How To Create a Class II SaMD Regulatory Strategy

A winning regulatory strategy for SaMD has five fundamental elements which reflect the key components of your future submission:

1. **The Right Regulation and Predicate**
2. **Risk Management**
3. **Software & Cybersecurity**
4. **Human Factors & Usability**
5. **Clinical Validation**

In this “How To” guide, I have listed a series of questions I would typically ask a client when creating a regulatory strategy with them along with notes throughout to help guide you in the right direction. Here is **STEP 5: CLINICAL VALIDATION**. Happy strategy formulating!

STEP 5: CLINICAL VALIDATION

Note: First, we want to identify any relevant studies previously accepted by FDA that could help us design a successful study.

- Do any of your competitors have any studies listed on clincaltrials.gov? *Note: When you search FDA’s 510(k) database sometimes a NCT number is listed. The NCT link will take you directly to the validation study conducted to support their application. If there is no NCT number but there is a clinical validation study referenced in the 510(k) Summary, then you can do a keyword search to find the study on clinicaltrials.gov.*
- Are there any international standards related to your device that may outline clinical study requirements? *Note: If there isn’t a standard for your device, you may be able to use study design elements from ISO standards that are closely related to your device. It may not give you the entire study design, but it may give you an endpoint or a study arm consideration, for example.*

Note: Next, we want to think through the study design and study logistics. A clinical validation study will be one of your most expensive investments so it’s important to design it to meet regulators’ expectations and think strategically about the data you’re collecting and how you’re collecting.

- What is the most appropriate primary endpoint to support the device's intended use? *Note: You may have a selected predicate that used a different primary endpoint and that may be ok. It's important to use the intended use to guide the primary endpoint, not just your predicate. Your primary endpoint should represent a benefit to patients/users, it will drive your study sample size and trial duration, and it should be objectively measured with validated tools or methods.*
- Are you considering a Patient Reported Outcome (PRO) as a primary endpoint? Is this PRO validated or it is novel? If it's novel, how do you plan to validate the novel PRO?
- What secondary endpoints should we consider including to support the device's intended use and to reinforce the primary endpoint?
- What secondary endpoints should we consider including to create market differentiation (think outcomes-based endpoints)?
- What secondary endpoints should we consider including to start building a body of health economics (think cost-effectiveness data)? *Note: While not the purpose of your clinical validation study (which is to demonstrate safety and effectiveness), it's a win-win if you can include health economic data if your device is not sold OTC/DTC and you will need data to capture reimbursement.*
- Based on your primary endpoint, what sample size do you need to statistically power your study? How does your sample size impact the number of study sites you'd want to include to facilitate enrollment rates that meet your business timeline?

  Note: While the minimal statistical power historically accepted by FDA and other regulators is 80%, you may want to consider a higher statistical power that gives you more confidence in your results, reduce the risk of missing a true effect, and ultimately a more compelling study to stakeholders.

  Note: More sites mean larger budget, but it should also mean faster study. Finding the right balance for your company is key.

  Note: Selecting study sites should be done very carefully. You want sites that can realistically enroll at your target pace. You want sites that are well trained and understand your technology. You want your sites to be geographically diverse. You want sites that are collaborative and available.
- What patient characteristics (such as age, sex, skin color, ethnicity, preexisting conditions) do we need to consider when setting enrollment targets? *Note: Your intended use population should guide your enrollment. Diversity matters. Your team needs to make plans for how you will enroll a diverse study population and using geographically diverse site can help you achieve that.*
  - How long does each study participant need to engage in the study for? How much time do you expect the study to take in total?

- How will you recruit study participants? Do you have a preexisting network of users? Would your intended users respond to social media advertisements, or do you need to use more traditional routes like outpatient clinics?
- Will you hire a Clinical Research Organization (CRO) to help you run the study? Are there any aspects of the clinical trial that your internal team can take on (such as protocol writing, statistical analysis plan) or will you outsource everything? *Note: There are many CROs out there so shop around to find the right fit for your company based on factors like cost, timeline, connection with sites of interest, real experience running studies for devices like yours, the ability to be a strategic partner, and a vested interest in your study's success.*