This document provides an outline of key elements to be defined and documented for a global regulatory strategy for a medical device. Every product raises distinct issues so the categories and issues in this document should be appropriately tailored for the device in question. Similarly, not all sections will apply for every new program. Since even the most diligently developed strategy is almost certain to change during the course of product and regulatory development, this document should be periodically updated to reflect internally and externally driven changes.

1 Executive Summary

This section provides a high-level overview of the device, its intended use, and the proposed development plan and regulatory strategy. This is a high-level summary of information further detailed in later sections of the document.

1.1. Name of Device

Identify the internal project name and proposed trade name for the device.

1.2. Indication(s)/Target Population(s)

Provide the proposed indications for use, target patient populations and anatomical sites, the use environment for which the device is intended (home, hospital), prescription vs. over-the-counter distribution, etc.

1.3. Device Description

Provide a high-level description of the device. Include, as appropriate, the various models that are proposed for marketing and a summary of device characteristics that are important from a regulatory perspective (depending on device, could include sizes, materials, features, performance specifications, software options, accessories, etc.).

1.4 Marketing Status

Describe the marketing history for the product, if applicable. Identify where and when the device was first approved. List the countries and regions where it has since gained marketing approval. Provide a listing of countries, timelines, and proposed indications (if they differ based on target market) for planned marketing applications.

1.5 Regulatory Plan

Provide a high-level description of how you expect the product to be regulated in major target markets and what key regulatory challenges are expected both for the investigational and marketing portions of the product lifecycle. Identify any significant jurisdictional discrepancies (e.g., product regulated as a device in one jurisdiction and as a drug or biological product in another). Include basic information about any key partnerships important from a regulatory perspective (e.g., another company involved in product development, testing, etc.).

1.6 Testing Plan

Provide a high level description of the studies that will be needed to secure regulatory approval or clearance. Depending on the device, these could include bench, animal, biocompatibility, software, and clinical studies. If clinical studies will be necessary, provide a brief description of the proposed clinical development program, including the types of studies to be conducted and the countries in which clinical

investigations will be conducted. Describe main study endpoints, duration of follow-up, and any differences between intended patient population and that being studied. Provide an overview of the intended timeline for the clinical investigations.

1.7 Key Regulatory Assumptions/Issues/Questions

Describe any critical assumptions, issues or questions, particularly those that could influence regulatory strategy or warrant pre-submission discussions with regulators.

1.8 Additional Strategic Points to Consider

Identify any other high-level strategic points appropriate for consideration in an Executive Summary.

2 Project Team

2.1 Team Members and Responsibilities

Identify the project team members and their contact information, along with their functional areas and specific responsibilities for this program. Include all major functions, such as engineering, manufacturing, quality, regulatory, clinical, reimbursement, marketing, as well as consultants and partner contacts where applicable. If the team is large, it might be helpful to present this in the form of a table. Who is responsible for providing information to support the regulatory submission? Who is responsible for internal review of the submission? Are there any specific directions on communications, e.g., "all communications with Contractor A must go through Project Manager A?" Are unique/ unusual resources required (e.g., chemistry and/or pharm-tox expertise for a device company's first combination product)?

2.2 Team Communications

Explain your team's communications strategies. Are there weekly team meetings? Are there communication constraints due to team memberships in multiple time zones? How will you maintain decision logs and meeting minutes? What is the governance model for the team?

2.3 Business Relationships

Provide names of other companies involved in the development and briefly describe the delineation of any major and/or unusual responsibilities. Highlight any regulatory approvals, clearances or master files needed that depend on other companies.

3 Product/Program Details

3.1 Device Nomenclature

- Internal Project/Product Name
- Proposed Trade Name
- Common/Generic Name
- FDA Classification Regulation (e.g., 21 CFR 870.4520)
- FDA Product Code (e.g., DXY)
- US Classification (I, II, III)
- EU Classification (I, IIa, IIb, III)
- Canadian Classification (I, II, III, IV)
- Other Country Classifications (as determined by target markets)

3.2 Device Description

Provide a description of the device. Include, as appropriate, the various models that are proposed for marketing and a summary of device characteristics that are significant from a regulatory perspective

(depending on device, this could include sizes, patient/fluid contacting materials and their duration of contact, principle of operation, features/options, performance specifications, software configurable features/operation, power source, single use vs. reusable, etc.). Tabular presentation may be helpful to illustrate the similarities/differences among the various models proposed for development. Include any accessories, particularly those that will require regulatory approval/clearance. Note: a separate regulatory strategy document may be appropriate for some standalone or significant accessories that require agency approval/clearance in their own right.

3.3 Indications for Use/Target Population

Provide the proposed indications for use, target patient populations and anatomical sites, the use environment for which the device is intended (home, hospital), prescription vs. over-the-counter distribution, etc.

3.4 Proposed Claims

Describe any claims proposed for the device for which Agency review/approval is required (or desirable). Does the proposed trade name of the device itself imply a device claim? Careful planning and obtaining supportive data for desired claims may help the product gain a competitive marketing advantage. What methods will be utilized to promote the device (e.g., conventional or newer methods such as social media, web, etc.?)

3.4 Target Markets

Identify each target country in which regulatory approval/clearance will be pursued. Identify any countries that will require unique regulatory strategies (e.g., due to significant differences in regulatory requirements, cost effectiveness evidence required, etc.). Identify any countries where another country's approval is first necessary. What are the key target market priorities for the company, so that regulatory submissions can be appropriately prioritized and timed? What languages will device labeling and product interfaces need to be written in? What are the regulatory application fees in the target markets? Is the potential revenue in a target market significant enough to justify the costs/time of pursuing regulatory approval? Note: countries with unique or significantly different requirements may warrant separate regulatory strategy plans.

3.5 Current Regulatory Status

Identify the countries where the device is in clinical trials, marketed and registered, if applicable. Identify application or license numbers where applicable. Describe any unique regulatory considerations for this or similar devices in a given market, such as expedited review status, humanitarian use designation, premarket registration exempt, *de novo* candidate, FDA "Class IIb" potential, etc. If a product has more than one indication, provide the above information for each indication if the information differs by indication.

3.6 Design and Manufacturing

Where will the device be designed? Where will it be manufactured? Will design and manufacturing sites require registration and/or inspection prior to and/or following regulatory approval, and if so, by what countries? What is the plan for manufacturing the product? Are there any unique supply chain issues with regulatory consequence? Will the specifications differ by country? What are the key quality and GMP issues for the product?

3.7 Target Product Profile

What is the team's plan for developing the Product Profile or Design Dossier? Who will be responsible for these documents and what is the timeline for their development? What are the plans for lifecycle management for the product? What changes are anticipated in the short and long term timeframes?

3.8 Standards

Which voluntary or mandatory standards will the product be designed to meet (consider horizontal

standards such as IEC 60601-1 as well as product-specific standards)? How will conformance be demonstrated? What certifications will be required? What test labs will be utilized?

4 Regulatory Strategy

4.1 Regulatory Objectives

What are the overall regulatory objectives? What are the "must-haves" in terms of indications, claims, timing, specific country approvals or other key priorities for the company? What are the "nice-to-haves?" Are there foundational elements that must be obtained from a regulatory perspective, e.g., are there future generations, modifications, indications or claims that will be predicated on and build on prior, initial or subsequent approvals/clearances?

4.1.1 Short-Term Regulatory Objectives

Describe the initial regulatory deliverables and their timing (e.g., complete proof of concept study by Q3 2011, file IDE, 510(k), PMA, MDL, supplement, amendment, etc. in Q2 2012). Provide broad objectives for major target markets.

4.1.2. Long-Term Regulatory Objectives

Describe future regulatory objectives (e.g., file for 2nd generation with ergonomic improvements in Q4 2013, file for additional indication in Q1 2014). Provide broad long-term objectives for major target markets.

4.2 Agency Contacts

Identify the regulatory Agency, Division or Department(s) that will be responsible for leading and/or consulting on the product review. For devices, this may include the lead reviewing division/branch for that product area, as well as human factors, compliance/manufacturing, software, biocompatibility, and other specialists. For combination products, reviewers from other Agency components responsible for the drug or biological product will often be part of the review team. Where known, include the names of responsible government personnel who will be responsible for the review of the product. Where known, describe typical areas of focus or concern for the review staff and division that will be involved.

4.3 Summary of Regulatory Approach and Precedents

Describe how the device will be regulated. What agency guidance is available to facilitate the product's development and testing? Has the company committed to any special studies or other requirements in prior discussions with the agencies for this or similar products?

Identify the options that may be available for the regulatory strategy, along with the benefits/advantages and risks/disadvantages of the different approaches. Which approach makes most sense given the company's objectives? Is the fastest regulatory approach (e.g., 510(k)) best, or might positioning of the product as a PMA provide greater long-term gains in terms of market exclusivity, claims or reimbursement, despite the longer approval time? How can the company best gain a competitive advantage through its regulatory strategy in target markets? Is exclusivity an option?

If the device will be compared to another device as the basis of its regulatory clearance (e.g., US 510(k) process), provide a detailed comparison of the proposed and predicate devices with respect to all key device characteristics that are significant from a regulatory perspective (e.g., indications for use, target population, intended environment, sizes, features, performance specifications, etc). Tabular format is especially helpful for this analysis. Identify any differences that may be significant from a regulatory perspective and how these will be resolved/ addressed.

Describe any publicly available information that can help influence the regulatory strategy, such as the regulatory pathway, labeling/promotion, successes and/or pitfalls for predicate/competitive products.

4.4 Regulatory Agency Communication Plan/Strategy

Are pre-submission meetings necessary/desirable to gain regulator understanding and/or agreement with significant preclinical (bench, animal, biocompatibility) testing plans prior to commencing the studies? Are they necessary for clinical investigation plans? Identify plans for pre-submission meetings and other key discussions to secure regulator understanding and agreement with proposed regulatory strategy.

4.5 Marketing Application Approach

Describe the regulatory pathway or type of marketing authorization expected for the product. For example, could the device be eligible for humanitarian device status? If so, in which countries? Are there special review procedures that will be followed (e.g., expedited or priority review, modular submission approach)? What types of filings will be prepared? Provide this information as completely as is known for each country where the product will be marketed.

How will the applications be submitted to the regulatory authorities? Identify the opportunities for harmonizing the contents of the applications to reduce repetitive authoring and publishing. Will the STED format (GHTF) be used? Describe application formats (paper, electronic, electronic with paper).

Identify the country/region/GHTF guidances that will be followed in the development of the filings. Identify any areas where there may be overlap or conflict.

4.6 Submissions Timeline and Resources

What are the target dates for key regulatory milestones (requests for agency meetings, submissions of meeting packages, agency meetings, submission of applications, progress reports, etc.)? What internal and external resources are required to meet the timelines?

4.7 Anticipated Regulatory Issues

Identify anticipated points that it will be necessary to discuss with Agencies. Depending on the product's stage of development, include all issues pertinent to preclinical, clinical, and manufacturing aspects. What are the key risks or barriers to the product entering worldwide markets? What is the plan to manage those barriers? Describe any critical assumptions, issues or questions, particularly those that could influence regulatory strategy or warrant pre-submission discussions with regulators.

4.8 Preclinical Testing Considerations

Describe the bench, animal, biocompatibility, software, electromagnetic compatibility, or other studies that may be necessary to support the investigational and/or marketing applications for this device. What existing data can be leveraged, and where will new studies be needed? Does the unusual design or nature of the device warrant that new test methodologies be developed that must be factored into timelines?

4.9 Clinical Investigation Considerations

Provide clinical protocol names/numbers (if available), type and phases of investigation to be conducted, and countries in which clinical investigations are or will be conducted. Describe main study endpoints and duration of follow-up. Discuss any differences between the intended patient population and that being studied, and how the differences will be bridged. Provide an overview of the intended timeline for the clinical investigations.

Additional factors that should be considered, as applicable, include the following: What clinical data or evidence is required to support marketing approval and claims? Will the product represent a sea change in medical practice that may require special strategies for physician adoption? What submissions are required prior to

clinical study initiation? Could certain studies be deferred until after approval? What are the requirements for acceptance of foreign clinical data? Are there regulatory advantages associated with conducting clinical studies in specific geographies? What data and activities are necessary to obtain adequate reimbursement for the product? Will the agency likely require a post-approval study as a condition of approval?

4.10 Special Considerations

Does this device present any unique considerations that are new for the company (e.g., device tracking required by 21 CFR 821)? Will more postmarket/vigilance reporting (MDR/MPR) be necessary given the type of product compared to previous company products? Is this device more likely to result in product corrections or recalls than other company products? Is this the company's first sterile device, or is a novel sterilization method contemplated? Will a controversial material used, or does the device incorporate material from a tissue or other biologic source? Does the device involve nanotechnology? Will stability testing be necessary (e.g., device with drug component)? Does the device involve closed loop drug delivery? Is the device a US preamendments Class III device still reviewed under 510(k)? Is the device intended for use in a special patient population that may earn regulator attention? Might patient labeling be needed? Has the device or its indication been the subject of controversy in the medical community?

4.11 Additional Considerations for Combination Products

Describe the proposed strategy for determining the product jurisdiction assignment. Describe the jurisdiction of similar products, or precedents established through intercenter agreements or other agency jurisdictional determinations. What is the combination product's primary mode of action? If the jurisdiction for this type of product is unclear or in dispute, describe timing and strategy for submitting a Request for Designation in the US. For devices used with a drug or used to deliver a drug, describe any special regulatory considerations, e.g., whether regulatory approval may be needed for changes for the companion drug (cross labeling) and how your company will work with the partner company to obtain those changes. What changes to your company's GMPs and adverse event reporting procedures will be needed to comply with agency expectations for combination products?

4.12 Applicable Industry Conferences/Meetings

Identify any key, topical conferences or agency-sponsored meetings during which discussions/announcements impacting the regulatory strategy are expected. This may include FDA panel/advisory committee meetings for related products or conditions, medical society meetings where key results will be presented, etc.

4.13 Anticipated Changes

It is difficult to "see around corners," but what changes could be reasonably anticipated over the proposed development timeline? What changes might the company decide to make? How might the regulatory environment change? For example, how might your device be affected by anticipated 510(k) changes?

4.14 Key Reference Materials

Include citations for associated filings, publications, guidances, foreign studies, etc.

5 Regulatory Strategy Monitoring and Update Plan

New information that may influence the regulatory strategy includes internally driven changes (e.g., new/revised device indications or claims, device modifications, new target markets), or externally driven changes (e.g., new regulatory requirements/guidance, agency approvals/rejections of similar products, advisory committee discussions relevant to the type of product or disease).In this section, explain your plan to periodically review and update the strategy document with your team. What methods will you use to determine if updates are needed, and how often will you plan to review and update the strategy document as needed?