General Comments

1. Generally, the requirement that all medical devices, other than custom-made medical devices, be listed on the ARTG makes sense.
2. A number of existing manufacturers of custom-made [and patient-specific] devices already satisfy TGA medical device regulations. It is important that any new regulations do not increase their costs, delay them or increase their business risk, as this would not be beneficial to patients. New regulations should be aimed at increasing the capability of non-conforming manufacturers.
3. Greater alignment should be provided between the proposed rules and rules/guidance adopted in territories where equipment is manufactured and where medical device manufacturers serving the Australian market are located, with the objective of ensuring that cost and time burdens due to differing regulatory requirements are minimised and supply, into the Australian market, of equipment and medical devices from offshore suppliers is not affected.
4. What implementation timeline and transition plan is the TGA proposing?
5. Will the TGA allow manufacturers to supply custom [and patient-specific] devices into the market that don't comply with all essential principles?

Proposal 1: New definitions for personalised devices

6. **The definition of *"patient-specific medical device"* is not required.**
    a. If a medical device is not a custom-made medical device then it is simply a commercially available medical device and should be subject to ordinary conformity assessment procedures, in accordance with its risk classification. This approach is consistent with that of the FDA and EU approaches.
7. **The *"commercially available medical device"* test in relation to custom-made medical devices requires greater clarity.**
    a. The requirement for there not to be a *"commercially available alternative medical device"*; (i) ignores the possibility that the prescribing practitioner may reasonably consider that custom-made a medical device will provide a superior clinical outcome to the commercially available alternative medical device; (ii) that the commercially available alternative medical device may be of a very old design, which has not been updated or improved on by manufacturers due to their "orphan" status; and (iii) lacks clarity in the instance where a manufacturer is already providing a custom-made medical device for that pathology (is it intended that if there is already a supplier of a custom-made medical device for a specific indication that no other suppliers will be allowed in the market?). Without a clear definition of the term *"commercially available alternative medical device"* it may be simpler and provide greater clarity if the term is deleted.
    b. There is no indication as to how *"rare patient conditions"* are practically defined or how the concept fits into the TGA's definition. Should the term become an explicit part of the definition? If so, should it be explicitly defined by the TGA or left to industry to make an informed judgement call? For example, the term could be; (i) aligned with Table 2 of the Orphan Drugs Programme discussion paper (May 2015) which is <0.88 per 10,000 population per year; or (ii) could be aligned with the FDA's definition of a *"sufficiently rare patient condition"* and leave it to industry to reasonably interpret this?
    c. Alternatively, the EU concept of *"industrial scale"* production and *"mass production"* could be applied to determine what is and what isn't a custom-made medical device, rather than

differentiating based on the design process (scaling templates based on anatomical references) which is currently common across all types of custom-made [and patient-specific] medical devices.

8. **A flow chart relating to the decision whether or not a device is a custom-made medical device would provide greater consistency and accuracy in decision making.**

   The flow chart could be similar to that provided by the FDA as Appendix III of Custom Device Exemption: Guidance for Industry and Food and Drug Administration Staff (issued 24 September 2014), with the question regarding the number of devices being deleted (refer item 10 below).

   Examples of what are and aren't custom-made medical devices may provide additional clarity.

9. **There should be no limit on the number of custom-made devices that a manufacturer can supply annually.**

   The supply side of the United States medical devices market is significantly greater than the population ratio and is capable of meeting United States market demand on the 5-unit maximum basis.

   There are very few custom-made medical device manufacturers servicing the Australian market. Therefore limiting the number of custom-made medical devices a manufacturer may have the effect of limiting the overall number of custom-made medical devices into the Australian market. Potentially to a level where demand is greater than supply. This may have the effect of delaying patient treatment and increasing implant prices. This may be compounded by off-shore manufacturers ceasing to supply the Australian market if the time and cost burden of the proposed rules makes the Australian market unattractive to off-shore manufacturers.

   It should be noted that the FDA limits the number of custom devices to 5 per year of a particular device type, not 5 per year in total[1].

10. **The TGA should not implement an application and approval process for the use of custom-made medical devices.**

    A compelling rationale as to how such a process would add value has not been presented in the consultation paper.

    The TGA may not possess the design and clinical skills and experience to process such applications on a timely basis and such a process would be at odds with the practitioner's responsibilities (including specific design characteristics) as set out in the definition for a custom-made medical device defined on page 9 of the TGA consultation paper. If the TGA were to disagree with the practitioner's prescription then what happens?

    At a practical level, practitioners routinely require a delivery time-frame for custom-made medical devices of 2 – 4 weeks. The TGA would need to be confident that it has sufficient experienced resource (for example that understood pathologies, design options, surgical approaches, et. al.) to assess and approve applications without impacting delivery timeframes. In the case of an oncology patient for example, delaying delivery of the implant could have serious implications on the patient's health outcome.

[1] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM415799.pdf

Proposal 2: Changes to the custom-made conformity assessment procedure

11. **There should be no requirement to obtain patient informed consent for custom-made medical devices [or patient-specific devices] or requirement to provide the patient with a copy of the manufacturer's statement for such devices.**

    The discussion paper mentions that informed consent is a current requirement in Europe. EU regulation 2017/745 only covers the requirement for informed consent in the context of clinical investigations, without reference to custom-made [or patient-specific] medical devices.

    No rationale has been provided in the consultation paper that identifies the benefits of obtaining informed consent or providing the manufacturer's statement in relation to custom-made medical devices [or patient-specific medical devices].

    Such a requirement would create a range of risks for the patient, practitioner and manufacturer, for example:

    a. the patient may for whatever reason decline to provide informed consent immediately prior to the surgery reducing available treatment options, negatively impacting health outcomes and leaving the manufacturer with a very costly implant it cannot recover the cost of; and

    b. the patient, as a lay person, may simply not understand or like the wording of the manufacturer's statement, even if that wording complies with the regulations. Reasons for this could include concerns around select non-compliance with the essential principles, which from a regulatory perspective are allowed for custom-made medical devices, but may not be understood by a lay person. Again, this could reduce available treatment options, negatively impact health outcomes and leave the manufacturer with a very costly implant it cannot recover the cost of.

12. **Annual reporting is sensible when case-by-case reporting is discontinued.**

    Electronic, internet based annual reporting (with a draft/save function), should be implemented generally in a form similar specified by the FDA in section VI of Custom Device Exemption: Guidance for Industry and Food and Drug Administration Staff (issued 24 September 2014).

Proposal 3: Changes to the definition of manufacturer

13. **An exemption should be provided for manufacturers not to be deemed to be the manufacturer of third-party devices where such are used in conjunction with custom-made [or patient-specific] devices.**

    Custom-made medical devices [and patient-specific medical devices] are often designed to be implanted in conjunction with third-party medical devices.

    This is especially relevant in revision surgeries where existing devices may be retained if they are well secured or in instances where the practitioner specifies their preference of ancillary components (for example a femoral head, liner and cup as part of a custom-made total hip joint).

    With reference to clause 3(c) on page 12 of the consultation paper, an exemption should be provided where manufacturers incorporate commercially available third-party medical devices (*"ancillary components"*) into larger custom-made implant systems.

    For example, the exemption could read:

    > *"Where a manufacturer incorporates an ancillary component or components into a custom-made medical device or system or designs a custom-made device or system to work in conjunction with such ancillary component and the manufacturer reasonably believes (where such belief may reasonably be formed through the experience of the manufacturer and/or the prescribing*

practitioner and without the benefit of information from the third-party manufacturer on the ancillary component or testing of the component, device or system) that incorporating such ancillary component or components into a custom-made device (system) will not change or negatively affect the function of either ancillary devices or the custom-made medical device (system), then the manufacturer shall not be deemed to be the manufacturer of the ancillary device."

Without this exemption manufacturers may not be prepared to provide custom-made medical devices in instances where existing medical devices are retained or where practitioners wish to use preferred components sourced from third-parties. This would limit practitioner choice, impact treatment pathways and increase costs.

14. **Healthcare facilities and practitioners should be encouraged to use 3D printed class 1 (excluding measuring, invasive and the like) medical devices, but they should be required to satisfy normal pre-market conformity assessment requirements for class 2a devices.**

    No rationale has been provided in the consultation paper for providing healthcare facilities and practitioners with such an exemption.

    The risks to patients are the same irrespective of whether it's a practitioner or commercial entity providing the devices, therefore the requirements on the provider should be the same. The argument that historically manufacturers have taken advantage of the custom-made medical device exemption applies equally and to the same degree to both commercial and non-commercial providers.

    Arguably the risks to patients from such devices are higher as non-commercial operators may not have the systems, training and experience to complete this work correctly. For example, they may not be properly trained in the regulations, segmentation, supporting the devices during build, materials, biocompatibility and the like.

    Other questions include:

    a. If the healthcare facility or practitioner requires the medical device to be worked on by a third-party (for example for it to be machined, cleaned or sterilised) then is the device still exempted?

    b. If a healthcare facility or practitioner is part of a research collective (for example an association between a healthcare facility and an academic institution or research organisation), then can that collective design and manufacturer exempt devices on behalf of the practitioner?

15. **The term *"medical device production system"* should be deleted as such a (inferred) system is not commercially available.**

    The TGA should provide a definitive list of devices that can be manufactured by healthcare facilities and practitioners as many of these groups do not have the training and experience to determine whether their product is class 2a or lower. Healthcare facilities and practitioners should be able to apply to the TGA to have the type of product they are seeking to manufacture added to this list over time.

    The issue considered in item 14 above is further complicated by the context of the use of the term *"medical device production system"*. The assertion is that there is a single manufacturer for the system and that such systems are or will be listed on the ARTG, by that manufacturer. In reality, any production system is likely to be comprised of a series of individual hardware and software components produced by unrelated manufacturers and without the overall system being validated by any single manufacturer.

    For example, the system could be comprised of:

    a. An imaging system for capturing data (possibly supplied by GE or Siemens);

b. A file transfer system for transferring big data sets to the engineer (possibly provided by a third-party service such as Hightail);

c. Segmentation software to convert the 2d data into a 3d model (possibly provided by Materialise);

d. Software for manipulating the model and designing the device (possibly Solidworks); and

e. A 3d printer for building the device (possibly provided by Stratasys or 3D Systems).

Therefore, the definition of a medical device production system should be expanded to include the various hardware components, as well as the software that both operates and links the hardware.

The supplier of the 3d printer should be required to validate the entire production system (including the specific build materials which in themselves should be suitable for the class and type of device being manufactured), in the same manner as a commercial operator is required to. The healthcare facility or practitioner should be required to:

f. keep records including the materials used, operating training on all equipment and software used in the production process); and

g. ensure that where the system is not validated by the supplier that it is validated annually by a suitably trained and experienced third-party.

It is possible that many of these components are not even listed on the ARTG. The TGA should undertake further analysis of this issue and in particular determine whether the manufacturers of such production components are willing to be classified as the manufacturer of a *"medical device production system"* as it is described in the discussion document.

Finally, in the circumstance where the healthcare facility or practitioner is part of a formal or informal group that operates such a system and where the facility or practitioner does not have substantial control over that group and its operations then the proposed exemption should not apply and the production facility should be treated as a commercial manufacturer, with the requirement to undergo conformity assessment.

Proposal 4: New classification for anatomical models and digital 3D print files

16. **Anatomical models should be classified in accordance with their intended use and the classification rules and not automatically be deemed to be class 2a.**

The comparison to x-ray film may be inappropriate. The rationale for x-ray film having a class 2 classification is not articulated and may simply be the legacy of an unrelated issue. In the United States x-ray film has a class 1 classification (refer 21CFR892.1840(i)(H)(B)(a)).

a. If the system on which the model is designed and manufactured is in itself validated to produce accurate and repeatable outcomes (models) then the models themselves are low risk (class 1). If the models are not accurate then it is either an equipment, operator or segmentation issue.

b. In reality, the degree of accuracy required in models varies significantly depending on the use of the individual models. Most models are representative only, where relatively low resolution and accuracy is perfectly acceptable for their intended use and the risks are low. Some diagnostic models, particularly cardiovascular models, require high degrees of resolution and accuracy and hence have higher risk. Models that may be used invasively such as cutting guides and the like should have a higher risk classification.

c. Operator training is a key driver of accuracy. Training in segmentation, build orientation and supports is important for higher risk models, but not as important for lower risk models.

d. Most models are relatively low cost (< A$1,000). Classifying them as class 2a may add significant cost to these models, which could impact their availability in the clinical setting.

Should industry be left to determine classifications, levels of resolution/accuracy and the like, as part of its conformity assessment obligations or should the TGA regulate these?