmer.	AC-powered device that delivers a brief pulse of magnetic energy to the back of the head to induce an electrical current in the subthalamic nucleus (STN).

to Cerena.” Cahn then drew Laup’s attention to the flowchart (Figure 1).

“However, the intended uses of the devices differ, so Cerena can’t be used as a predicate for DailyStim. Interestingly, the intended use of DailyStim is very similar to that of Activa, which is a Class III PMA-approved device.”

Laup interrupted nervously, “Is it going to be the PMA pathway for DailyStim then?”

“No, that’s not what I meant,” Cahn interjected. “Activa is a high-risk implanted device. The risks associated with DailyStim are only low-to-moderate. Furthermore, a combination of general and special controls should be sufficient to provide a reasonable assurance of DailyStim’s safety and effectiveness.<sup>15, 16</sup> It is possible that the benefit our low-to-moderate device provides for patients may

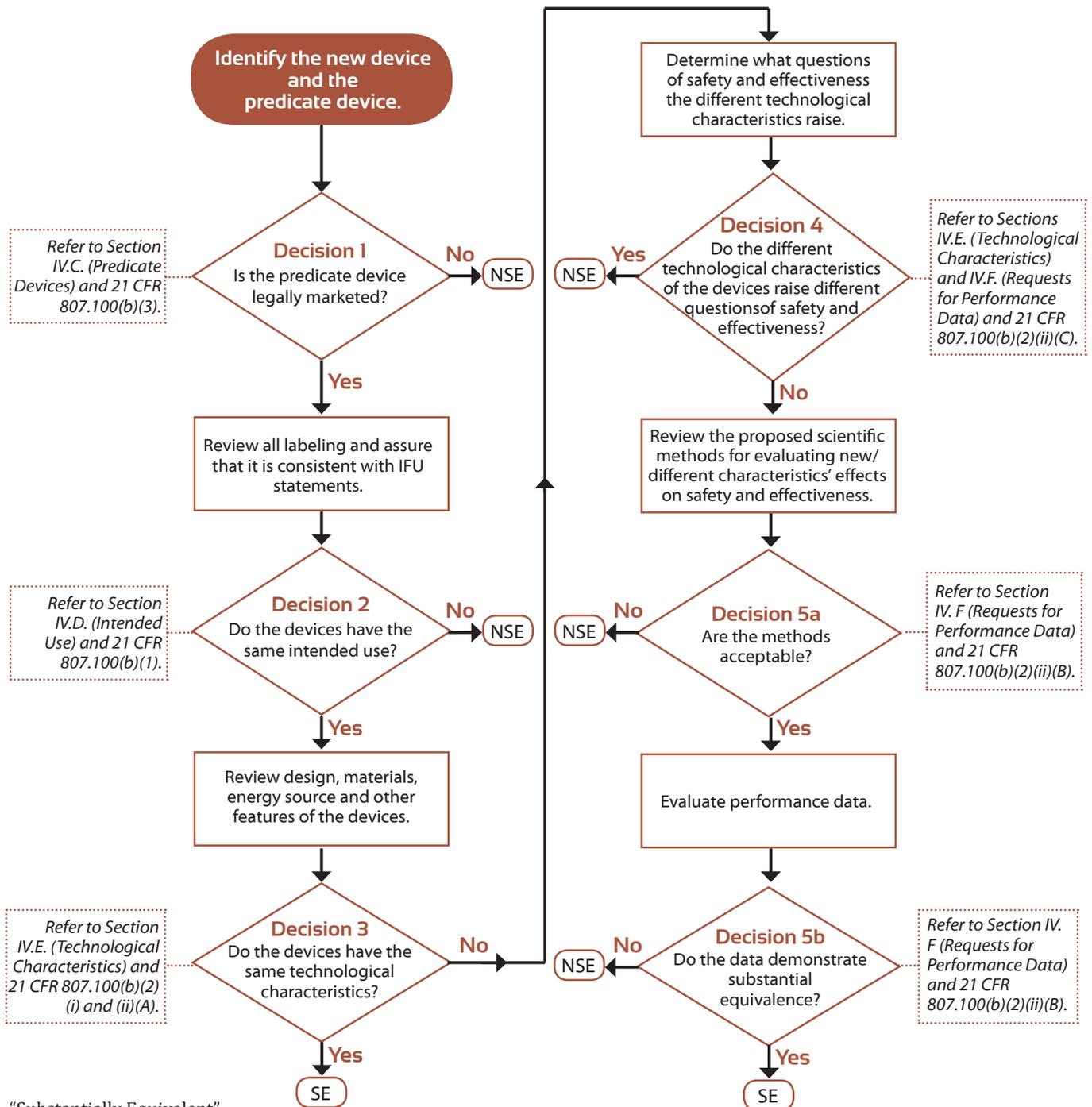
not be as high as that provided by a high-risk device like Activa, but we do know from our research that DailyStim will be beneficial to patients who suffer from PD. I think we have a shot at qualifying for the *de novo* pathway. Let me investigate

<sup>15</sup> *De Novo Classification Process*

<sup>16</sup> Section 513(a)(1) FD&C Act

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FIGURE 1: 510(k) DECISION-MAKING FLOWCHART



SE = "Substantially Equivalent"  
 NSE = "Not Substantially Equivalent"  
 IFU = "Indications For Use"

\*Refer to the appropriate section in "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notification [510(k)]"  
<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM284443.pdf#page=30>

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a few things and we can talk again later this week.”

## Ways to Investigate Whether your Device is Appropriate for the *De Novo* Pathway

On Thursday, Cahn interrupted Laup in the laboratory again. This time, the interruption was welcome.

“I believe we should qualify for the *de novo* pathway as DailyStim is a novel device that only poses a low-to-moderate risk to users.”

Laup was still concerned. “Are you sure? Not that I doubt you, but I’d hate to go through the submission process only to find out that we’re wrong. Is there a way to make sure FDA will consider the *de novo* as an appropriate path for DailyStim before we proceed?”

“You read my mind!” Cahn replied. “Section 513(g) of the FD&C Act [21 U.S.C. 360c(g)] provides a means for us to obtain a formal determination regarding the classification and the regulatory requirements that apply to our particular device through a Section 513(g) Request for Information. The provision states that FDA has a 60-day window to provide a determination regarding the classification and regulatory requirements applicable to a given device. Specifically, according to guidance<sup>17</sup> on procedures for Section 513(g) requests, and based upon the information provided in the 513(g) submission, FDA will

provide its determination regarding whether the device

1. Is an unclassified preamendments device type, and therefore subject to the 510(k) requirement,
- OR
2. Appears to be a postamendments device type that has not yet been reclassified (or for which a PMA has already been approved), and therefore subject to the PMA requirement,

OR

3. Appears to be a classified device type. In this case, FDA will generally identify the apparent generic type of the submitted device (e.g., classification regulation) and classification, as well as the type of regulatory submission, if any, required to market the device.

“Besides the formal determination given in response to a 513(g) request,” Cahn continued, “we could also request informal feedback on specific questions through a type of Q-Submission<sup>18</sup> (a request for feedback from FDA) called a Pre-Submission, or Pre-Sub Request.”

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<sup>17</sup>FDA and Industry Procedures for Section 513(g) Requests for Information under the Federal Food, Drug, and Cosmetic Act

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM209851.pdf>

“Which one should we submit to FDA to find out if our device is suitable for the *de novo* pathway?” Laup asked.

“Well, the turnaround time for a response from FDA will be similar for either process,” Cahn explained. “But there are pros and cons to each approach. The 513(g) approach appears to be more structured, so we might be able to put together the required information faster and save some time in the long run (Appendix A). However, there is a user fee for the 513(g) submission. On the other hand, the Pre-Sub process has no user fee, but it would take more time to put together.

“There is one final caveat that you should be aware of,” Cahn added. “According to FDA, neither a 513(g) nor a Q-sub response will constitute final agency action. Such responses only provide determinations regarding the classification and regulatory requirements applicable to the device based upon the information that we provide in the 513(g) submission. We won’t find out FDA’s final decision on whether we are a Class I, II, or III device and if we have authorization to market our device until we submit the actual *de novo* request.”

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<sup>18</sup>Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf>

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“I understand,” Laup responded. “Let’s prepare a 513(g) request so we can receive a more formal determination from FDA.”

## Preparing the *De Novo* Request

Eight weeks after CranialCare submitted their 513(g) submission for the DailyStim, Cahn received FDA’s determination. “Laup! Great news!” Cahn exclaimed, bursting into the lab. “FDA says that the *de novo* pathway may be appropriate for DailyStim.”

Laup let out a sigh of relief. “Fantastic! I’m so glad we double checked with FDA. Could you imagine the time and money we would have wasted if we had prepared a *de novo* request only to find we weren’t eligible? So, are we ready to submit the *de novo* request? Tell me more details about the submission process.”

Putting on his regulatory hat, Dr. Cahn explained, “The *de novo* process is available for classifying into Class I or Class II the following: (1) low-to-moderate risk devices that have been found not substantially equivalent (NSE), or for which no legally marketed predicate device is available, and (2) devices for which general controls, or general and special controls, are sufficient to establish a reasonable assurance of safety and effectiveness.

“There are two options available for submitting a *de novo* classification request for novel devices of low-to-moderate risk like DailyStim,”

Dr. Cahn continued. “Option one: we could first submit a 510(k) to FDA, wait for them to make an NSE determination, and then submit our *de novo* request. Or, since we have determined that there is no predicate device upon which to base a claim of substantial equivalence, our second option is to submit a *de novo* submission right away for the FDA to make a risk-based classification of DailyStim into Class I or II (informally called a ‘direct’ *de novo* submission).<sup>19, 20</sup>

“Based on our prior research on predicates and FDA’s response to our 513(g), I suggest that we proceed directly with a *de novo* submission for DailyStim. We’ll need to demonstrate that our device poses low-to-moderate risk and that based on what we know about the device, it meets the statutory standards for classification into Class I or II under Section 513(a)(1) of the FD&C Act (i.e., **general controls** or general and **special controls** provide a reasonable assurance of the **safety** and **effectiveness** of the device).”

Cahn handed Laup a sheet of paper. “Here is a figure from FDA’s draft guidance<sup>21</sup> describing the *de novo*

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<sup>19</sup>The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM284443.pdf>

<sup>20</sup>New Section 513(f)(2) - Evaluation of Automatic Class III Designation, Guidance for Industry and CDRH Staff

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080197.pdf>

pathway. This is the regulatory process we’ll follow for DailyStim. (Figure 2)

“This figure assumes that we haven’t submitted a 510(k) prior to filing the *de novo* request,” Cahn pointed out. “As *de novo* devices are by definition low-to-moderate risk, the amount of data we will need to collect may be less than if we were submitting a PMA application. However, FDA will still require data and other information to determine whether general or general and special controls are sufficient to mitigate the risks associated with use of the device, and to ensure a reasonable assurance of safety and effectiveness.”

“Now,” Cahn continued, “It is very important that we follow FDA’s medical device regulations as we gather data for the *de novo* submission. Specifically, you and your staff will need to adhere to **Good Laboratory Practices (GLP)**, **Good Clinical Practices (GCP)**, and **Current Good Manufacturing Practices (cGMP)**. This may seem like a lot of work, but spending a little more time on this now will save us time and money in the future.”

“Got it,” said Laup. “As we’re gathering and documenting our data, I think we should keep in mind how FDA will evaluate our device. Do you have any idea what they will be looking for or is this something we should ask FDA?”

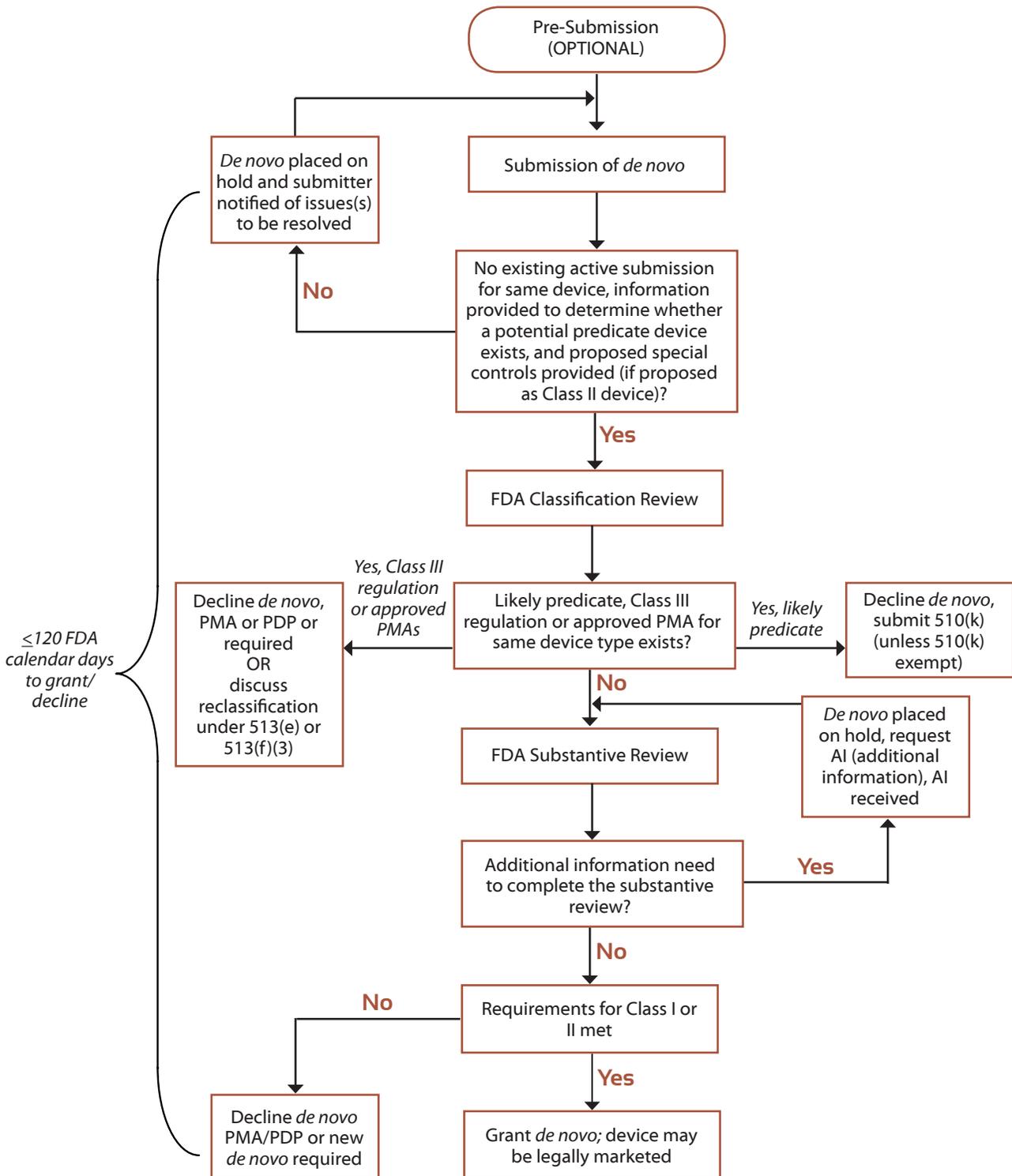
“Asking FDA for clarification is never a bad way to get started,” Cahn replied.

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<sup>21</sup>*De Novo* Classification Process

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FIGURE 2: STEPS AND ESTABLISHED TIMEFRAME FOR A DIRECT *DE NOVO* SUBMISSION



Source: De Novo Classification Process (Evaluation of Automatic Class III Designation) – Draft Guidance Issued August 14, 2014  
 (Note: Draft guidance is subject to change and is not for implementation)

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM273903.pdf>

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“But I think I have a fair idea of what they are looking for. As I mentioned earlier, besides establishing that our device does not have a predicate, we will also have to provide evidence that the device can appropriately be classified into Class I or II and that general or general and special controls are sufficient to mitigate the known risks associated with use of the device and to provide a reasonable assurance of safety and effectiveness.

“While reviewing our argument that DailyStim is a low-to-moderate risk device, FDA will rely upon valid **scientific evidence** to establish a reasonable assurance of safety and effectiveness. Both **clinical** and **nonclinical** data may play a role in FDA’s review of our *de novo*. Furthermore, FDA makes a benefit-risk determination for all *de novo* decisions based on FDA’s **benefit-risk guidance**.<sup>22</sup> So one of the first things we should do is create a **risk assessment plan** to address all risks associated with use of the device. After we address and

provide methods to mitigate all the risks, we’ll compare the clinical benefits to the overall residual risk. To have our *de novo* request granted, we must be able to demonstrate that DailyStim’s benefit versus risk profile would be acceptable to FDA.

“Once we have gathered all of the necessary information we will package it into the *de novo* submission. Here is the list of items that should be included in the submission per FDA.”<sup>23</sup>

Cahn handed Laup another printout (**Appendix B**). “I’ll gather the items covering the routine information about our company while you and your team compile the rest of the required data on our device.

“FDA has 120 days to review our *de novo* submission and make a final decision, but this timetable may be delayed if we do not provide adequate information and FDA has to ask us for more data. Let’s make sure we do everything we can now to address this list so that we can proceed through the *de novo* process as rapidly as possible.”

## Conclusion

“Okay!” said Laup. “There is a lot to be done, but these meetings were a great way to get us focused and prepared. We have a novel product that is low-to-moderate risk that can help people suffering from PD and we’ve finally identified a regulatory pathway that will benefit physicians and patients by getting DailyStim to market in a timely fashion. After so much work and planning, I’m excited to get started on this!”

“As am I,” Cahn smiled. “I’ll let you get back to work, but let’s talk about scheduling a Q-sub meeting to get FDA’s input on the design of our nonclinical and clinical trials when your team reaches that step.”

“Another meeting!” Laup groaned. She laughed and continued before her partner could give her a lecture on the necessity of Q-sub. “Just kidding. I’ll keep you updated on our progress. Thank you again for all your hard work. We’re finally going to make a positive contribution to the quality of life of patients living with PD. I have the *de novo* process, and you, to thank for that.”

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<sup>22</sup>Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval & *De Novo* Classifications

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM296379.pdf>

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<sup>23</sup>*De Novo* Classification Process

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## APPENDIX A: RECOMMENDED INFORMATION FOR INCLUSION IN A 513(g) SUBMISSION

Information Required	Description
Cover Letter	<p>Your cover letter should identify your request as a “513(g) Request for Information” and include the following:</p> <ul style="list-style-type: none"> <li>✓ Date of the request</li> <li>✓ Name of the device</li> <li>✓ Your specific question(s) concerning the class in which the device has been classified and/or the regulatory requirements applicable to a device</li> <li>✓ Requestor’s name, address, telephone number, fax number, and email address</li> <li>✓ 513(g) requestor’s signature</li> </ul>
Description of the Device	<p>As applicable, the description of the device should include the following:</p> <ul style="list-style-type: none"> <li>✓ List of materials and components used in/with the device</li> <li>✓ Photographs, engineering drawings, and/or samples of the device</li> <li>✓ Summary of the device’s operational principles</li> <li>✓ Description of the type and amount of energy to be used or delivered by the device</li> <li>✓ Description of similar devices in commercial distribution in the United States, if available</li> </ul>
Description of What the Device is to be Used for	<p>This includes the following:</p> <ul style="list-style-type: none"> <li>✓ The disease or condition with respect to which the device is to be used</li> <li>✓ Prescription versus over-the-counter use</li> <li>✓ Part of the body or type of tissue applied to or interacted with</li> <li>✓ Frequency of use</li> <li>✓ Physiological purpose (e.g., removes water from blood, transports blood)</li> <li>✓ Patient population</li> <li>✓ Any other labeling information related to the patient use of the device</li> </ul>
Proposed Labeling or Promotional Material	<p>Provide any proposed labeling, including:</p> <ul style="list-style-type: none"> <li>✓ Proposed promotional material for the device or</li> <li>✓ Any labeling or promotional material of a similar, legally marketed device.</li> </ul> <p>If no proposed labeling is available for the described device or for a similar legally marketed device, this should be noted in the cover letter.</p>

Source: FDA and Industry Procedures for Section 513(g) Requests for Information under the Federal Food, Drug, and Cosmetic Act  
<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM209851.pdf>

# USING THE *DE NOVO* PROCESS TO CLASSIFY AND BRING TO MARKET AN INNOVATIVE, LOW-TO-MODERATE RISK DEVICE



## APPENDIX B: RECOMMENDED INFORMATION FOR INCLUSION IN THE *DE NOVO* REQUEST

Information Type	Information to be Included in All <i>De Novo</i> Petitions
Administrative Information	Applicant name, contact name, address, phone, fax, e-mail.
Regulatory History	Describe any prior submissions to FDA for the device, including any 510(k)s and related NSE decisions, IDEs, Pre-Subs, and/or previously withdrawn or declined <i>de novos</i> .  For any previous submissions where FDA provided feedback, identify how you have responded to the identified issues.
Device Information and Summary	Provide the device name, device description, indications for use statement (including prescription and/or over the counter), and a description of all main functions, technological characteristics, components, and accessories. Include a summary of the directions for use/usage instructions. Identify the target population including demographics information, diseases, and/or symptoms to be treated, etc.
Classification Recommendation	Recommended Class (I or II) and recommended applicability of 510(k) requirement (exempt or not exempt). Describe why you believe general controls or general and special controls are adequate to provide reasonable assurance of safety and effectiveness. If you are proposing Class II and believe the device type should be exempt from 510(k), justify why premarket notification should not be required.
Proposed Special Controls (for Class II Devices ONLY):	Provide proposed special controls along with cross-references to other information within the submission demonstrating that the device meets these special controls.
Supporting Protocols and/or Data	<p>Summary of Benefits: Provide information supporting the effectiveness of the device. Cite the available data/studies supporting effectiveness. This section may include references to available published literature, where applicable.</p> <p>Summary of Known and Potential Risks to Health: List each risk and identify the reason for each risk (tracing back to risk analysis, clinical testing, etc.). Summarize the studies completed and how they support safety.</p> <p>Supporting Protocols and/or Data: Provide a summary of all performance and clinical testing that provide a reasonable assurance of safety and effectiveness for your specific device and that demonstrate that general controls or general and special controls are sufficient to provide a reasonable assurance of safety and effectiveness. The summary should include the objective of the testing, a description of study design, and a description of the results. For human subject testing, the summary should also describe the study population, selection and exclusion criteria, duration, data collection methodology, observed adverse reactions, and statistical analysis. The summary should include links to appendices, etc., that contain the detailed final protocols and supporting data.</p>
Summary of Benefits	Provide information supporting the effectiveness of the device. Cite the available data/studies supporting effectiveness. This section may include references to available published literature, where applicable.
Summary of Known and Potential Risks to Health	List each risk and identify the reason for each risk (tracing back to risk analysis, clinical testing, etc.). Summarize the studies completed and how they support safety.

# USING THE *DE NOVO* PROCESS TO CLASSIFY AND BRING TO MARKET AN INNOVATIVE, LOW-TO-MODERATE RISK DEVICE

## APPENDIX B: RECOMMENDED INFORMATION FOR INCLUSION IN THE *DE NOVO* REQUEST

Information Type	Information to be Included In All <i>De Novo</i> Petitions (continued)
Risk and Mitigation Information	Provide a table showing the proposed mitigation(s) for each risk. Identify which mitigations are general controls and which are special controls. Provide specific section and page numbers where the details on each recommended mitigation (e.g., specific testing required) can be found in the submission.
Benefit-Risk Considerations	Provide a discussion demonstrating that, when subject to general controls or general and special controls, the probable benefits to health from use of the device outweigh any probable injury or illness from such use. <sup>1</sup>
Device Labeling	Proposed device labeling that clearly indicates the proposed intended use and indications for use, limitations contraindications, etc. <sup>2</sup>

Information Type	Information to be Included in All <i>De Novo</i> Petitions
Classification Summary	<p>For direct <i>de novos</i>, describe your search for legally marketed devices of the same type. Provide a list of regulations, approved PMAs, and/or product codes that may relate to or are potentially similar to the subject device. You should also provide a rationale for why the subject device is different from and/or does not fit within any identified regulations, PMAs, and/or product codes.</p> <p>If the same device (same technology and same indication(s) for use) has been previously found NSE due to lack of a predicate, new intended use, or different questions of safety and effectiveness, only the relevant 510(k) number should be submitted for this section along with a summary of this search performed since the NSE was issued.</p>

Information Type	Additional Information to be Submitted for a <i>De Novo</i> Request Preceded by a 510(k)
Change Summary	Describe in detail any changes made to your device or proposed indications since any prior Pre-Sub or 510(k), as appropriate. This summary should include changes to the device as well as changes to test protocols and/or labeling.

Source: De Novo Classification Process (Evaluation of Automatic Class III Designation) – Draft Guidance Issued August 14, 2014 (Draft guidance is subject to change and is not for implementation)

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM273903.pdf>

<sup>1</sup>For information on benefit-risk determinations and factors considered, please see Guidance for Industry and Food and Drug Administration Staff - Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approvals and *De Novo* Classifications <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm267829.htm>

<sup>2</sup>Labeling is defined in section 201(m) of the FD&C Act, 21 U.S.C. 321(m), as “all labels and other written, printed or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.” Labeling may include package inserts, instructions for use (for patients and/or physicians, as applicable), service manuals, etc.

# USING THE *DE NOVO* PROCESS TO CLASSIFY AND BRING TO MARKET AN INNOVATIVE, LOW-TO-MODERATE RISK DEVICE

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## GLOSSARY

**Approval:** Approval of a medical device must be obtained from the FDA by demonstrating that the device is reasonably safe and effective, and that the benefits outweigh the risks for the intended patient population before it can be put into commerce. The term “approval” of a medical device is used in the context of the “approval” of a **Premarket Application (PMA)**.

**Clearance:** Clearance of a Class I or Class II medical device not exempt from 510(k) must be obtained from the FDA by demonstrating that the device is substantially equivalent (SE) to a legally marketed predicate device before the device is put into commerce.

**Clinical Investigation (Trial or Study):** A systematic investigation conducted to evaluate the safety and effectiveness of a medical device using human subjects or specimens.

**Current Good Manufacturing Practices (cGMP):** Production and testing practices that help ensure safe, effective, and quality products. In the United States, cGMP Regulations are promulgated by the FDA under the authority of the FD&C Act (Chapter IV for food; Chapter V, Subchapters A, B, C, D, and E, for drugs and devices). The “c” stands for “current”, reminding manufacturers that they must employ up to-date technologies and systems to comply with the regulation. It is the manufacturers’ responsibility to be current.

**Device Classification:** The Food and Drug Administration (FDA) has established classifications for approximately 1,700 different generic types of devices and has grouped them into 16 medical specialties referred to as panels. Each of these generic types of devices is assigned to one of three regulatory classes based on the level of control necessary to assure the safety and effectiveness of the device. The

three classes and the requirements which apply to them are:

Device Class and Regulatory Controls:

1. Class I General Controls
  - With Exemptions
  - Without Exemptions
2. Class II General Controls and Special Controls
  - With Exemptions
  - Without Exemptions
3. Class III General Controls and Premarket Approval

**De Novo Classification:** New devices that FDA has not previously classified into Class II or Class I are “automatically” or “statutorily” classified into Class III by operation of section 513(f)(1) of the FD&C Act, regardless of the level of risk they pose.

To limit unnecessary expenditure of FDA and industry resources that could occur if lower risk devices were subject to **Premarket Approval (PMA) under Section 515 of the FD&C Act**, Congress enacted section 513(f)(2) of the FD&C Act as part of the Food and Drug Administration Modernization Act of 1997 (FDAMA). The process created by this provision, which is referred to in FDAMA as the “Evaluation of Automatic Class III Designation,” is referred to as the “*de novo* process.”

In 2012, Section 513(f)(2) was modified by Section 607 of FDASIA. This new law provides two options for *de novo* classification. First, any person who receives a “not substantially equivalent” (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may, within 30 days of receiving notice of the NSE determination, request that FDA make a risk-based classification of the device under section 513(a)(1) of the Act. Alternatively, any person who determines that there is no legally

## USING THE *DE NOVO* PROCESS TO CLASSIFY AND BRING TO MARKET AN INNOVATIVE, LOW-TO-MODERATE RISK DEVICE

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marketed device upon which to base a determination of substantial equivalence may request that FDA make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k).

If the *de novo* request is granted, the device is placed into Class II or Class I, and a new classification regulation is created. The device may be marketed immediately and can serve as a predicate device for future 510(k)s.

If the *de novo* request is declined, or if the device is ineligible for *de novo*, the device remains in Class III and will require a PMA prior to going to market.

**Different Technological Characteristics:** As defined in Section 513(i)(1)(B) of the FD&C Act [21 U.S.C. § 360c(i)(1)(B)], devices are deemed to have different technological characteristics when there is a significant change in the materials, design, energy source, or other features between the two devices.

**Effectiveness:** There is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results. [21 CFR Part 860.7(e)(1)]

**General Controls:** General controls include the following:

- Establishment Registration of companies required to register under 21 CFR Part 807.20, such as manufacturers, distributors, repackagers, and relabelers
- Medical Device Listing with FDA of devices to be marketed
- Manufacturing devices in accordance with GMP in 21 CFR Part 820 (Quality System Regulation)
- Labeling devices in accordance with labeling regulations in 21 CFR Part 801 or 809

- Submission of a Premarket Notification, or 510(k), before marketing a device

For additional information please refer to

<http://www.fda.gov/medicaldevices/device-regulationandguidance/overview/general-and-special-controls/default.htm>

**Good Clinical Practices (GCP):** A set of guidelines that must be followed when conducting clinical trials to ensure that the rights and well-being of the trial participants are protected and that the data generated in the trial is valid. GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials involving human participants. The guidelines were developed in order to provide drug clinical trials with a unified standard across the European Union, Japan, and the United States and were labeled ICH-GCP at the International Conference on Harmonization (ICH), 1996. For medical devices, ISO 14155:2011 Clinical Investigation of Medical Devices for Human Subjects–Good Clinical Practice was developed and is the global standard for medical device GCP.

**Good Laboratory Practices (GLP):** A set of principles that provides a framework within which laboratory studies are planned, performed, monitored, recorded, reported, and archived. GLP helps assure regulatory authorities that the data submitted are a true reflection of the results obtained during the study and can therefore be relied upon when making risk/safety assessments.

**Guidance Documents:** Documents prepared for FDA staff, applicants/sponsors, and the public that describe the agency's interpretation of or policy on a regulatory issue. They do not create or confer any rights for or on any person and do not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

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Draft guidance documents are for the public to comment on and suggest changes for, but are subject to change and are not for implementation. [See 21 CFR Part 10.115 (b), (d), and (g)]

**Good Guidance Practices (GGP's):** Good guidance practices (GGP's) are FDA's policies and procedures for developing, issuing, and using guidance documents. Please refer to the following links for additional information:

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=10.115>

<http://www.fda.gov/downloads/AboutFDA/Transparency/TransparencyInitiative/UCM285124.pdf>

**Intended Use/Purpose:** Intended use means the general purpose of the device—or what the device does. The intended use of a device is the general purpose of the device or its function (not to be confused with the indications for use or IFU of the device). The IFU is disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient population for which the device is intended. By definition, the intended use of a device encompasses the IFU.

**Medical Device:** An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, “or accessory” that is the following:

1. Recognized in the official National Formulary, the United States Pharmacopeia, or any supplement to them
2. Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in man or other animals
3. Intended to affect the structure or any function of the body of man or other animals
4. Does not achieve its primary intended purposes through chemical action within or on the body of a human or other animals and that is not dependent upon being metabolized for the achievement of its primary intended purposes [Section 201(h) of the FD&C Act]

**Nonclinical Investigation:** A systematic investigation conducted to evaluate the safety and effectiveness of a medical device using non-human subjects or specimens, primary or secondary cell lines, or computational models.

**Predicate Device:** A legally marketed device to which a new device may be compared for a determination regarding substantial equivalence.

**Premarket Approval (PMA):** The FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices. Any PMA application for a Class III medical device, including all information submitted with or incorporated by reference therein (21 CFR Part 814.3). Class III devices are those that cannot be classified as Class I or Class II devices because insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, and either (1) are purported to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health; or (2) present a potential unreasonable risk of illness or injury.

**Premarket Notification–510(k) Clearance:** Section 510(k) of the FD&C Act requires device manufacturers to notify FDA of their intent to market a medical device at least 90 days in advance. This is known as Premarket Notification, also called PMN or 510(k). In a 510(k), FDA determines whether the device in question is substantially equivalent to a device already placed into Class I, Class II, or Class III requiring 510(k), unclassified requiring 510(k), or a legally marketed preamendment device.

Specifically, medical device manufacturers are required to submit a Premarket Notification if they intend to introduce a device into commercial distribution for the first time or reintroduce a device that will be significantly changed or modified to the extent that its safety or effectiveness could be affected. Such change or modification could relate to the design, material,

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chemical composition, energy source, manufacturing process, or intended use.

**Product Code:** The name and product code identify the generic category of a device for FDA. The product code assigned to a device is based upon the medical device product classification designated under 21 CFR Parts 862–892.

**Regulatory Pathways:** Before a medical device can be introduced into the U.S. market, manufacturers of medical devices may have to submit evidence to demonstrate product safety and effectiveness to the Office of Device Evaluation (ODE) and to the Office of In Vitro Diagnostics and Radiological Health (OIR) of the Center for Devices and Radiological Health (CDRH) at FDA. There are various submission processes and respective applications for evaluation. PMA, PMA Supplement, Product Development Protocol (PDP), Humanitarian Device Exemption (HDE), IDE, IDE Amendment, IDE Supplement, *de novo* classification request, and 510(k) are programs administered by ODE and OIR. They are also called regulatory pathways.

**Residual Risk:** Risks not adequately addressed by the general and special controls outlined in a risk management plan. A device may be marketed even with residual risk as long as the residual risk is acceptable and appropriate methods are in place to obtain relevant post-market information.

**Risk Assessment:** Process comprising a systematic use of available information to identify hazards and to compare the estimated risk against given risk criteria to determine the acceptability of the risk.

**Risk Management Plan:** Systematic application of management policies, procedures, and practices to the tasks of analyzing, evaluating, controlling, and monitoring risk.

**Safety:** There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh the probable risks. [21 CFR Part 860.7(d)(1)]

**Scientific Evidence:** Evidence that serves to either support or counter a scientific theory or hypothesis. The strength of scientific evidence is generally based on the results of statistical analysis and the strength of scientific controls, for example, information from well-controlled clinical studies.

**Significant and Non-Significant Risk Devices:** A “significant risk device” presents a potential for serious risk to the health, safety, or welfare of a subject. These devices are either intended as an implant or are substantially important in diagnosing, curing, mitigating, or treating disease (e.g., dental lasers, embolization devices for urological use, collagen, and bone replacements).

A “non-significant risk device” does not pose a significant risk to human subjects (e.g., external monitors for insulin reactions, general biliary catheters, MRIs within specified parameters).

**Special Controls:** Special controls may include, but are not limited to, the following:

- Special labeling requirements
- Mandatory performance standards
- Postmarket surveillance
- Nonclinical and/or clinical testing
- Other specific types of performance testing

For additional information please refer to:

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/GeneralandSpecialControls/ucm2005378.htm>

**Substantial Equivalence:** As part of the 510(k) process, FDA may issue an order of substantial equivalence if it determines that, as compared to the legally marketed predicate device, the new device has the same intended use and the same technological characteristics as the predicate, or it has the same intended use and different technological characteristics and the different technological characteristics do not raise different questions of safety and effectiveness.

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## STUDENT ACTIVITIES

### SESSION 1

#### I. Review the following materials before Session 1:

##### 1. CDRH Learn Materials

- a. Review the “*De Novo* Program” presentation and slides under the “How to market your device” tab

<http://www.fda.gov/Training/CDRHLearn/ucm126230.htm#collapseTwo>

- b. *De Novo* Program

<http://www.fda.gov/downloads/Training/CDRHLearn/UCM421766.pdf>

- c. Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and *De Novo* Classifications

(Approximately 20 minutes)

<http://fda.yorkcast.com/webcast/Viewer/?peid=bac3f2698df14fa98388409da5cba6831d>

##### 2. Information on Parkinson’s Disease (PD)

- a. The Michael J Fox Foundation for Parkinson’s Research

<https://www.michaeljfox.org/foundation/michael-story.html>

- b. Muhammed Ali Parkinson Center

[http://www.thebarrow.org/Neurological\\_Services/Muhammad\\_Ali\\_Parkinson\\_Center/index.htm](http://www.thebarrow.org/Neurological_Services/Muhammad_Ali_Parkinson_Center/index.htm)

- c. National Parkinson’s Foundation

<http://www.parkinson.org/parkinson-s-disease.aspx>

- d. NIH Senior Health: Parkinson’s disease

<http://nihseniorhealth.gov/parkinsonsdisease/whatisparkinsonsdisease/01.html>

- e. Mayo Clinic: Parkinson’s disease

<http://www.mayoclinic.org/diseases-conditions/parkinsons-disease/basics/treatment/con-20028488>

- f. Parkinson’s UK

<http://www.parkinsons.org.uk/content/side-effects-parkinsons-drugs>

##### 3. Mandatory Reading<sup>1</sup>

*Note: A Draft Guidance is subject to change and is not for implementation.*

- a. Draft Guidance: *De Novo* Classification Process (Evaluation of Automatic Class III Designation)

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM273903.pdf>

- b. Evaluation of Automatic Class III Designation (*De Novo*) Summaries

<http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm232269.htm>

- c. Draft Guidance: Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications [510(k)] with Different Technological Characteristics

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM404773.pdf>

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<sup>1</sup>FDA Guidance Documents are documents prepared for FDA staff, applicants/sponsors, and the public that describe the agency’s interpretation of or policy on a regulatory issue. They do not create or confer any rights for or on any person and do not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. Draft guidance documents are for public to comment and suggest changes for, but are not for implementation. [See 21CFR10.115 (b), (d), and (g)].

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- d. Factors to Consider when Making Benefit-Risk Determinations in Medical Device Premarket Approval and *De Novo* Classifications

<http://www.fda.gov/downloads/medical-devices/deviceregulationandguidance/guidancedocuments/ucm296379.pdf>

## 4. Optional Reading

- a. General/Specific Intended Use

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073944.htm>

- b. Use of Standards in Substantial Equivalence Determinations

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073756.pdf>

- c. New Section 513(f)(2) – Evaluation of Automatic Class III Designation, Guidance for Industry and CDRH Staff

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080197.pdf>

- d. FDA and Industry Procedures for Section 513(g) Requests for Information under the Federal Food, Drug, and Cosmetic Act

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM209851.pdf>

- c. Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf>

## II. Answer the following questions before Session 1—Fundamental concepts:

- 1. What are the key elements that FDA will consider to determine if a device is appropriate for the *de novo* process?

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM273903.pdf> (pg. 5, Section 3.1)

- 2. How do you justify that the *de novo* is the correct regulatory pathway for DailyStim?

## SESSION 2

### I. In-class group discussion (instructor guidance required):

- 1. Using the information presented on DailyStim in the case study, discuss the following:
  - a. State the intended use of DailyStim.
  - b. Identify DailyStim’s key technical characteristics.
  - c. Examine DailyStim and list all potential risks to patients.
  - d. Propose mitigation strategies for each identified risk.
  - e. Determine all the benefits of DailyStim and justify how DailyStim’s benefits outweigh the identified risks.
- 2. Use the CDRH Medical Device database to do the following:
  - a. Identify potential predicates for DailyStim.
  - b. Find a PMA device that could be similar to DailyStim.

# USING THE *DE NOVO* PROCESS TO CLASSIFY AND BRING TO MARKET AN INNOVATIVE, LOW-TO-MODERATE RISK DEVICE

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## III. Additional References

1. The Federal Food Drug & Cosmetic (FD&C) Act  
<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/default.htm>
2. Sub Chapter II – Definitions § 321. Definitions [p. 32, paragraph (h)]  
<http://www.gpo.gov/fdsys/pkg/USCODE-2010-title21/pdf/USCODE-2010-title21-chap9-subchapII-sec321.pdf>
3. Biological Evaluation of Medical Devices Part 1: Evaluation and Testing  
<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM348890.pdf>

- c. *De Novo* Classification Request Example (DEN130007): AXIOS Stent and Delivery System  
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm?ID=DEN130007>

2. Additional submission examples can be found via the following links:
  - a. Device Classification under Section 513(a)(1)(*De Novo*) Database  
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm>
  - b. Evaluation of Automatic Class III Designation (*De Novo*) Summaries  
<http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm232269.htm>

## SESSION 3: STUDENT PROJECT AND PRESENTATION—RECOMMENDED INFORMATION FOR INCLUSION IN A *DE NOVO* REQUEST

### I. Review the following materials before beginning the project:

1. Example Submissions:
  - a. *De Novo* Classification Request Example (DEN130034): ReWalkTM  
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm?ID=DEN130034>
  - b. *De Novo* Classification Request Example (DEN110019): Neuropsychiatric EEG-Based Assessment Aid for ADHD (NEBA) System  
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm?ID=DEN110019>

### II. *De Novo* Team Project

*Note: This case study may be used as part of an academic requirement such as a thesis, senior project, or graduate project. A Draft Guidance is subject to change and is not for implementation.*

After reviewing the materials above and your in-class group discussion minutes or notes, prepare the various sections of a *de novo* submission for DailyStim. (Alternatively, you may use a specific device you are working with as part of a class project for this exercise.)

Refer to Attachment 2 of the draft *de novo* guidance “*De Novo* Classification Process (Evaluation of Automatic Class III Designation)”

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM273903.pdf>.