Response to *Proposed regulatory changes related to personalised and 3D printed medical devices*

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Prepared by the Centre for Implant Technology & Analysis (CITRA)

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Background

Royal Perth Hospital (RPH) is one of Australia's largest (450 beds) and busiest hospitals, providing a broad range of tertiary-level services for adults. The hospital is Western Australia's oldest and has a long history of innovation and excellence in medical research and patient care. RPH has one of the busiest Emergency Departments in Australia and the second biggest trauma workload in the country. RPH is part of the East Metropolitan Health Service.

The Department of Medical Engineering & Physics at RPH has Australia's oldest Biomedical Engineering service, established in 1969. The department was formally recognised as a State-wide service and renamed the Centre for Implant Technology & Analysis (CITRA) in 2013. It provides a service to all patients in Western Australia, supplying custom made medical devices (including surgical planning models) across a wide range of specialities for adult and paediatric patients of all of the major hospitals in Western Australia, public and private.

While we use 3D printing as a large part of our current service, we have been producing custom medical devices for more than 40 years; well before the invention of 3D printing. We designed and manufactured the world's first custom medical implant designed from CT data, a Class III shoulder arthrodesis plate[1] that remains *in situ* after more than 30 years. In 2006 we designed and supplied the world's first 3D printed custom acetabular implant, the example device discussed in the TGA proposal paper. Over our 40+ year history we have provided more than 1000 custom medical devices to Western Australian patients, including scores of Class III custom implants and hundreds of 3D printed surgical planning models. Some examples of World or Australia first devices are given in Appendix 1: RPH Bioengineering History.

Given this history it is both surprising and disappointing that we were not invited to participate in the TGA-hosted workshop on 10 August 2017, or even made aware that it was occurring. It is our firm belief that no hospital in Australia (and few in the world) has a comparable history or breadth of bioengineering experience across a wide range of custom made medical devices.

[1] J Bone Joint Surg Br. 1986 Mar;68(2):208-12

Executive Summary

Recommendations

Change the title to better indicate the breadth of the proposal, perhaps “Proposed regulatory changes related to custom and personalised medical devices”.

Clarify the definition of ***patient-specific medical device***, in particular what makes them different to a custom medical device.

Clarify how a process to produce a ***patient-specific medical device*** could be validated.

Clarify how a ***medical device production system*** could be validated, with particular attention to the role of the skilled operator in such a system.

Also change the wording in the definition from “no commercially available alternative” to “no mass-produced alternative”.

NER Registered Biomedical Engineers working with clinicians in tertiary hospitals should be exempt from the responsibilities of a Medical Device Manufacturer for both patient-specific and custom devices.

Not-for-profit manufacturers should be given either an exemption from any fees or substantially reduced fees to reflect the difficulty in funding added compliance costs. Failure to do this will likely stifle innovation in the medical device design and manufacture and result in poorer patient outcomes.

No limit on the number of custom made devices that a manufacturer can supply in one year.

No application and approval process for custom made devices. If such a process is implemented, it should contain provisions to allow rapid response to the need of trauma patients (e.g. like the existing Authorised prescriber scheme or Special Access Scheme notification pathways)

There should be a transition period of at least five years for any substantial changes to the current regulations.

A copy of the manufacturer’s statement should also be provided to the medical practitioner requesting the custom device.

All patients referred to a hospital for an Class IIa or lower device produces with a ***medical device production system*** should be considered their patients, regardless of the source of the referral and so exempt from the responsibilities of a Medical Device Manufacturer.

Anatomical models, both non-physical digital models and physical models, should be covered by a separate clause and not lumped in with image recording devices.

Tissue engineered devices or devices incorporating biologicals produced as part of registered Clinical Trials should be exempt from these changes, to allow non-manufacturers to undertake research and development in this area.

Currently running Clinical Trials should remain exempt from the proposed changes (grandfathered).

General comments

Scope

The proposed regulatory changes are significant and far more wide ranging than only for devices manufactured using 3D printing.

The emphasis on 3D printing technologies, in the title and throughout the text, obscures the scope of the proposed changes and could mislead people who do not read the whole document closely.

We suggest changing to better indicate the breadth of the proposal, perhaps "Proposed regulatory changes related to custom and personalised medical devices".

Costs

These proposed changes will have a substantial effect on our operation, as we produce many custom medical devices under the current regulatory framework. Many will now no longer be considered custom devices, if this proposal is adopted.

Achieving compliance with the proposed regulations (.i.e. becoming an official medical device manufacturer and being listed in the ARTG for the vast range of devices we supply) would impose a significant cost impost onto our service. As a public hospital, we supply our devices at no cost to the patient. We do not have the resources to achieve greater regulatory compliance nor do we have either a budget or an income stream to pay for compliance costs, unlike for-profit medical device manufacturers.

For many years, for-profit manufacturers have been generally uninterested in developing solutions for "one-off" cases. In contrast, it is our mandate to treat all patients referred to our service to the best of our ability, which has enabled patients to be successfully treated who would otherwise have poor outcomes. For example, the patient who received the world's first custom-made device designed from CT data would have had his arm amputated without this device. Instead, he has enjoyed 30+ years of functional use of his arm.

The solutions first developed in our department within the public hospital system have often pioneered the way for substantially similar offerings from commercial medical device manufacturers, greatly benefitting countless patients Australia-wide. It is questionable whether such devices would have been brought to market if they were not first attempted by hospital departments such as ours, willing to take on difficult and unprofitable cases. Certainly, the lead-time to market for such devices would be greatly extended if services such as ours did not exist.

History of single use device regulations

The impact of this proposed change is analogous to another regulatory change imposed by the TGA relating to the re-use of Single Use medical Devices (SUDs). High cost SUDs were routinely re-processed for re-use in hospitals throughout Australia over a period of decades with no reported adverse events. This enabled significant cost savings to the health system with no impact on clinical care or patient safety. The TGA mandated that from 1 July 2007, SUDs could no longer be re-used unless they were "re-processed" by a medical device manufacturer. The TGA envisioned that hospitals would become licenced medical device manufacturers to continue re-processing SUDs. The reality is that more than 10 years after coming into effect, no

hospital in Australia is accredited to re-process SUDs. This single regulatory change resulted in additional costs in the order of millions dollars [2](and counting) to the various health systems throughout Australia with no demonstrated improvement to patient care or safety.

Similarly, with the current proposal the TGA is suggesting that hospitals that provide custom made devices will become licenced medical device manufacturers. The experience with SUDs suggests that no hospital will become a manufacturer and this activity will cease entirely in Australia.

This would result in significant cost increases as equivalent services are sourced from for-profit companies and/or imported into Australia. Unlike the changes to SUD regulations, however, this will have a detrimental impact on patient care. Patients within our catchment receive same-day or next-day devices or models in response to emergency referrals, such as trauma cases. This is only possible by having the service located within a hospital with the referring clinician on-hand to provide guidance; operating on a cost-recovery-only basis; and having decades of experience providing such a service.

It is easy to foresee that the removal of this service due to increased regulation will result in an inferior standard-of-care being provided to patients.

Likely impact

The history of SUD remanufacturing has shown that public hospitals have no will to become medical device manufacturers. It is not the core business of a hospital to be a medical device manufacturer and seeking a budget allocation from scarce funding to become one is unlikely to be fruitful.

If these proposals are adopted it is highly likely that services such as ours will simply cease to exist. This will result in significant and ongoing increased costs to the public health system, the loss of knowledge and skills in medical device design and manufacture (reducing Australian competitiveness in a field in which we are currently World-leaders), and inferior outcomes for patients who have come to expect a high level of care.

The TGA should also understand and appreciate the impacts that these proposed regulatory changes will have to other hospital services who currently supply custom made medical devices. These potentially include maxillofacial prosthetics, orthotics and prosthetics, providers of mobility aids and custom wheelchairs, radiology and surgeons who make “on table” medical devices.

Alternative or additional strategies

Give consideration to:

> An exemption from becoming a medical device manufacturer to all tertiary hospital departments who employ suitably qualified bioengineers designing and manufacturing devices in conjunction with clinicians in a hospital environment to treat patients. (“suitably qualified bioengineers” could be assessed as NER registered Biomedical Engineers (or equivalent)).

[2] Based on WA Health cost analysis of the failed SUD remanufacturing project

Or if an exemption from regulation is considered undesirable, to:

> Exempt non-profit and charitable institutions (including all public hospitals) from any and all fees payable to achieve and maintain regulatory clearance as a medical device manufacturer.

Responses to proposals

Direct quotes from *Consultation paper: Proposed regulatory changes related to personalised and 3D printed medical devices* are shown as:

> Text from TGA proposal, highlighted as required, followed by page number in proposal
> **(page n)**

Our responses are grouped by section as in proposal.

Introduction

> It is important to note that, like conventionally manufactured mass produced medical devices, 3D printed mass produced medical devices are not custom-made and are regulated under the existing risk based framework.
> **(page 6)**

This point needs more emphasis throughout the text. 3D printing is just another manufacturing technology like CNC machining or investment casting.

The repeated emphasis on 3D printing in this proposal distracts from the main thrust, which is – substantially changing the definition and regulation of formerly custom devices and introducing a new but currently poorly defined grouping of "personalised medical device".

> However, strict regulatory oversight is not the case with the majority of similarly high risk 3D printed implants in Australia, which are currently captured under exemptions for custom-made medical devices.
> **(page 6)**

What evidence is there that this is occurring, and what figures does the TGA have regarding the number of such devices? Is this different to devices made by CNC machining?

Proposal 1: New definitions for personalised devices

There are a number of passages in this proposal that are unclear.

> …custom made medical device - means any device …
>
> for which there is no commercially available alternative medical device.
> **(page 9)**

Why is "no commercially available alternative" the test for a custom device?

A custom device could be made for any reason; it would still be custom if it fulfils the other criteria, regardless of the availability of a commercially available alternative. Further confusing the issue there are commercial suppliers of custom made medical devices.

If the intent was "for which there is no mass produced alternative", then perhaps adopt this wording.

How would a device be deemed to be an alternative? Clearly there could always be an alternative device, if the quality of the result is ignored. If the suitability of alternative devices is considered, then who makes the determination and on what basis?

Mass produced devices which need to be adapted to meet the specific requirements of any professional user and ***patient specific devices*** shall not be considered to be custom-made devices.
(page 9)

It should be made clearer that this only covers devices that are intended by the original design to be adapted to the individual.

It is common in our practise to develop a custom device by modifying a mass produced device in some way beyond the original intention of the manufacturer.

Perhaps change to "***Mass produced devices*** which are intended to be adapted to meet …"

patient-specific medical device – a medical device based on a standard device template model that is matched to a patient's anatomy using techniques such as scaling of the device based on anatomic references, or by using the full anatomic features from patient imaging, and which is produced through a process that is capable of being validated.
(page 9)

The definition of ***patient-specific medical device*** needs considerable clarification.

What does "a standard device template model that is matched to a patient's anatomy" mean? For example, all acetabular reconstruction cages could be considered variations on a standard device template, as they will all share similar characteristic components, functions and design constraints. The process is however much more than just taking an existing design, scaling to suit and subtracting the patient bone. Is this term intended to refer just to the latter process? Even then, it is uncertain what would become patient-specific and what will remain custom.

The phrase "a process that is capable of being validated" is also vague. Any custom device under the current regulations should be produced through a process that can be validated. The process should be part of a Quality System and the resultant the device must satisfy the Essential Principles, Risk Analysis and requested functions. Checking that it does satisfy all these would be validating the process. Does the TGA propose a method to validate processes, or will there be guidelines specifying what "a process that is capable of being validated" should be?

mass produced medical devices – medical devices that are produced in production runs or batches of the same product.
(page 9)

How is "mass produced" defined? If by number of devices, how will the limit be determined?

Would this definition include manufacture of blanks or partially completed devices that then have further manufacturing operations to produce the final (possibly custom) device? An example would be our scapular fusion plate, where a standard blank is made in bulk that then has to be extensively customised (bent, twisted and shaped) to suit the patient's anatomy and the requirements of the fusion.

medical device production system – a collection of products, including specified raw materials, that is intended to be used by a health care practitioner to produce a finished medical device and that may include the input of a digital patient image file.

The system output must be validated with the specified components. The classification of the system is determined by the classification of the finished device.
(page 9-10)

This should be determined by the highest classification of the devices it is intended to produce.

Excluding 3D printed patient specific medical devices from the custom-made definition would result in these devices being regulated under the existing framework for medical devices. This is based on the risk classification level of the device and is designed to have increasing oversight as the risk level increases. For example, non-invasive 3D printed prostheses would be class I devices and would not require third party oversight, while a joint implant device would be class III and require both design and manufacturer QMS certification by a third party.
(page 10)

3D printing is merely a production technology, and using it should not automatically make a device custom-made any more than investment casting from a wax master does.

Questions for consideration – Proposal 1

Should the number of custom made devices that a manufacturer or sponsor can supply in one year be limited? The FDA limits this number to 5 per year in the USA, a country whose population is more than 10 times that of Australia.

No. There is no risk management reason to limit the number of custom devices from a manufacturer. For example, a company that specialised in custom devices could conceivably make many devices a year and do a much better job than one with a production focus that only made a few custom devices.

The population of the USA is not relevant. There are also many more device manufacturers in the USA, so the supply of custom devices is not unduly limited by this restriction. That is not the case in Australia.

Should the TGA implement an application and approval process for the use of a custom made device? This is the approach taken by Health Canada.

No, unless there is a rapid approval process (in the order of an hour) to allow for the occasional emergency (e.g. printing a trauma planning model). This would be a greater issue in WA due to the large time difference from the East coast in the summer due to daylight saving time.

Something like the current special access provisions for drugs, where an application can be assumed to be approved once sent, could work.

Do you have any other comments or suggestions about the proposed definitions?

This proposal is the most substantial change to the current regulations, and all the rest of the changes flow from it. Yet the proposed definitions are very unclear. Before this matter can progress the TGA must develop better definitions of the proposed new type of medical device

If implemented, these changes should have an extended transition period, not less than five years, for existing manufacturers who have operated under the current regulatory regime since the TGA Act of 1989.

Other comments and suggestions

Currently there are no ***medical device production systems*** certified by the TGA. Nor is any guidance as to what one may look like or the process that should be used to validate one.

How does the TGA propose to certify a ***medical device production system***? The results of any medical imaging based system are highly dependent on the skills and experience of the operator. For example, dealing with metal artefacts in CT scans requires a great deal of judgement based on knowledge of the anatomy, pathology and other circumstances of a particular case. No existing software product can do this without a skilled human operator, so how will the system be validated in itself, independent of the operator?

In general, the devices cited as examples in this proposal are not produced by monolithic systems designed for medical device production that would be amenable to validation and listing as a ***medical device production system***.

It is more usual, indeed almost universal, to have one or more software systems operated in conjunction to produce a digital model, which is then physically rendered by a completely separate system comprising software, hardware and specified raw materials.

We use a range of software products, from expensive FDA-approved imaging software to open-source 3D packages, using whichever package is best for the needs of a particular case. It is highly unlikely that most of these software packages will become ***medical device production systems***, which will severely impact the range of software tools we can use and hence, the quality and timeliness of the service we can provide.

Based on our experience with 3D-printing surgical planning models, we have often had our expensive, corporate 3D-printers fail and have resorted to printing time critical models for trauma cases on inexpensive "hobby" printers. The judgement that this is acceptable is made by experienced bioengineers following appropriate risk-analysis procedures. It is likely that only large manufacturers of 3D-printers will produce certified ***medical device production systems*** whilst smaller companies would not. This would reduce the flexibility of our service and would negatively impact on the service we could deliver.

Proposal 2: Changes to the custom made conformity assessment procedure

- that the manufacturer's statement about a custom made device is provided to the patient receiving the device. This is the current requirement in Europe.
- that the TGA be allowed to enter and inspect custom made device manufacturing sites, in accordance with the authority it has to inspect all other medical device manufacturers.
- a manufacturer in Australia or sponsor of custom made devices to provide an annual report to the TGA of the custom made devices it has supplied.
- documentation about an implantable custom made device to be maintained for a minimum period of 15 years, the current specification of a 5 year retention period is inadequate.
  (page 11)

The suggestions in this proposal seem generally reasonable and should not be onerous to implement.

Questions for consideration – Proposal 2

Are there any issues or unintended consequences that may arise out of these proposed changes to the custom made conformity assessment procedure?

Who would bear the cost of TGA inspection? For commercial manufacturer's this would obviously be part of doing business. However Public Hospitals do not have funding available for this, nor do they generate an income stream from the sale of devices.

Holding documentation for 15 years will also incur a cost, as will the added reporting requirement. These will obviously be smaller than the inspection costs, but the issue remains that Public Hospitals will not have the funds to pay for these activities.

How will reporting to TGA be done, and what information will be required? An electronic system that could accept bulk data in a standardised and clearly defined format would be preferable. In that way in-house record systems could be adapted to produce the required reports at minimal cost.

Will TGA make the number and type of devices produced public? This may be an issue for commercial providers.

If there are issues, can you provide suggestions for addressing them?

Not for profit manufacturers should be given either an exemption from fees or a substantially lower fee schedule to reflect the difficulty in funding added compliance costs.

This is particularly the case with Public Hospitals and other State funded bodies, where fees paid to TGA are just a transfer of money from State to Federal governments.

Other comments and suggestions

We suggest that a copy of the manufacturer's statement should also be provided to the medical practitioner requesting the custom device.

Proposal 3: Changes to the definition of manufacturer

Customised devices

The text suggests that raw materials for the manufacture of dental crowns are medical devices. While accepted practise, calling a raw material a device is odd.

The TGA does not believe it is sufficient to only regulate the raw material for a 3D printer. 3D printing is more than assembling or adapting a device for a particular patient; it is a manufacturing process that has an impact on the finished devices' compliance with the essential principles. Some additional clarification around this provision is required. **(page 12)**

Investment casting of a dental material is also a manufacturing process with potential impact on compliance in the same way that 3D printing is. A material that is provided for 3D printing dental crowns should be considered the same as a material provided for casting dental crowns, and regulated in the same way.

That is, the supplier of the material should outline the processing parameters required to produce a finished device of adequate quality. The parameters are very different to those for investment casting, but the philosophy is the same.

The issue of the fidelity of the crown's shape is a different matter. When making a crown from an impression then the impression process should be validated, separately from the casting process. The materials and methods for taking an impression may not be from the same process as those for casting the final crown. Similar considerations apply to scanning & 3D printing. And scanning should be considered separately.

A new paradigm for health care facilities and practitioners as manufacturers

It is proposed to add a new exclusion from the responsibilities of being a manufacturer. This would apply to health care practitioners or hospital laboratories that use ***medical device production systems*** (as defined in proposal 1 above) that are included in the ARTG to produce medical devices of risk classification Class IIa and lower for use in treating their own patients. **(page 13)**

The phrase "their own patients" needs clarification. What will determine who a service can regard as "their own" patients?

For example, any patient referred to our Service for a custom medical device becomes our patient. As we are a State service of WA Health, the "healthcare provider" in our case is the Health Department and our patients come from across the State.

See also below in "Other comments and suggestions".

Questions for consideration – Proposal 3

Are there any issues or unintended consequences that may arise out of these proposed changes to the definition of manufacturer regarding ***customised devices***?

The definition remains unclear.

The phrase "change the purpose" should be better defined. How much can the purpose be changed? It depends partly on how narrowly the manufacturer defines the purpose, of course. For example, if a device is used in a novel way but achieves the same effect, does that change the purpose?

Are there any issues or unintended consequences that may arise out of these proposed changes regarding the use of ***medical device production systems***?

This provision will reduce innovation in the medical modelling market in Australia.

It may reduce competition by forcing small suppliers of medical devices out of the market and concentrating supply with a few large manufacturers.

Many systems and machines currently used for innovative medical device production were not developed for medical devices. Often medical use is a small part of their market and they will not have the resources or inclination to validate their system for medical device production.

If there are issues, can you provide suggestions for addressing them?

The raw materials for dental crowns are sold with instructions for how to process them to achieve a compliant medical device. These instructions include the conditions that the casting machine must achieve, but there is no restriction on the manufacturer using a different casting machine, provided it can achieve the specifications required by the raw material manufacturer.

3D printing should be regulated similarly. A manufacturer of a raw material should specify the conditions required to produce the expected final product and test procedures to ensure that the final product is fit for purpose.

Other comments and suggestions

This proposal suggests that health care facilities suppling ***patient-specific medical devices*** can be exempt from the responsibilities of a manufacturer provided they use a ***medical device production system***. This is another newly introduced term with a nebulous definition, as discussed in our response to Proposal 1.

In theory this proposal will free hospitals from becoming device manufacturers if they use a ***medical device production system***. In practise, trying to do so will have a substantial impact on our services. As noted in our response to Proposal 1, we often need to use consumer 3D printers for emergency cases. As these will not be part of a ***medical device production system***, if we have not become device manufacturers we would be unable to provide an emergency model.

The proposal further notes that any exception for using a ***medical device production system*** for Class IIa and lower devices, only applies to health care facilities supplying devices for "treating their own patients". There is no definition given of what would be considered our patients. We would generally consider any patients who have been referred to our service as our patients. As noted above, we are a centralised service providing custom anatomical models across Western Australia. If "our patients" are only patients for the hospital where we are located, it could mean every hospital in WA would need to establish a duplicate of our service at great expense.

We also supply models to private referrals. Could we provide devices to private patients referred to us and remain exempt? If not, this would apply different rules (and level of scrutiny) to providing a model to a private patient compared to providing the same model for the same surgeon and the same patient referred to us through the public system.

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

Software that records patient diagnostic images should also be captured by this rule..
(page 14)

The phrase "records patient diagnostic images" is ambiguous. For example, a Picture Archiving & Communication System (PACS) contains instances of DICOM objects that in turn can hold medical images in digital form but could hold other data. Does the PACS record medical images?

For medical imaging, it would seem reasonable to consider it is the device that images the patient (CT scanner, ultrasound, MRI, etc.) that records the diagnostic images. The PACS stores those images. Data for an anatomical model would likely be taken from the PACS. Would it be the scanner software, the PACS software or both that is captured by this rule?

5.4 Medical devices intended to record diagnostic images

A medical device that is intended by the manufacturer to be used to record diagnostic images is classified as Class IIa. This includes software and anatomical models intended for diagnosis or investigation of the anatomy.
(page 15)

Models do not "record diagnostic images". It could be argued that they record information derived from diagnostic images, but then so can pieces of paper.

The phrase "diagnostic images" could also be an issue. Imaging data acquired to produce a model is often not diagnostic, but taken for treatment planning or recording purposes.

Is the phrase "software and anatomical models" intended to refer to digital and physical anatomical models respectively? A digital model is in fact data, which can be viewed and manipulated by any suitable software. Or is this phrase intended to refer to any software used to view and analyse medical imaging data? The wording of the heading suggests the former meaning, but the phrase "digital 3D print files" focuses again on the use of a digital model to produce a physical model. Such models are made and used in diagnosis or treatment planning without ever being made into a physical model.

These ambiguities should be resolved.

The phrase "investigation of the anatomy" would be better as "treatment planning". If an anatomical model is not being used for diagnosis or treatment, it should not be considered a medical device. The proposed wording would capture the common use of models for patient counselling, as that is part of the treatment planning process.

Manufacturers of anatomical models would be required to hold appropriate conformity assessment evidence for a Class IIa device. This would not apply to hospitals or healthcare practitioners if they used a ***medical device production system*** to produce the anatomical models for treating their patients, and the ***medical device production system*** was included in the ARTG.
(page 15)

Why restrict this clause to only hospitals or healthcare practitioners? If the ***medical device production system*** is validated, then why not allow the same exemption for commercial providers to use them to produce models?

See also comments on ***medical device production system*** previously.

Questions for consideration – Proposal 4

Are there any issues or unintended consequences that may arise out of the proposed change to the classification of anatomical models and software?

It is likely that restricting the supply of anatomical models will encourage people to go offshore and have models printed and posted to Australia. Medical imaging data is easily shared across the Internet and the models are cheap to post. Would be these treated like the importation of any other medical device for personal use? If not, how would this trade be policed?

The proposal also misses the issue of non-physical models. A non-physical or digital model must be made before a 3D printed model (or any 3D printed object) can be produced. Current methods of producing digital models include extracting surfaces from medical imaging data and 3D scanning of the patient. The digital model should also be considered a medical device

A further consequence of the changed wording is that this now includes clinical photographs.

If there are issues, can you provide suggestions for addressing them?

A separate clause to cover anatomical models, both digital and physical, derived from medical imaging data would be much clearer. They could still be Class IIa devices, but a separate clause would avoid some of the language problems of trying to group them with X-ray film and the like. The terminology should also reflect the broad range of data used to generate models of patient anatomy and the range of uses to which those models are put.

Given the issues of people generating their own models, it is probably reasonable to treat them in the same way as medical devices imported for personal use.

Other comments and suggestions

Proposal 5: New arrangements for devices with human material

Questions for consideration – Proposal 5

To ensure the most efficient and effective assessment of these products, it is proposed that medical devices that contain as a component, but that are not wholly comprised of, human origin material are not biologicals, but are Class III medical devices. Regulation 4.1 should be amended to require conformity assessment for medical devices that contain a biological (human origin) component.
(page 16)

What about a device composed wholly of human origin material that has been extensively altered? An example would be a bone fixation pin machined from treated allograft bone. These are commercially available in the USA.

We would suggest that all Class III devices should require the same conformity assessment, regardless of the presence of human origin biomaterials. Any biomaterial component should then be subject to additional regulation as a biological if required.

Are there any issues or unintended consequences that may arise out of the proposed change to the pathway for medical devices that incorporate materials of human origin?

This is not a mature area of device development and the technologies and approaches used for tissue engineered implants are changing rapidly. Any changes to the Regulations need to be drafted carefully so that they don't stifle the innovation needed to progress in this area. Most innovations in this field will arise from groups who are not medical device manufacturers. Currently they can produce tissue engineered products incorporating device-like components without becoming manufacturers, but the proposed changes will stop that

If there are issues, can you provide suggestions for addressing them?

Tissue engineered devices or devices incorporating biologicals produced as part of registered Clinical Trials should be broadly exempt, to allow non-manufacturers to undertake research and development in this area.

This exemption could be restricted to hospitals, if desired.

Currently running Clinical Trials should be made exempt (grandfathered).

Other comments and suggestions

Notes on appendices

Appendix 1 – Background on 3D printing

With conventional manufacturing methods the design of the interior channels would be limited by the necessity to remove the shape from a mould, or else would require the joining together of two or more pieces; with 3D printing a single-piece object with the desired design can be achieved.
(page 17)

The descriptions of 3D printing in this section are a bit confused & not strictly correct. Lost-wax investment casting can achieve a single piece design with interior channels, for instance.

Reliance on software

3D printing is a digital technology and, as such, is reliant upon the correct application of software to achieve successful outcomes. 3D printing utilises two major software components, one is a 3D software model of an object and the other is a translation of the object software model into printer-specific software that controls the build. A range of different software platforms are available for both of these components and the process of translating the object model to a printer-ready state is not always straightforward. Sometimes additional software platforms are required to add final corrections or refinements to the translated model prior to printing.

The pattern, or build file, for a 3D printed object is essentially a map for the printer's computer that controls the movement of the energy source and/or the raw material. The build file for a 3D printed object can be thought of as the coordinates on a digital grid for a number of adjacent 2D slices of the desired object.

The quality of a 3D printed object is heavily dependent upon the correct application of complex software interfaces.
(page 18)

This is potentially misleading, and no more characteristic of 3D printing than of CNC machining, for example.

In particular, it is entirely possible to take a file provided by someone else and without making any changes to predefined settings pass it through the software provided with a 3D printer and

to the printer to produce a reasonable quality part. It is not correct that the result is *dependent on the correct application of complex software interfaces*.

This certainly *is* the case with CNC machining, which is much more reliant on complex software and always requires a high degree of user expertise to achieve a quality part.

Appendix 2 - Medical applications of 3D printing

Anatomical models

> Different tissues in the body have different identifiable properties that are represented uniquely in the software images.
> **(page 20)**

Not strictly true, and the source of several problems when trying to produce accurate 3D models. Multiple tissues can and do map to the same quantity (e.g. multiple tissues and materials can have the same Hounsfield Unit number in CT).

Non-invasive prosthetics

> Therefore, manufacturing devices using patients' scanned body images and 3D printing, versus the currently widely used moulding method, may provide better flexibility and opportunities for creating devices that are better tailored to specific anatomical characteristics of individuals.
> **(page 21)**

This has been more driven by speed & cost considerations (centralising manufacturing without having to transport plaster casts, for example) than by a need to better tailor these devices.

Reference issues

Page 5, Footnote 2

The use of *ibid* here makes this a reference to the Dictionary of the Regulations (i.e. the source of reference 1) rather than to the Act, which was probably intended.

Page 27, Footnote reference

Di Prima et al, Additively manufactured medical products – the FDA perspective, May 2016, https://www.researchgate.net/publication/303750500_Additively_manufactured_medical_products_-_the_FDA_perspective [accessed 2/07/2017].

This should reference the actual journal article https://link.springer.com/article/10.1186/s41205-016-0005-9 (open access), not the ResearchGate upload.

Appendix 1: RPH Bioengineering History

Examples of World and Australia-first custom made medical devices supplied by our department include:

- **1984** Design, manufacture and first-in-human use of a medical device derived from CT data. The shoulder arthrodesis is still *in situ* 30+ years after surgery.
- **1997** First use of a modular Hip Spacer, a custom made device designed and manufactured to treat infected joints allowing the patient to mobilise whilst the infection is treated. This is now routine clinical practice with several competing commercial products now available.
- **1998** First use of custom arthrodesis compression nail, for allograft arthrodesis of long bones following tumour resection. The nails apply compression post insertion to ensure good apposition of the intercalary allograft to the host bone.
- **2000** Australian-first production of custom titanium implants for cranioplasty.
- **2001** Australian-first use of custom CNC machined radiotherapy compensators (in conjunction with SCGH).
- **2001** Custom ^{125}I brachytherapy eye plaque for unusually large tumour.
- **2006** World first use of 3D laser melted (SLM) titanium acetabular reconstruction hip implants. Again, this is now routine clinical practice with several competing commercial products now available.
- **2010** World first double titanium cranioplasty (shortly followed by the second in 2011).
- **2013** Australian-first use of custom titanium implants for orbital reconstruction.
- **2013** First-in-human clinical trial of a tissue engineered construct using resorbable ceramics and allogeneic mesenchymal stromal cells for cranial reconstruction – patients re-growing their own cranial bone *in situ* from donor stem cells.
- **2014** World first case of intra operative 3D printing of a surgical planning model.
- **2015** World first combined cranio/orbital reconstruction manufactured from a single piece of titanium, assisted by a 3D-printed resection guide
- **2016** World first custom stoma plate designed to eliminate leaking in difficult stomas.