AdvaMed
Advanced Medical Technology Association

701 Pennsylvania Avenue, NW
Suite 800
Washington, D.C. 20004–2654
Tel: 202 783 8700
Fax: 202 783 8750
www.AdvaMed.org

January 8, 2019

Bureau of Policy, Science and International Programs
Therapeutic Products Directorate
Health Products and Food Branch
Health Canada
Holland Cross, Tower B
1600 Scott St.
Address Locator 3102C3
Ottawa, Ontario K1A 0K9

Re: Licensing Requirements for Implantable Medical Devices Manufactured by 3D Printing; Draft Guidance

Dear Sir or Madame:

The Advanced Medical Technology Association ("AdvaMed") appreciates the opportunity to provide comments on the Health Canada draft guidance, "Licensing Requirements for Implantable Medical Devices Manufactured by 3D Printing" ("3D Printing Draft Guidance").

AdvaMed is the world's largest association representing manufacturers of medical devices, diagnostic products, and medical technology. AdvaMed's member companies range from the largest to the smallest medical product innovators and manufacturers, with nearly 70 percent of our members generating less than $100 million in annual sales. AdvaMed's member companies produce innovations that transform health care through earlier disease detection, less invasive procedures, and more effective treatments, including the use of 3D printing.

AdvaMed appreciates Health Canada's efforts to outline premarket expectations for implantable Class III and IV medical devices manufactured using 3D-printing technologies. We strongly believe that the use of this technology in medical devices has already rapidly advanced and will continue to increase in the future. Given the ever-growing prevalence of 3D techniques in global manufacturing of medical devices, we appreciate Health Canada's work on this issue both inside and outside of Canada. We note that Health Canada is a member of the IMDRF Personalized Devices Working Group ("WG"). We hope that our comments can help inform Health Canada's current thinking, both as it relates to its own regulatory regime, and as it participates in the harmonization effort with its fellow regulators at IMDRF.

We offer general comments on the draft guidance below, followed by comments related to specific parts of the draft guidance.

General Comments

Health Canada should revise the 3D Printing Draft Guidance to better align with "Guidance on Supporting Evidence to be provided for New and Amended License Applications for Class III and Class IV Medical Devices."

While the introduction to this document is clear that the 3D Printing Guidance should be read in conjunction with the "Guidance on Supporting Evidence to be provided for New and Amended License Applications for Class III and Class IV Medical Devices" ("License Applications Guidance"), the structure (order) and content of the 3D Printing Guidance does not always align with the referenced guidance. For example, the Preclinical Studies section of the 3D Printing Draft Guidance does not align with the License Applications Guidance and asks for information requested in the manufacturing section of the License Applications Guidance. The device description section of the 3D Printing Draft Guidance may be confusing as it only addresses materials and manufacturing processes and is silent on the description of the finished device itself.

Revising the 3D Printing Draft Guidance to better align with the License Applications Guidance could bring clarity to differences in expectations for Class III and Class IV devices. Specifically, the License Applications Guidance asks for significantly less information on manufacturing and quality controls for Class III devices. It is unclear in the 3D Printing Guidance if this expectation carries through to 3D-printed devices, or if there are higher expectations for Class III 3D-printed devices. In this vein, it would be helpful if Health Canada would clarify in the 3D Printing Draft Guidance what it would expect in an application versus what is more applicable for review during a quality management systems audit.

Understanding that Health Canada may not wish to duplicate all the information from the License Applications Guidance in the 3D Printing Draft Guidance, it would be helpful if throughout the text, the 3D Printing Draft Guidance included statements to clarify that information is in addition to the License Applications Guidance or is intended to clarify the specific expectations for 3D-printed devices.

In addition, we would recommend that Health Canada restructure the document to better reflect the manufacturing process flow. 3D Printing is a manufacturing process (additive manufacturing) and manufacturers will follow Design Control and Product Realization processes (Design Inputs, Design Outputs, Design Verification, Design Validation, Installation Qualification, Operational Qualification, Process Qualification and Production Validation). The structure and flow of the guidance does not always follow this process and we believe it would be helpful to restructure the document accordingly.

Health Canada should include guidance or definitions regarding point-of-care manufacturing of 3D-printed devices.

We recommend that Health Canada include guidance or definitions regarding point-of-care manufacturing of 3D-printed devices. Other global regulators such as Australia's Therapeutic Goods Administration ("TGA") have observed and are working to address the public health concerns related to rapid increase of 3D Printer installation and manufacture of medical devices in hospital facilities, with little or no oversight. We are concerned that this activity is not covered either by the licensing of Class III and IV medical devices or the Special Access Program and could become exploited as an unregulated path to medical device manufacturing in a manner that compromises patient safety and public health.

Health Canada should clarify use of term "validation" throughout the document.

The term "validation" is used frequently throughout the 3D Printing Draft Guidance for testing that is typically conducted as characterization or verification. We believe revision is needed to provide clarity on the intent to validate versus verify individual process steps.

Health Canada should replace "patient specific" with "patient matched" throughout the document to be consistent with the International Medical Device Regulators Forum ("IMDRF") "Definitions for Personalized Medical Devices."

We appreciate that in the 3D Printing Draft Guidance, Health Canada adopts the definitions developed by the IMDRF in the recently issued final document "Definitions for Personalized Medical Devices." We believe that harmonized definitions represent a helpful step towards the goal of a harmonized regulatory pathway for devices manufactured using 3D printing. IMDRF recently released the final version of that document.

The working group chair explained that in the final version, the WG "removed the term 'patient-specific' from the document in favor of 'patient-matched' as 'patient-specific' could be misconstrued as 'custom-made,' whereas 'patient-matched' is more descriptive of the devices in this category."[1] We recommend correspondingly updating this document to replace "patient specific" with "patient matched" to reflect the changes made to the IMDRF document.

* * *

AdvaMed thanks Health Canada for its consideration of these general comments and the specific comments that follow. Please do not hesitate to contact me at 202-434-7230 or jwolszon@advamed.org if you have any questions.

Respectfully Submitted,

/s/

Jamie Wolszon
Associate Vice President
Technology & Regulatory Affairs

Attachment

[1] http://www.imdrf.org/docs/imdrf/final/meetings/imdrf-meet-180321-china-beijing-presentation-working-group-update-pmd.pdf (last accessed December 17, 2018).

ADVAMED COMMENTS

LICENSING REQUIREMENTS FOR IMPLANTABLE MEDICAL DEVICES MANUFACTURED BY 3D PRINTING HEALTH CANADA DRAFT GUIDANCE

Additions indicated with an underline.
Deletions indicated with strikethrough.

Line(s) No.	Change	Reason
84-89	Please refer to Section 4.3.1 of the "Guidance on Supporting Evidence to be provided for New and Amended License Applications for Class III and Class IV Medical Devices" for the description of the finished device. This section supplements that discussion with additional information regarding the expected level of detail (e.g., summary information or detailed specifications) for the material properties.	As written, the device description section is unclear as it omits any discussion of a description of the finished device and focuses entirely on the starting material. We assume the intent of this section of the 3D Printing Draft Guidance is to augment the final paragraph in Section 4.3.1 of the License Applications Guidance with information specific and relevant to 3D-printing materials and processes. For purposes of clarity, we would recommend adding an instructional statement in this draft guidance to specifically refer to the License Applications Guidance for the description of the finished device, and the information in the 3D Printing Draft Guidance provides additional information regarding the expected level of detail (e.g., summary information or detailed specifications) for the material properties.
123-124	An amendment application may also be required if potential effects on safety and effectiveness of the finished device are identified. A manufacturer may document internally in their change management system why such changes do not require an amendment. Changes that trigger an amendment ~~These~~ may include:	Few of the implant devices subject to the 3D Printing Draft Guidance are likely to contain software. We propose revisions to the 3D Printing Draft Guidance to reflect what we believe to be the intent of this section, i.e., manufacturing changes that would have a significant impact on the finished device. If supplier changes do not impact the material, we believe that supplier change should be part of the quality management system and this information does not need to be included in the regulatory license application or require a change submission.

ADVAMED COMMENTS

LICENSING REQUIREMENTS FOR IMPLANTABLE
MEDICAL DEVICES MANUFACTURED BY 3D PRINTING
HEALTH CANADA DRAFT GUIDANCE

Line(s) No.	Change	Reason
	changes in material (i.e., ~~supplier,~~ incoming material specification, ratio of recycled powder) ~~software changes (i.e., change or update of build preparation software)~~ ~~Changes to the printer or printing process which may effect the finished device~~ and other manufacturing changes that would significantly affect the finished devices, including significant changes to the build preparation software or printing process, beyond the validated range.	In addition, we believe it would be helpful to clarify that the manufacturer may document internally in their change management system why such changes do not impact safety or efficacy, and thus not require an amendment.
126	~~The design philosophy should describe the advantages of using 3D printing as a manufacturing process (i.e., patient-matched devices, devices with complex geometry and/or non-standard sizing) compared to conventional manufacturing methods.~~ The features that enable the device to be used for the medical conditions and purposes for which it is manufactured, sold or represented by the manufacturer should be described. A brief description of the underlying science/technology, design concepts and/or theoretical principles supporting the device's function should be provided, linking them to the claimed indications or use. For 3D-printed devices this could include patient-matched device aspects, devices with complex geometry and/or non-standard sizing.	We propose this revision to promote alignment with the License Applications Guidance.

ADVAMED COMMENTS

LICENSING REQUIREMENTS FOR IMPLANTABLE
MEDICAL DEVICES MANUFACTURED BY 3D PRINTING
HEALTH CANADA DRAFT GUIDANCE

Line(s) No.	Change	Reason
134	2.2 Safety and Effectiveness ~~Requirements~~	We propose this revision to promote alignment with the License Applications Guidance.
139-146	We believe references to process validation should be removed from this section and discussed in the manufacturing and quality controls section of the document as preclinical studies are conducted on finished devices as verification activities, not manufacturing processes.	We propose this revision to promote alignment with the License Applications Guidance.
149	With respect to the printer, the following evidence should be provided: ~~A summary of the cleaning and maintenance processes for the printer.~~	We believe that printer cleaning and maintenance should be part of the quality management system and this information does not need to be included in the regulatory license application.
157	~~If multiple build paths are used, each build path should be documented and validated.~~	Each build path for patient-matched products by definition will be different as the build path will be unique to each patient. As written, the language in the 3D Printing Draft Guidance would result in a new submission for each patient-matched device. Lines 153-156 provide the appropriate considerations for validation of the print bed space and no additional text is needed.

ADVAMED COMMENTS

LICENSING REQUIREMENTS FOR IMPLANTABLE MEDICAL DEVICES MANUFACTURED BY 3D PRINTING HEALTH CANADA DRAFT GUIDANCE

Line(s) No.	Change	Reason
163-173	Consider adding examples tailored to technologies other than powder bed fusion-based technologies.	This section appears written from the perspective of powder bed fusion-based technologies and does not address other current liquid-based technologies (stereolithography, ink jetting) or emerging technologies (2 photon, direct energy deposition).
211	Clarify if the shelf life of recycled powder is specific to polymers.	We believe this information would provide helpful clarity.
223	~~maintenance of final device files and printer logs for later retrieval~~	We believe that maintenance of final device files and printer logs should be part of the quality management system and this information does not need to be included in the regulatory license application.
225-28	Evidence of biocompatibility from non 3D-printed previously licensed devices or materials is not generally considered sufficient to support biocompatibility of 3D-printed devices due to differences in the manufacturing process (even with adherence to recognized material standards specific to 3D printing). Subsequent to that first testing, a company would evaluate the change, e.g., materials, manufacturing or process change, and consider whether retesting is needed.	While the referenced statement discusses new 3D-printed devices with differences in manufacturing from non 3D-printed licensed devices, it does not discuss the situation in which a new 3D-printed device leverages currently licensed 3D-printed devices. We would propose adding language indicating that biocompatibility test information from a previously licensed 3D-printed device can be leveraged without retesting in a new application in certain circumstances. Clarity regarding expectations for devices that use a 3D-printed version as a predicate would be helpful, specifically instances where retesting is not necessary and justification for omission of retesting can be provided.

ADVAMED COMMENTS

LICENSING REQUIREMENTS FOR IMPLANTABLE MEDICAL DEVICES MANUFACTURED BY 3D PRINTING HEALTH CANADA DRAFT GUIDANCE

Line(s) No.	Change	Reason
239	Provide examples of device types that typically warrant clinical studies.	Expectations for when clinical studies will be required are vague. Discussion on how manufacturers can approach this, or examples of device types that would typically warrant clinical studies, would be helpful.
280-282	For 3D-printed devices that are patient-matched, Health Canada recommends additional labelling information since ~~clinical staff, device manufacturers, or a designated third party might modify the design of a patient-specific device.~~ these devices are matched to an individual patient's anatomy.	Clarifying edit.
312	Patient-matched medical device ~~(or Patient-specific medical device)~~	Revised for consistency with final version of IMDRF definitions document.
391	IMDRF ~~Proposed~~ Document International Medical Device Regulators Forum, Definitions for Personalized Medical Devices (October 18, 2018)	Revised to reflect issuance of final version of IMDRF definitions document.
Endnote 1	~~Throughout this guidance document the terms patient-specific devices and patient-matched devices are used interchangeably.~~	Revised to reflect final version of IMDRF definitions document.

ADVAMED COMMENTS

LICENSING REQUIREMENTS FOR IMPLANTABLE
MEDICAL DEVICES MANUFACTURED BY 3D PRINTING
HEALTH CANADA DRAFT GUIDANCE

Line(s) No.	Change	Reason
Endnote 4	IMDRF ~~Proposed~~ Document International Medical Device Regulators Forum, Definitions for Personalized Medical Devices (October 18, 2018)	Revised to reflect issuance of final version of IMDRF definitions document.