Adoption and Diffusion of Disruptive Technologies: The Case of 3D Printing in the Medical Device Industry

White Paper II: Business Models, Barriers, and Solutions

Enabling Capability Platforms
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Ethics Declaration

This report is a result of project number 21946 and was granted ethics approval by the RMIT University Human Research Ethics Committee.

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Executive Summary

With the aging population and the increasing cost of healthcare in Australia, disruptive technologies can play a major role in improving patients' experiences and reducing the cost for health care system. A prominent example of such disruptive technologies is 3D Printing (3DP), which according to a recent CSIRO's medical device industry roadmap report, is identified as an opportunity area for growth in Australia's evolving manufacturing industry. Existing evidence suggests that utilising 3DP in medical sector can be potentially beneficial for patients, health care system, industry growth, and export. However, the widespread adoption and diffusion of this technology is currently slow.

In order to tackle this problem, RMIT University's Enabling Capability Platforms (ECPs) funded a research translation project running from 2017 to 2020, which involves a wide spectrum of stakeholders in the industry, i.e., manufacturers (large firms and SMEs), surgeons, patients, hospitals, research centres, regulatory bodies (TGA), insurers, and industry associations. The outcome of this project has been documented in two White Papers. The first one comprehensively investigated Opportunity Areas, Stakeholder Mapping, Road Mapping of the industry, and also the application of 3DP in the industry (published in November 2018). Four opportunity areas were identified in this project: Business Model, Technology, Material Science, and Regulations. The second (current) White paper digs deeper into the Business Model opportunity area and further investigates the non-technical and business-model-related barriers to adoption and diffusion of 3DP medical devices.

In particular, we have adopted multi-stakeholder perspectives, as a unique endeavour, in order to investigate the following issues in this White Paper:

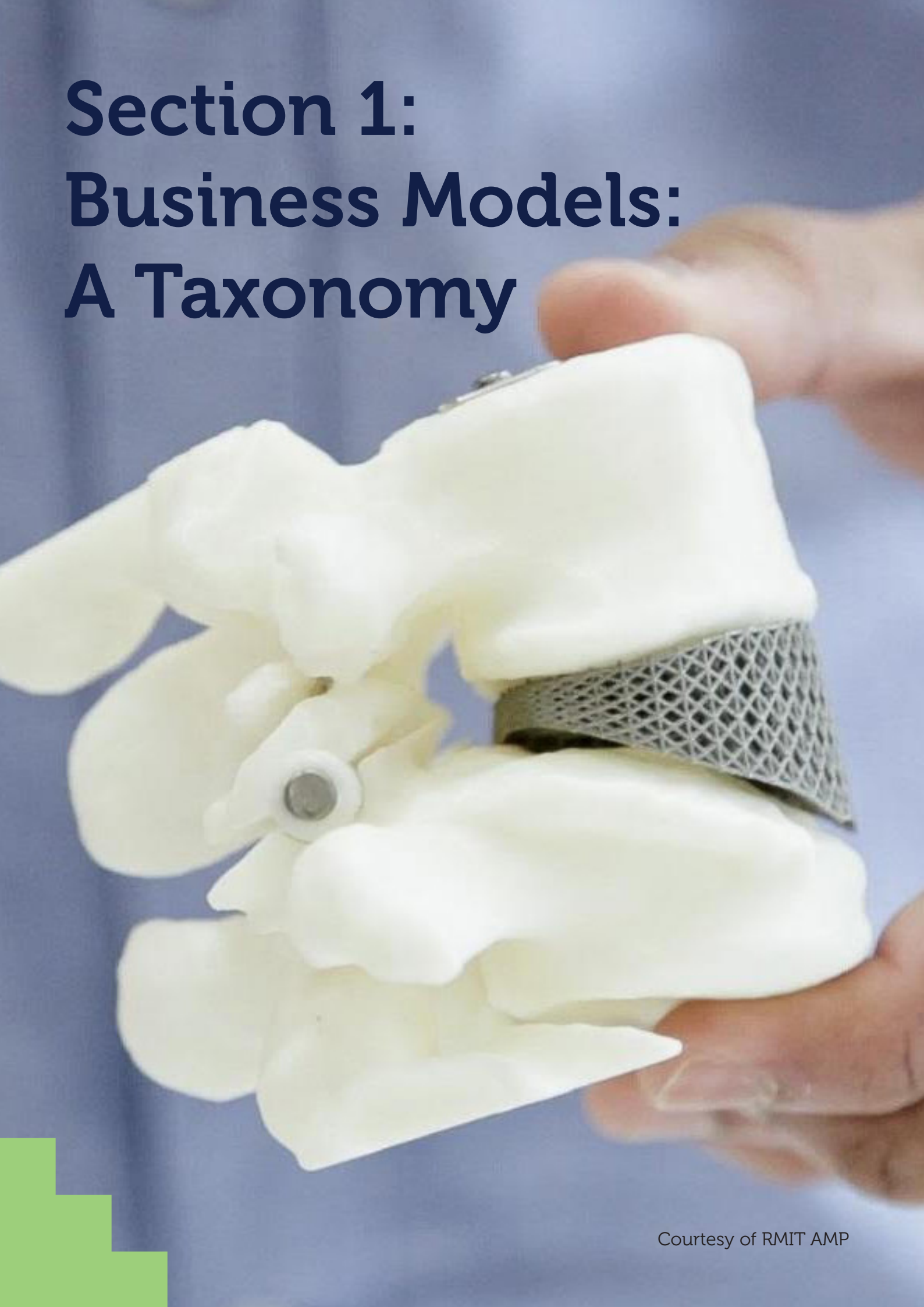
- Identifying various Business Models in the industry, both currently practiced and potentially future ones (Section 1)
- Identifying non-technical and business-model-related barriers hindering a wider adoption of 3DP in medical device industry (Section 2)
- Mapping the identified barriers against the Business Models and weighing their severities (Section 2)
- Conducting a Root-Cause Analysis for each barrier in order to identify where each barrier comes from (Section 3)
- Identifying complex Catch-22 scenarios in conducting Root-Cause Analysis (Section 4)
- Offering recommended solutions to overcome the barriers and the associated Catch-22 scenarios (Section 3 and 4)
- And finally, proposing future avenues for developing practical tools that enhance the engagement of various stakeholders in the industry and hence a wider adoption of 3DP (Section 5)

This White paper is the first ever effort to dig deep into the non-technical barriers associated with the blockage in the adoption of 3DP technologies in medical device industry, particularly in Australia. Our main findings point that technology, material science, or regulatory framework are not necessarily impeding the growth of the industry. The less investigated, non-technical, stakeholder related, and 'soft' barriers can be the main blockages for a wider adoption of 3DP in medical device industry. Eight barriers were identified through this research. Two examples of such barriers are (i) lack of adoption by surgeons and (ii) lack of endorsement by insurers.

Moreover, our findings show the importance of collaboration between various stakeholders to achieve higher goals in realizing the potential of disruptive technologies such as 3DP in medical device industry. However, this is not usually straightforward since various stakeholders typically have different interests. This can lead to a number of complex and inter-dependent barriers (caused by various stakeholders), which we denoted them as Catch-22 scenarios. We then pinpoint the root-causes of each barrier. Finally, we propose possible solutions to remedy the root-causes, which would eventually mitigate the barriers. Hence, it can enable a wider adoption and diffusion of 3DP in medical device industry.

The findings in this White Paper report, and the project as a whole, will be beneficial for industry actors such as SMEs, large manufacturers, and service bureaus. It will help them have a holistic and multi-stakeholder perspective about the prospect of the current and future business models, associated barriers to the business, and potential solutions. It is also beneficial for governmental research agencies, such as IMCRC and CSIRO, to design targeted grants for areas with market failure blockages that require third party interventions. It can be helpful for regulatory bodies to explore smoother, faster, and more transparent regulatory pathways which can be particularly useful for SMEs. Last but not least, the findings in this White Paper are beneficial for health insurers to facilitate their informed decision making about the coverage of certain high-risk 3DP medical devices.

Section 1: Business Models: A Taxonomy



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SECTION 1 – BUSINESS MODELS: A TAXONOMY

Business models in medical device industry can be categorised broadly into centralised types vs. decentralised types (see Figure 1). The centralised type is when one company/ organization takes control of all the stages of manufacturing, from design and printing to post processing and sterilisation of the device. The benefit of this type of business model is that the company has full control on the manufacturing stages, hence the complication concerning the liability of failed products is minimum. The problem with this business model is that it requires heavy investment in machineries and equipment in order to own everything in-house.

Currently, the centralised business model is practised mainly by large firms such as Stryker. On the contrary, the decentralised business model is when a company outsources parts of the manufacturing to another party, for example outsourcing the printing to service bureaus. This is mainly due to the economies of scale and/or the lack of in-house facilities (such as 3DP machines or sterilisation chambers).

Currently, the decentralised model is mainly pursued by SMEs, such as OMX Solution or Anatomics. In rare occasions, smaller companies, such as Oventus, also tried the centralised business model, but now they are shifting to the decentralised model in order to be more cost-effective. As an SME representative made it clear:

> "It would be impossible for a small company that print high end orthopaedic implants to financially justify a titanium 3D printer."

The centralised business model can be further broken down into In-House and Hospital-Based models. The In-House model is when a company operates and manages every stage of manufacturing in its own facilities (which can be co-located in one place or different locations).

Currently, the conventional type of the In-House model is the common practice type for large companies. In this business model, the company designs, prints, post processes and sterilises the devices within its own facilities. Apart from the conventional type, Centralised In-House business model can also be subscription-based. In this model, a (large) company provides all the stages of production, from design to post processing and sterilisation. As a large firm representative pointed out:

> "We can have subscription service where we have the core patent and people can come to us to add onto it as a new version where that update is sent into the cloud."

A possible example of the subscription-based model is the leasing digital templates of CAD/CAM models regulated by the TGA. This could be used for a range of medical devices where their dimensions can be aligned with a patients' anthropometry[1].

The Hospital-Based model is similar to the In-House Centralised business model, except for the fact that large companies, such as Stryker, have their own facilities inside the hospital, next to the operating theatre. This is currently not happening.

[1] And there are regulatory notes on the template-based design. The TGA, based on new definitions, is saying the manufacturer still need to get approval for the template. Just because the manufacturer is customising it, it doesn't mean it's 'custom-made', hence the manufacturer cannot bypass the custom-made regulatory pathway and is not to able to get exemption. The reason is that in this case, the manufacturer is customising a template and not making a new patient-specific device.

Large companies are open to adopt this business model if they get an offer from hospitals authorities, because this business model can facilitate the idea of Just-In-Time implants, therefore, large companies can keep the full control over the process and avoid liability concerns. Hospitals seem to have some initial positive views on this model, as noted by a hospital representative:

> "Maybe if they [large companies] said we want to have a manufacturing site here and we want it to supply Australia, that could happen."

However, SMEs have opposing views. An SME representative noted,

> "Hospitals have a hard time enough operating, let alone having to take on external company representatives."

Nevertheless, some SMEs seem to have approached hospitals recently. As a hospital representative pointed out,

> "Smaller companies interested in 3D printing have approached the hospital already and were interested in having an office or a lab with some engineers so the surgeons can talk with the engineers. They did not envisage titanium 3D printing to happen on-site though. They wanted something that made it easier for clinicians to be aware of the companies' services and have access to them."

In general, the decentralised business models are more common in the medical device industry than the centralised models. As a 3DP machine producer said,

> "The whole 3DP process to produce a medical implant revolves around far more processes than just the printing. Those processes are very rare to find in a single location."

Simply put, the process consists of first, powder procurement and then sorting the powder accordingly. Next, designing and qualifying the file followed by printing. Afterwards, it comes to the measurement of the device and checking the consistency of its manufacturing (not for one-off devices). Later, the devices need to go through a machining or finishing process, and then a polishing process followed by a quality check control according to certain ISO standards. Finally, it will be time for device sterilisation. A 3DP machine producer emphasized,

> "By the time you get the part at the end of the process, it will have gone through multiple companies. At the moment, almost every company has to go to a few locations to be able to get that finished product."

However, the decentralised business model does not seem to be a favourable model from investor's perspective:

> "I think decentralised doesn't work. There are too many steps. It should be mass produced [in a centralised manufacturing model]."

Decentralised business model can be further broken down into Service Bureau model and Hospital-Based model. The Service Bureau model is the one when a company (mostly SMEs) designs the device's CAD file and then sends the file to printing and/or sterilisation service bureaus that can be located nationally or internationally. Currently, the national services bureaus, such as CSIRO's Lab22, are the common practices. Two issues are raised by the SMEs representatives. First,

> "There is a need for more 3D Printing bureaus with ISO 13485 certification"

Second, the limited number of such service bureaus are mainly industry-specific, which means they operate and serve one single industry, e.g., medical device industry. An SME representative pointed out that instead of this, we can have Trans-Industry Service Bureaus where there are service bureaus that service multiple industries at the same time, hence reaching full-capacity of 24/7 production.

Another possible future scenario can be to send the CAD file to overseas service bureaus. In this case, not only can they print the device geographically close to the overseas patient and reduce the lead time and cost, but they can also reduce the printing cost if the targeted market is a low-production-cost place. As an SME representative noted,

> "Given the niche market of 3D printed implants and specifically maxillofacial surgery, you absolutely have to take your business globally."

Moreover, from the perspective of foreign owned large companies, e.g., Stryker, it also makes sense to have global service bureaus close to customers, in this case Australian customers.

There are two main questions when it comes to international service bureaus and going global. The first question is when to go global. SMEs, particularly the ones with single, dominant, and innovative product, such as Oventus, seem to go global when they are done with the R&D and design, and have already got their patent.

> "For us the design of the device was the point of differentiation and it was what our patent was about. Doing that R&D rapid turnaround to get multiple iterations of the device was key. We did that in Australia because it was quicker to do it here than anywhere else. Once the design is frozen, the bespoke devices need to be printed close to the customer. For us to print in Australia and ship it to the US and have issues with customs, then sent to another site before being sent to the dentist- you can lose a week at least and that is a disadvantage when compared to competitors who are manufacturing in the US."

The second question concerning going global is "where to start to go global?" There seems to be a quite straight forward mapping exercise in this industry. The reason is that a 3DP medical device, particularly an implant, is a highly customised, patient-specific, and expensive treatment.

> "You're in the 1st world health economy which means your number 1 target is the U.S. Then Europe, then the rest. We have put China onto the bottom of our list, because of the nature of the business and the payment reliability. Our recent presence in India is perhaps an exception and would not have happened if it weren't for a contact. We are working with Aus-Trade on a mapping exercise with India."

as an SME representative stated.

Another type of decentralised business model can be Hospital-Based model in which instead of sending the CAD file to typical service bureaus, the CAD designing company (mostly SMEs but can also be larger firms) sends the file directly to a hospital where the device can be printed and sterilised. In this case, the liability of printing and the control over the printing process is owned by the hospital (unlike the Centralised Hospital-Based model, where a company representative holds the full control over the process). This model is only a future possibility and it is not currently practiced.

However, there are some economic and quality concerns about this model. Most of the stakeholders are pessimistic about the realisation of the business model where the hospitals become the ultimate manufacturers (as noted by representatives of large manufacturer, SMEs, insurer, and research institutions). An exception is an industry representative noting that

> "3D Printing in hospitals might occur in a country with a higher population, such as China."

This will be elaborated in Section 2.1.4. There are also bureaucratic barriers for hospitals to take on the manufacturing role. As a hospital representative mentioned,

> "Hospitals currently provide a list of services for the government for payment. When they step outside their current business model, they are probably very concerned."

Hospitals are also fairly conservatives by nature. Another hospital representative noted,

> "I am just thinking for implanted devices, the risk of infection and other risks that could lead to litigation, hospitals might be pretty conservative about."

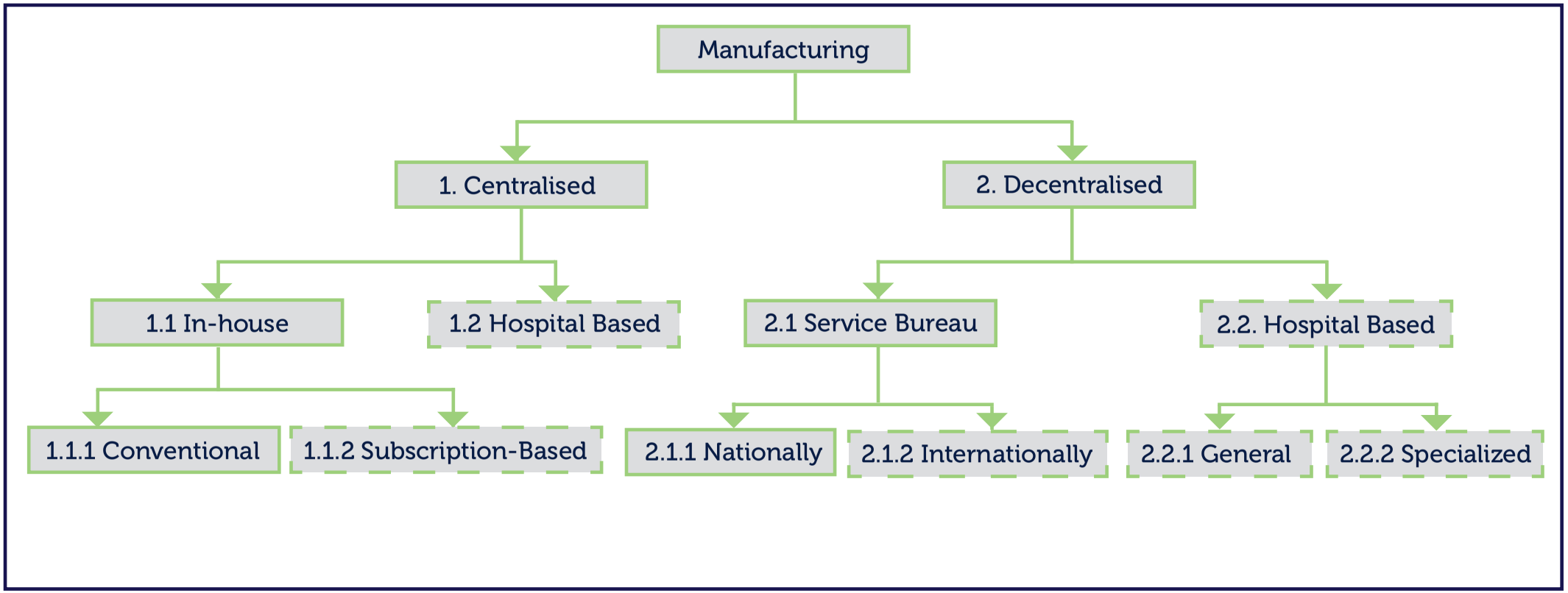
And finally, another hospital representative said,

> "There is also pressure from companies, big companies in particular. They, I think, believe that, [if there is going to be any hospital/-based model], then some sort of centralised [hospital-based] manufacturing is desirable, instead. They will amplify the risks when talking about manufacturing medical devices to hospitals, saying that they are needed to take care of device manufacture."

Nevertheless, assuming Decentralised Hospital-Based model can be implemented in the future, the two available routes include general and specialised manufacture, in which the former is about engaging all hospitals in printing and surgery of all types of 3DP devices, while the latter model is about designating specific hospitals dedicated to specific types of surgery (for instance, hypothetically, St Vincent hospital in Melbourne is dedicated to metal hip implant, while Wollongong hospital specializes in spine implant). In this vein, a private health insurance representative stated,

> "I suspect that there will be even some variations of Hospital-Based business models. For example Doctor centric- there's no doubt that doctors will someday be doing their own stuff, although it is not exactly Hospital-Based models"

Figure 1: Business Model Types



Note: Solid boxes indicate currently practiced business models. Dashed boxes indicate possible future business models.

Section 2: Business Models And Barriers

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SECTION 2- BUSINESS MODELS AND BARRIERS

Whether the business models are currently in place, or have potential to be adopted in the future, there are barriers that impede the utilisation of 3DP in medical device industry. Based on our extensive qualitative data collection during 2018 to 2019 through workshops and a series of post-workshop face-to-face interviews, eight barriers were raised by a wide range of stakeholders that were specific to the scope of business models. They are:

1. Lack of surgeons' adopting 3DP medical devices
2. Lack of insurers' endorsement in 3DP medical devices
3. Liability issues with decentralised manufacturing
4. Concerns (quality and economic feasibility) with hospital-based manufacturing
5. Lack of global harmonization in regulatory requirements
6. Protection of Intellectual Property Rights (IPR)
7. Lack of affordable sterilisation bureaus
8. Funding opportunities for SMEs

Some of these barriers are significantly easier to resolve than others, which is why a member of an industry association stated,

> "Some of these barriers can be categorised as 'perceived barriers' compared to 'real barriers'."

Nevertheless, in the following Section, we will explain what each of these barriers is about. This is further clarified in sections 3 and 4 of the report where root-cause analysis is conducted on each barrier in order to investigate 'why' these barriers exist and what can be done to remove or ease them.

2.1 Explanation Of The Barriers

2.1.1 Lack of surgeons' adoption of 3DP medical devices

Surgeons (alongside patients) are one of the primary end users of 3DP devices and they are possibly more influential than patients whether or not to choose 3DP devices. This is why surgeons have a paramount role in the adoption and diffusion of 3D medical devices, specifically the class 3 medical devices, e.g., orthopaedic implants.

Through the interviews held, concerns were expressed that the majority of surgeons are not (at least yet) willing to adopt 3D printed devices. This was mainly due to the lack of confidence among surgeons concerning the 3DP devices, which we will further discuss in detail in Section 3.1. Nevertheless, surgeons' lack of endorsement is crucially impeding the adoption and discussion of 3DP medical devices. As a researcher stated,

> "Certainly, surgeons' endorsement is the top barrier, as without surgeons it is difficult for companies to invest in this sector. Certainly, they are both needed, but surgeons will be needed to pull this technology before large manufacturers to make these devices."

Although the majority of surgeons seem to be fairly hesitant to adopt the 3DP implants, there are still few early-adopter surgeons that are pioneering the implementation of 3DP implants.

Dr. George Dimitroulis is an example of such with specialisation in maxillofacial surgery. He is also the founder of 'OMX Solutions', a company that specialises in producing 3DP titanium patient specific implants established in 2016 in Melbourne.

They primarily focused on tetra-mandibular joint replacements but have expanded the field to other implants later. Dr. Peter Choong (an orthopaedic surgeon) is another example of the pioneering surgeons who support the adoption of 3DP implants. He is the Head of Department of Surgery at St. Vincent's hospital and a key figure in BioPen project.

The project entails the use of a 3D printer pen filled with stem cell ink to "draw" new cartilage into damaged joints (e.g., knees) to repair damaged areas as opposed to the current methods of surgery which involves grafting or inserting non-biological prosthetics (e.g., titanium implants).

Another key surgeon in the endorsement of 3DP implants is Dr. Paul D'Urso who practices neurosurgery and is the founder of Anatomics (est.1996). Originally Anatomics started with the manufacturing of custom cranial implants but now has expanded to a spectrum of custom implants, ranging from sternum to shoulder implants.

Although still amounting to a minority rather than majority of the surgeons community, these three examples reflect the surgeons who actively practising and supporting 3DP medical device implantation.

2.1.2 Lack of insurers' endorsement of 3DP medical devices

In our first White Paper [1], medical device reimbursement was ranked as the third most impactful barrier in response to a survey among variety of stakeholders. Medical device reimbursement, through the prosthesis-list reimbursement protocol, is influenced by insurers' endorsement.

The reimbursement procedure works effectively for devices listed on the prosthesis list. If the patient has the appropriate level of private health insurance coverage, the device manufacturer reimbursement will be provided.

Examples of this procedure working effectively are the temporomandibular joint (TMJ), fossa replacement, and surgical guide by OMX Solutions. The three devices totalling $14,991 are fully covered by the minimum costs paid by private health insurers, which means if a patient that requires the devices has the appropriate health coverage, he/she will only need to pay the gap payment for the medical professionals, if required.

However, if the device is not enlisted on the prosthesis-list, this creates a large barrier for both medical device manufacturers to manufacture the 3DP devices and also for the patients to adopt them.

Firstly, the barrier for 3DP medical device manufacturers stems from the expensive product development process of novel patient-specific devices. It is expensive because the engineering and manufacturing costs are specific to one device and cannot be offset by economies in the scale of high-volume production.

Therefore, there is limited financial incentive for manufacturer to design, manufacture and be willing to go through the regulation process for a device that will be produced in low volume, in many cases as a one-off device. That is why the reimbursement from insurers is crucial for financial viability of such medical device development.

Secondly, the lack of affordable devices, which are not listed in the prosthesis-list, is also a barrier, mainly because it kills the demand from the end use side, i.e. the patients. It is widely believed that cutom-made 3DP devices (such as implants) tend to be more expensive than traditionally made off-the-shelf implants for patients.

However, as more data is collected, previous reports have indicated that it can possibly supply evidence on whether there are costs saved through the reduction in operation time, rehabilitation time, hospital stay and reduced revisional surgeries [2-4].

Moreover, making healthcare more affordable for patients could provide the methods with acquiring more data, while also resulting in better patient outcomes.

2.1.3 Liability issues with decentralised manufacturing

Decentralised manufacturing is the current model taken by almost all SMEs to manufacture 3DP medical devices. It entails outsourcing numerous steps of the procedure to bureaus. However, if a medical device were to fail, having other parties involved in its manufacturing will definitely raise the question of who is liable.

Such liability issue has become a highly ranked barrier for companies, especially SMEs, to pursue the manufacturing of 3DP medical devices [1]. For the legal ambiguities present in decentralised manufacturing, stakeholders have expressed their concern that the risk is not worth it unless someone is willing to take the responsibility. This will be further discussed in detail in section 3. And this is particularly an issue for SMEs because they are 'small'. As an SME representative noted:

> "I think the disadvantage with contracted [or decentralised] manufacturing is that you are now relying on others for the manufacturing. When you are small, you are not that important to a contracted manufacturer. It is only when you become a reasonable size when a contracted manufacturer will respond quickly."

Furthermore, in a 2017 consultation paper published by the TGA, the liability aspect is addressed through the proposal of changing definition of a manufacturer. What this proposal addresses is that, currently, the party who modifies an implant to adapt the device for an individual patient does 'not' constitute as the manufacturer.

An example of this is dental implants made by dentists. They modify a crown to fit a patient and they are not counted as a manufacturer given that they follow guidelines of the actual manufacturer of those crowns.

However, if they were to opt for 3DP crowns, the producer of the raw materials of the crown would be the manufacturer while the dentist still isn't (thus not liable).

This is not reflective of the true distribution of the liability. With that reasoning, the TGA wants to revise the definition of a manufacturer of a 3DP device to ensure that proper liability is attached to the parties involved in the production of a 3DP device.

Even though such proposition to change the definition of manufacturer and hence the distribution of liability is understandable, nevertheless, a potential consequence of this change in the definition would leave some parties, who are in the current supply chain of the production of 3DP devices, vulnerable and hesitant and may lead them to opt out from participating in the supply chain.

Such opting out can be a double-edged sword because on one hand, there is more clarity about liability in the industry, but on the other hand, there will possibly be fewer actors, particularly SMEs, in the industry (hence fewer innovations).

2.1.4 Concerns (quality and economic feasibility) with Hospital-Based Manufacturing

Hospital-based manufacturing is not a current practicing business model. It is rather a potential business model (in Figure 1, Models 1.2, 2.2). An example of the realisation of such potential business model is through the Just-In-Time project, where the idea is to print the 3DP implant next to the surgeons' operating theatre [5]. However, there are objections and concerns about this potential business model which are mainly regarding the quality of medical devices that can be produced in a hospital environment and also the economic feasibility of the venture.

First, concerning the quality capability of hospitals as the manufacturers of 3DP devices, stakeholders noted that if hospital-based manufacturing is widely adopted, it would be only for low-risk devices such as bio-models for surgery planning, as opposed to high-risk devices such as implants. However, it is extremely unlikely for a hospital to own and operate a manufacturing precinct because it drastically deviates from their current business model and capabilities. A researcher involved in investigating hospital-based manufacture states,

> "I don't think hospitals will ever run a manufacturing facility. It will always be operated by an independent manufacturer. It might be located in or next to the hospital."

In addition to the large routine change, manufacturing quality issues arise as hospitals would require additional trained staff, running a QMS to obtain ISO 13485 certification, and disrupting existing protocol to accommodate for an engineering and manufacturing precinct with certain cleanroom and sterilisation capabilities.

Second, economic feasibility is a major concern depending on the adoption rate of the technology. If 3DP devices are exclusively adopted for extreme cases, the return on investment will be very low. A manufacturer that owns an EBM printer says,

> "There is no way a hospital will be able to fill up one 3D printer. In my view there is no chance unless it is massive. If you look at the fixed costs in running the machine; the people, depreciation (of the machine), running QMS, polishing, sterilisation, all that stuff. The volume of cases will not come close to covering these costs."

Even if manufacturing 3DP devices are to be widely adopted by hospitals, for example in the large market of knee and hip replacement implants, the concerns about quality and routine change, for a bureaucratic organisation such as a hospital would still be present.

2.1.5 Lack of global harmonisation of regulatory requirements

Australia's Therapeutic Goods Administration (TGA) is the regulatory government body responsible for setting the quality standards which medical devices are built upon. Currently, there is no harmonised global regulatory framework at hand. Nevertheless, there is an ongoing global initiative in which numerous regulatory bodies across the world are aiming to produce a universal standard and consequently, aid a global medical market to flourish at the highest possible quality in medical devices being sold. This is particularly important for SMEs in Australia, who mainly produce patient-specific one-off devices, since the Australian market is too small for them. A global harmonised regulatory framework will enable international decentralised manufacturing and hence export of the devices (Figure 1, Model 2.1.2).

However, such global harmonisation might have unintended side effects as well. On one hand, Australia's current standards for medical devices are extremely high. On the other hand, the global harmonisation initiative taken by the TGA and the other equivalent bodies across the world (e.g., FDA, Health Canada, etc.) is perceived by a researcher to be potentially average considering the standards,

> "Global harmonisation is a double-edged sword. The TGA is globally noted as a high standard of regulation. Harmonising all requirements might increase the risk of medical devices that are manufactured and supplied in Australia."

Having the standard averaged could result in Australian medical devices to be manufactured in a level of quality lower than prior to the implementation of global harmonisation.

2.1.6 Protection of intellectual property

Intellectual Property (IP) protection is a key aspect to a business product and is extremely resource consuming (time and money) to patent a device. For medical device manufacturers in Australia, this process can cost an SME approximately $50k for a new device and it takes months to years to be processed. The barrier raised is those companies, especially SMEs, have been the theft of IP, which not only threatens an SME's standing in a market but also negates the substantial amounts of money they put into patenting their medical devices. An SME representative has stated,

> "Patent protection and intellectual property is a big barrier. It really is and we just don't have the money to fight the big companies. If a big company did come along and copy what we've done, they have the deep pockets to fight us and drain your resources no matter how many patents you have. And each patent is costing me between $30,000 to $50,000.... So now the board has decided we need to patent in America and western Europe. Anywhere else is a waste of time, even in Australia is a waste of time, because Australians aren't going to copy. They're only 2% of the market and too few Australian companies. There is plenty in America and America has a vicious market. The Europeans are ruthless as well and the Chinese don't care."

Due to the experiences the SMEs had, some are no longer willing to patent their medical devices in Australia. Instead, they file their patents only in larger and more competitive markets, such as North America, Europe, and China. The benefit does not outweigh the risk and the cost to patent a device in Australia is not deemed worth by the SMEs.

2.1.7 Lack of affordable sterilisation bureaus

Sterilisation is an important procedure for most medical devices and it is especially important for implantable devices. Most large manufacturers own and operate sterilisation equipment, whether they use ethylene oxide, gamma ray irradiation, or autoclave sterilisation procedures. For SMEs, however, there are only 3 bureaus in Australia that provide this service and in these places,

> "The sterilisation cost is enormous, as you pay for the entire volume of the machine. If you cannot sterilise multiple devices at once, each sterilisation process is $5000". This directly increases the cost of the medical device substantially for the patient and the reimbursement body. A SME medical device manufacturer states, "sterilisation facilities are a significant productivity issue in the country, let alone in MedTech. There is an acute shortage of sterilisation facilities. If you want anything sterilised, it's a monopoly."

2.1.8 Funding for SMEs

Acquiring funding for SMEs is a conventional problem in Australia and not specific to the 3DP medical device industry. It is negatively affecting innovative SMEs that are looking to invest in manufacturing equipment, expand overseas, and protect their Intellectual Property (IP). And it is still surprising that SMEs in medical device industry are facing the lack of funding, because the medical device industry is to some extent the 'convergence' of three strategic growth opportunities that CSIRO's road map have identified: additive manufacturing (3D Printing), precision healthcare, and advanced materials [6, 7]. This creates a barrier for SMEs. One SME representative who was looking to establish a manufacturing facility states,

> "The biggest problem we have in all of this is finding the funding. In Europe you can get a 3D Printer at 5 % interest rate and the bank will give you the money right away but here, you won't get approved for a loan. We had to raise equity and it was really tough to raise equity in a market people aren't familiar with. We thought it would take 3 months, but it took 9 months."

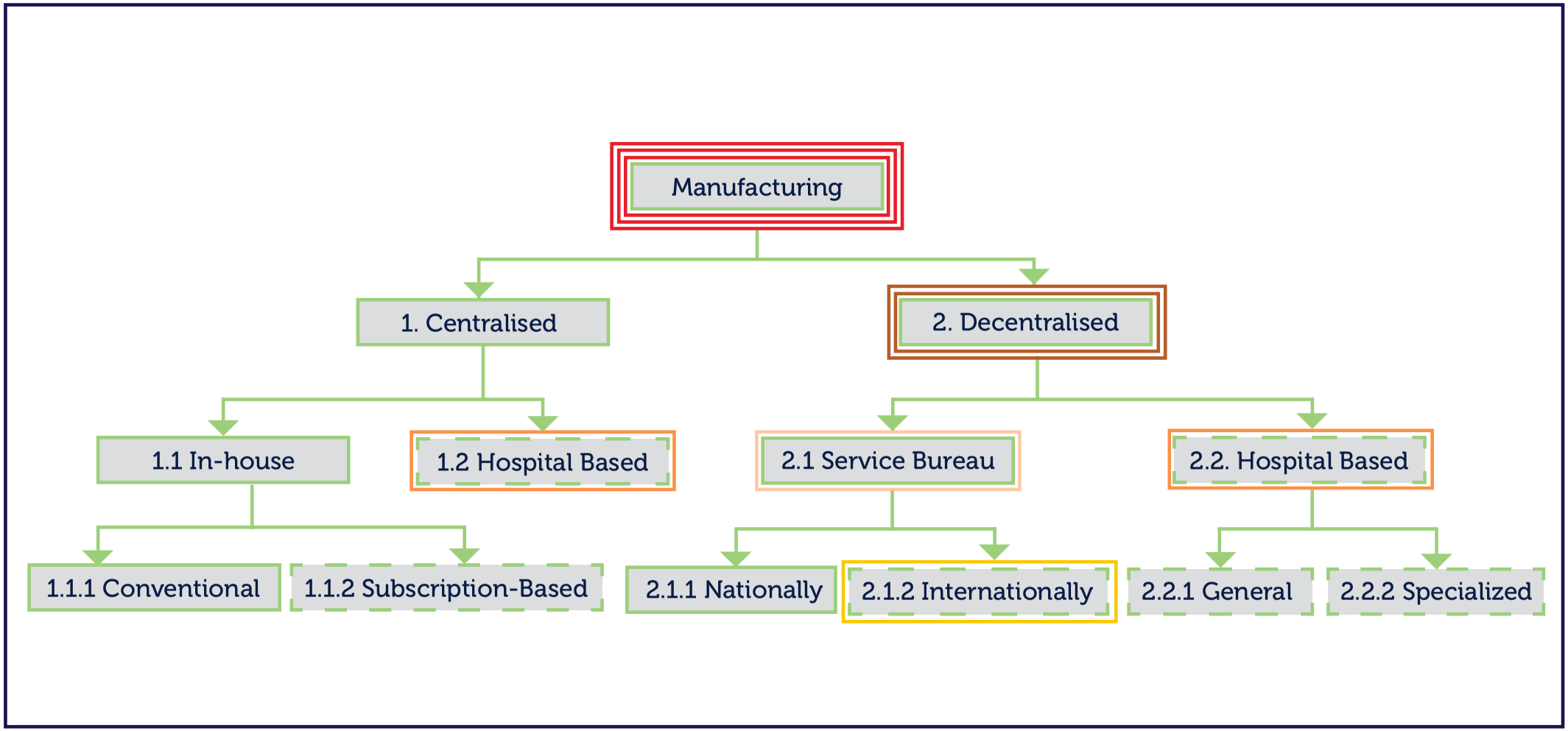
2.2 How Barriers Affect Business Models

The barriers explained in section 2.1 have implications in regard to the business models described in section 1 of the report. Stakeholders have expressed where the barriers pose a threat to both current and future business models. Some barriers pose an immediate threat to all types of business models but others were discussed to be barriers for certain types of business models. Moreover, some barriers are a threat to current business models, while others are more of a threat to future potential ones. In this section, it will be discussed how the aforementioned barriers impede the business taxonomy of section 1.

BARRIERS:

- Lack of surgeon 's adoption
- Lack of insurers' endorsement
- Protection of IP
- Funding for SMEs
- Liability issues
- Quality concerns
- Lack of Sterilisation Bureaus
- Lack of global Harmonisation of Regulatory Requirements

Figure 2. Impact of Barriers on Business Models



Lack of surgeon's adoption

Surgeons, SMEs and researchers have deemed the lack of surgeon adoption as an immediate barrier towards the adoption and diffusion of 3DP medical devices. It is clear that without surgeon adoption, there will not be enough demand, hence the businesses won't pursue 3DP medical device manufacturing, regardless of which types of manufacturing are in place (centralised or decentralised ones). This barrier essentially affects both larger firms and SMEs.

Lack of insurers' endorsement

Insurers' endorsement of the technology is critical in 3DP medical device manufacturing, similar to surgeons' endorsement, regardless of which types of manufacturing are in place. It is particularly important for SMEs that invest most of their time and money to satisfy medical device regulations. The low return on investment limits companies from innovating in the industry because the required resources (such as capital and time) are quite high in order to conduct R&D, satisfy TGA regulations, and prosthesis list evaluation before generating income.

Protection of IP

The protection of IP has been posed to be a barrier with financial ramifications but has not ultimately hindered the stakeholders in the design and manufacturing of their medical devices. This barrier is closely linked to the Funding for SMEs, as funders expect to have some I.P. protection, such as patents for the SMEs product. The development of the patent application is a costly process and often requires spending tens of thousands of dollars which SMEs do not have if they are new entrants to the market. This can create a Catch-22 scenario[2], with SMEs requiring funding to apply for the I.P. protection and the funding bodies requiring the I.P. protection before they commit their resources.

Funding for SMEs

The lack of funding for SMEs will impact both centralised and decentralised business models, depending on the services or products that the SME provides. For example, an SME that is looking to invest in 3D printing, post processing, and sterilisation equipment for a centralised manufacture model will be severely affected as the capital required could be in excess of one million AUD. An SME, that uses a decentralised manufacturing business model, might look to manufacture offshore, outsourcing the manufacture, and sterilisation in the targeted country to reduce logistical costs. That would also require funding to extrapolate their Australian patent to the targeted country, as well as satisfy all regulatory requirements.

[2] By the Catch-22 scenario, we are formally referring to a dilemma or difficult circumstance from which there is no escape because of mutually conflicting or dependent conditions.

Liability issues

The issue of liability with decentralised manufacturing has been posed to be an intermediate barrier. It is something to be kept in mind by SMEs that follow the decentralised business models. However, it does not display any prevention of a business model but has made current SMEs very selective about the parties contributing in their supply chain to ensure that the QMS procedures taken, pose the lowest risk possible. The effect of the surrounding liability issues would pose a restriction on how many bureaus can be sought by SMEs to engage in business with but stakeholders have not voiced any impedance to their business by the liability issues with decentralised manufacturing.

Quality concerns with hospital-based manufacturing

Quality and economic feasibility of hospital-based manufacturing exclusively affects business models 1.2 and 2.2. Most stakeholders did not rate this as an immediate barrier because there needs to be many stages of development before it is a viable business model. Some of these developments include studies that determine the economic feasibility of the business model. There will be money saved compared to the current inefficient method of sending surgical loan kits in various sizes to the theatre for one operation. However, whether that saved amount covers the costs of the machinery and the trained staff is still needed to be investigated.

Lack of Sterilisation Bureaus

The lack of affordable sterilisation bureaus affects the SMEs that use service bureaus to manufacture, post-process, and package their devices. Large manufacturers are typically unaffected due to the fact that they have the capital to purchase their own sterilisation equipment. Most interviewed stakeholders see it as a temporary barrier, one of whom states,

> "Maybe that is just a stage in the evolution of the industry because there are very few SMEs looking to sterilise their parts. It might be a barrier now but surely if it's a large problem it can be fixed, someone enterprising will start a business in that."

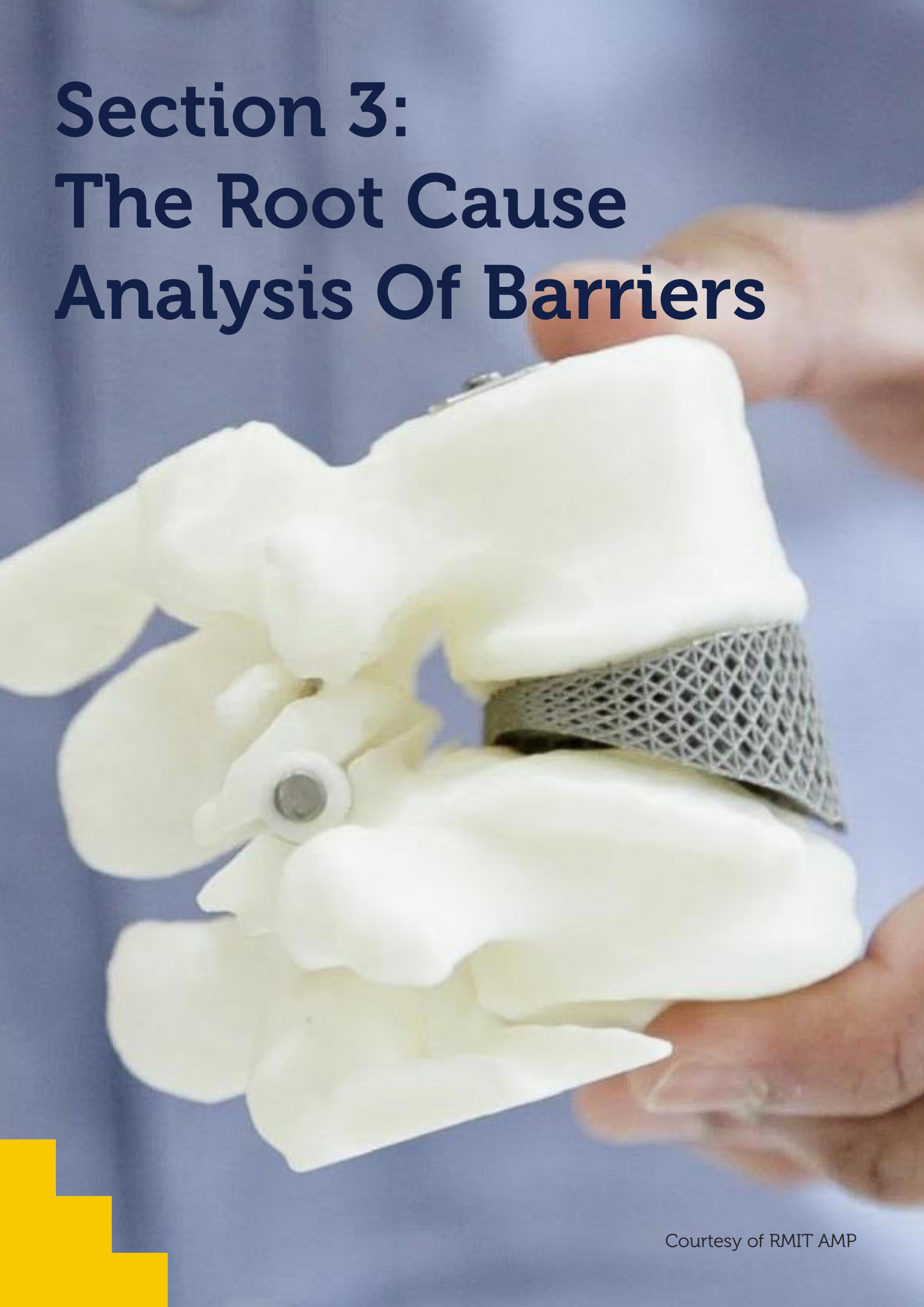
Lack of global Harmonisation of Regulatory Requirements

Stakeholders agree that this barrier is not an immediate threat to their business but will pose future issues once their business expands into a global scale. An SME member has declared,

> "That's our aim. To go global since Australia is only 2% of the market"

This reflects that in order for Australian businesses in the medical industry to be profitable, they do need to go global to take full advantage of revenue opportunities and to be able to compete against global competitors.

Section 3: The Root Cause Analysis Of Barriers



Courtesy of RMIT AMP

SECTION 3 - THE ROOT CAUSE ANALYSIS OF BARRIERS

In this section, we will dig deeper into each identified barrier to investigate where these barriers really come from. We will do it through Root-Cause-Analysis.

3.1 Lack of Surgeons' Adoption of 3DP Medical Devices

Lack of surgeon endorsement has been mentioned by a variety of stakeholders to play an immediate and substantial barrier to the current adoption and diffusion of 3DP medical devices in Australia. This is because surgeons, alongside the patients, are the ultimate end-users of the 3DP medical devices. Through the interviews, a deeper insight into 'why there is a lack of surgeon endorsement' was obtained. As stated by the stakeholders, and in particular a surgeon, the root causes of lack of surgeon adoption are based on

1. Lack of evidence
2. Hesitancy to change
3. Lack of creativity in medicine's educational system.

Each of these aforementioned root causes will be discussed in the following section.

3.1.1 Root causes

Lack of Evidence

Non-adopting surgeons not only need clinical evidence, but also they often need 'long-term' evidence on the effectiveness of novel 3DP medical devices. For example, as one of the early adopting surgeons of 3DP device said,

> "The feedback we get when we go to conferences and we have a table to present our stuff, they [other surgeons] say "where's the evidence? This paper is only 3 years old; I want 10."

However, since the implantation of 3DP implants is a recent advent and the technology is still in constant change and development, surgeons in support of 3DP medical devices adoption believe that it is redundant to ask for such long-term evidence. A supporting surgeon stated,

> "In 10 years, this device won't exist anymore because we'll have a better device. And testing a device that's 10 years old makes no commercial sense. No one is going to pay the researcher to look at a 10-year-old device that's not on the market because it's useless to publish"

In any rate, it is complex to determine the root cause of the lack of evidence required by surgeons. This is because while surgeons require more evidence (which can be produced primarily by medical device manufacturers), the manufacturers, at the same time, require surgeons' endorsement to produce further medical devices. This signifies a complex and interrelated 'Catch 22' scenario. Hence, this root cause and its associated solutions will be discussed in detail in a dedicated Section 4 of this report.

Hesitancy to change

Hesitancy to change has been listed as a prominent root cause of the lack of adoption of 3DP devices by surgeons. Digging further into it, hesitancy to change has its own root causes:

i. Due to the Tall Poppy syndrome

ii. Indirect pressure from surgeons in related areas

iii. Jealousy amongst surgeons

iv. Surgeons being time poor

Firstly, the hesitance to change among surgeons can be partially due to the Tall Poppy syndrome, which is a typical generic cultural aspect in Australia. The focus could be on either the surgeon or the 3DP medical device industry. Secondly, there is indirect pressure and resistance from the other surgeons in related areas. 3DP devices offer direct solution and new routes for surgical methodology, which raises 'hesitance to change' for other surgeons in related fields. This even seems to pose a threat to the current routines of the other surgeons in related fields. Such an issue was stated by an interviewed surgeon,

> "So we were producing the surgical morbidity from an 8-hour procedure to a one-hour procedure. Fully functional jaw with teeth. Whereas the current model is taking a leg bone and trying to reconstruct a jaw, with no teeth, in where the patient is in hospital for 2-3 weeks and half of them get infected legs. So, there's also the morbidity of that. So, I introduced to them [hospital] here is a jaw we could do and suddenly the plastic surgeons said "No, you're going to take our work. Don't worry about the patient but it's our work" and I would argue "What about the patients themselves?", "No that's not important, the important thing is the politics and we [plastic surgeons] have a job to do and you are here to kill it."

As an interviewed researcher stated, these ties with surgeons are risk-averse and conservative in nature. Thus, causing them to look only towards what has been well proven before being practised.

Third, 'jealousy' among fellow surgeons seems to be a related root cause for the lack of widespread adoption of the 3DP among them. As one of the stakeholders (surgeons) stated,

> "The closer they are to you, the less likely they are to adopt it. "Surgeon X has made a device but I'm not going to use it because the wide spread adoption of the device makes Surgeons X famous. I'm jealous of the fact that he's made it and I don't want him to be famous."

This reflects the sentiment that surgeons would not adopt the devices partially because they do not want to endorse another surgeon that is willing to offer new methodologies of a current surgical practice, which is the patient specific implementation of 3DP medical devices instead of modified off-shelf implants. And on top of this, the late-adopter surgeons seem to have an even harder time to endorse and adopt a technology that is associated with a fellow surgeon's new start up.

And finally, the forth root cause is the fact that surgeons are typically time poor. According to an interviewed researcher, surgeons are very busy and they prefer to do what they already know best.

> "They rather do what they know than take the time to jump into a new method/technology. That goes down to adoption of technologies"

As an interviewed researcher stated, this goes in tandem with surgeons being conservative in nature. They are slow to adopt because the adaptation would take a lot of their highly finite time in their high demand schedule.

Lack of creativity in medicine's educational system

Another root cause for the lack of surgeon adoption is the lack of creativity in medicine-related educational system. Creativity, in principle, is about bringing new solutions out of new avenues of thought and challenging the status quo. However, as an interviewed surgeon who is also a founder of an SME in 3DP devices stated,

> "There is an issue of lack creativity in medicine, where it's very textbook based and the opposite to art school where creativity is encouraged. That's stopping us from progressing and we need more people to be relaxed about opening up their minds and not closing it. The 6 engineers I have employed are all under 26, I could have gotten older ones with a lot of experience, but they would have resisted. The young ones came out and wanted to learn whatever I needed done. They were very adaptable. They are here to learn and want to continue to learn"

The concern of the lack of creativity with medical professionals, such as surgeons, has been deemed to be a reason that surgeons close their minds to implementing new possibilities offered by 3DP implants for patient specific applications. The consequence of surgeons who do not adopt 3DP devices due to textbook approaches is the perpetuation of implanting only off-the-shelf implants because that was what they were taught. Furthermore, the lack of creativity in medicine has left the interviewed surgeon hiring biomedical engineers who were beyond a textbook- approach methodology and were also willing to adapt to new techniques to address any given project

Courtesy of RMIT AMP

3.1.2 Solutions

Solution 1: Endorsement from key surgeons

As noted above, tall poppy syndrome is detrimental for surgeons to adopt 3DP devices. This syndrome is not only a part of surgeons' culture, but it also is a part of Australian culture. Nevertheless, there are proposed solutions to address it. It was discussed by an interviewed stakeholder that tall poppy syndrome can be abrogated by creating and spreading an in-favour influence to the adoption of a new technique/technology which is endorsed by the 'key' opinion leaders (i.e. high ranking and respected surgeons). Accordingly,

> "Then they [non-adopting surgeons] will think "because of this big professor is using it then maybe I should start using it". Then comes in the FOMO syndrome; Fear of Missing Out. Then they all start getting on board. So, the best thing to do is to get key opinion leaders on board. Without these key opinion leaders coming on board, it's very hard to convince the common garden surgeons to use anything."

It was also mentioned that having key-opinion leaders from far parts of the world would also help the adoption of 3DP devices by surgeons.

> "The further away the surgeon is, the more likely they are to adopt it. Like the professor in Glasgow, a world-respected authority; "I heard about you, I've come to see you". Then my [surgeon] friends possibly will get the FOMO here. And in general, once the ball gets rolling with key opinion leaders in every nation adopting, the Australian's will start to use it. But not before. They will follow, they will not lead."

Having the endorsement from all over the world would perpetuate a global level reputation in which the Australian surgeons would want to have a part and therefore can dissolve tall poppy syndrome and increase the adoption and diffusion of 3DP devices.

Solution 2: Collaboration between stakeholders

Collaboration between stakeholders has been another discussed solution to address the lack of surgeons' adoption. Collaboration between stakeholders offers communication between them to showcase each member's capabilities and what the other stakeholder exactly needs. Having surgeons collaborating alongside researchers and industry members has been a key point for medical device SMEs. However, SMEs are not the only beneficiaries. The surgeons would benefit from this as well.

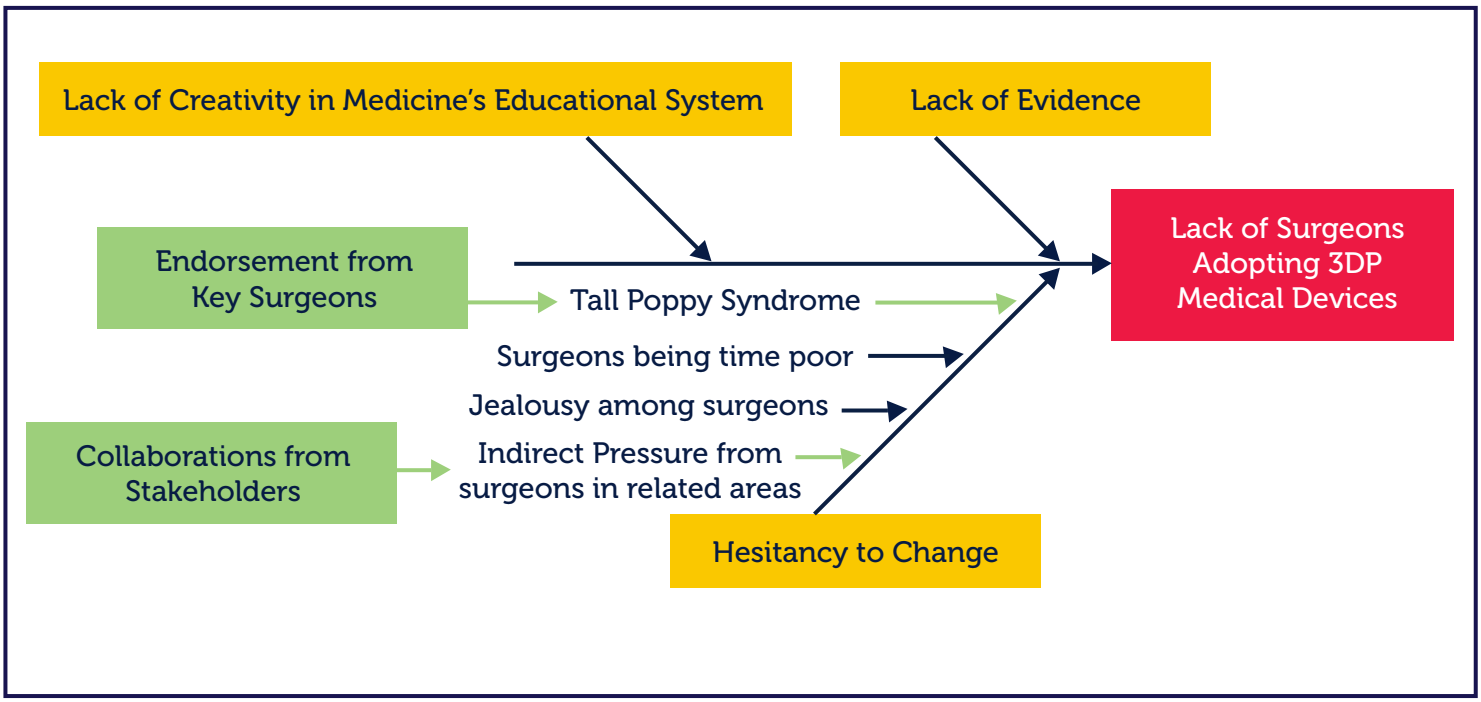
As a researcher has stated,

> "The BioFab lab is successful due to its design, where you have the medics and engineers working together. That's where you get the greatest adoption; the co-designing. It's important that surgeons collaborate with manufacturers and designers."

What the surgeons would be immediately appealed with, would be knowing that their concerns could be addressed by a team of engineers and researchers in which every member would have input on the development of a 3DP medical device.

These recommended solutions target the root cause of the surgeons' hesitancy to change and they are depicted in figure 3. The recommended solutions for the 'Lack of Evidence' root cause will be discussed in section 4.1.

Figure 3. Root-Cause diagram for lack of surgeons adopting 3DP medical devices with recommended solutions



3.2 Lack of Insurers' Endorsement of 3DP Medical Devices

Insurers are generally hesitant to cover custom-made medical devices manufactured in low volume with no evidence of cost-effectiveness. This results in difficulties in getting medical device reimbursement via prosthesis list, which creates barriers (in terms of being more expensive) for medical device manufacturers and patients with private health insurances. This is explained in detail in sections 2.1.2 and 2.2. The lack of insurers' endorsement stems from three root causes:

1. The lack of clearly favourable clinical and economical evidence
2. Disruptive devices not fitting into the categories of existing devices
3. Custom-made device exemptions

3.2.1 Root causes

Lack of Evidence

The first root cause for low insurers' adoption stems from the lack of favourable clinical and economical evidence, which is, interestingly enough, also a root cause of the lack of surgeons' adoption (Section 3.1.1). As a private insurer representative stated,

> "Give us the evidence that this provides at least the same value as current options. The committee at the prosthesis list want proof of value and comparative value; clinical evidence is not just for safety and effectiveness of the device but also proves it's worth (financially)."

Similar to "lack of evidence" noted by surgeons in 3.1.1, this root cause is interrelated and signifies a complex 'catch 22' scenario. Hence, the root cause will be discussed in detail in the dedicated Section 4 of this report.

Disruptive devices not suitable for established categories

Those firms who have developed novel devices solving existing problems in innovative ways are facing a roadblock when it comes to getting their devices reimbursed by private health insurers. For a private health insurer to cover the cost of a device, the device needs to be in a list called 'prosthesis list'. It is the list of surgically implanted prostheses that the private health insurers must pay benefits for under three conditions: First, if the patient has appropriate health insurance coverage; second, if the device is administered as a part of hospital treatment; and third, if the surgery is listed on the MBS. To have your device enlisted on the prosthesis list, a committee of 21 members, 2 of whom being private health insurance representatives, assess the device and makes recommendations on the most clinical and cost-effective devices.

However, if a device is radically new (and innovative), it is often difficult to classify the device in the established categories of prosthesis list. This poses a problem for insurers' reimbursement, particularly for SMEs. In the case of OMX Solutions for instance, they developed a custom anchor for the jaw joint instead of letting it hang unsupported, causing pain, strain and potentially further injuries on surrounding muscles and bones.

> "The jaw anchor is so new that they don't know where to put it and if a new Medicare number is needed then they're not going to be happy to quickly act. They want proof; lots of proof and patience. Then the TGA says you can't do more than 6 patients because you need to have it proved first"

A regulations expert from a large medical device company further provides reasoning of the root cause

> "If it doesn't fit into anything at the moment, that is already a difficulty to determine it's worth for reimbursement."

Custom-made device exemptions

It is unanimously pronounced by stakeholders that the custom-made medical devices regulatory process requires revisions [1].

> "Regulatory processes need to be matched accordingly with the risk associated with the medical device"

One of the reasons why insurers are not ready to adopt 3DP medical devices is because there is room for manufacturers to exploit the regulatory procedure for custom-made medical devices and not provide the appropriate high degree of risk management for a high risk device.

> "The concern for insurers is that major suppliers would abuse the loophole of custom implants being exempt to mass manufacture, via 3D printing, to sell unregulated devices claiming it's custom-made"

Currently, the custom-made devices are not required to undergo premarket approval assessment. They need to comply with the Essential Principles of medical devices, however, they do not require a certified QMS to be established. It should also be noted that an SME representative thinks the insurers understand that for true one-off unique implants, the custom-made medical devices need to be supported by insurers. They just express their concern that if the device is labelled 'custom-made' under the guise of being 3D printed, there is a potential for exploitation of the custom-made medical device regulations.

3.2.2 Solutions

Solution 1: Planning for Reimbursement during early stages of product development

For the case of disruptive devices that do not fit into the categories of existing ones or are not relatable to the existing devices on the market, the recommended solution is that manufacturers of 3DP devices keep the regulation and reimbursement in mind since the early' stages of their product development. This can aid in formulating the proposal to the Prostheses List Advisory Committee (PLAC). The proposal can clinically and financially investigate the effectiveness of the 3DP medical device. Such investigation can analyse the ongoing costs that might stem from further injuries if preventative measures are not taken and therefore, can comprise the comparison of using the device versus not using the device by patients.

Ultimately, insurers will pay for the demonstrated improvements in a patient's outcome. A hospital representative states,

> "Maybe if it [medical device] really works, that would be fine, and it could substitute an existing technology or method of treatment that might have ongoing costs. People discovering how to make things cheaper in the future is also a possibility. I do think that in the end, for these devices to get onto the market they need to be paid for [by private health insurers], who are very conservative with what they are willing to pay for."

A representative of insurers also importantly added

> "What I'm disappointed in is not in the evidence, or lack thereof, I am disappointed that somebody has not yet tried presenting the evidence in a way that there is a light at the end of the tunnel"

What the PLAC committee is looking for is both clinical evidence, i.e., safety and clinical effectiveness, and also financial effectiveness of the new devices. Moreover, if the PLAC requires more evidence than what is provided from the 'default' 6 patients who received the implants via custom-made medical device exemption, then the manufacturer must proceed with the ARTG enlistment for the medical device, giving the ability to manufacture more devices for more patients to retrieve more data.

Solution 2: Collaboration with the TGA's Consultation papers

The recommended solution to address the custom-made medical devices exemption, which increases the insurers' hesitation to endorse the device, is that all stakeholders, particularly insurers, participate in the consultations organised by the TGA and the IMDRF.

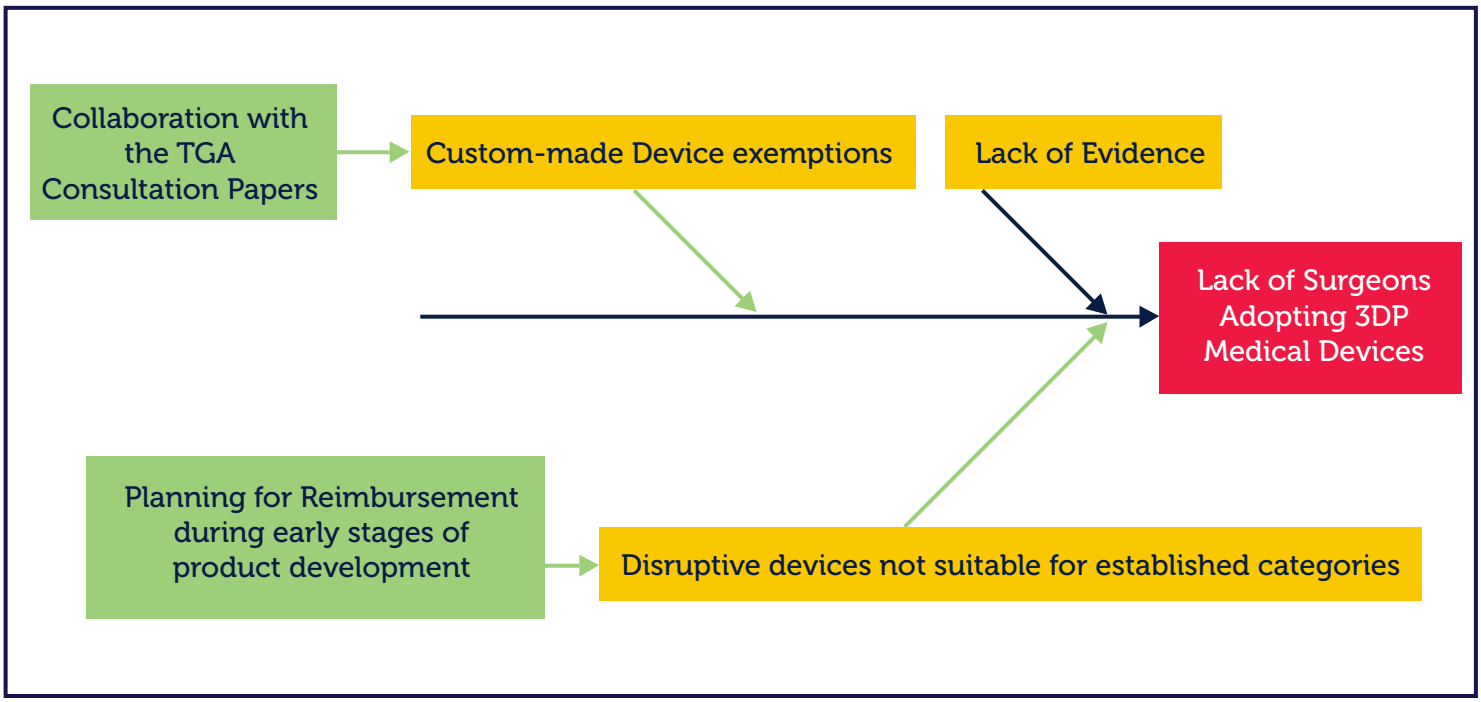
Since August 2017, the TGA has actively sought feedback on how personalised medical devices are regulated in Australia and it has taken initiative to globally standardise definitions through an IMDRF working group. Thus far, there have been two consultation papers, the latest of which proposes adopting new definitions for personalised medical devices with the three subcategories of 'custom-made medical devices', 'patient-matched medical devices', and 'adaptable medical devices' [8,9].

If the latest proposal is accepted and becomes a regulation, medical devices that fit the new 'custom-made' definition will still be eligible for exemption. However, there is an additional regulation that allows the TGA to inspect device manufacturing sites. The second category of 'patient-matched medical devices' will no longer be eligible for exemption and will require the standard conformity assessment based on the risk classification of the device. The third category of adaptable medical devices will also require a standard conformity assessment because it will cover mass-produced devices that have the ability to be modified at the point of care.

The consultation period was finished on the 31st of March 2019 and the submitted feedback is likely to be posted on the TGA's website by the end of 2019. In general, participating in the discussion that will form the new regulations will reduce the risk associated with the custom-made medical devices and increase the probability of health insurers' endorsement if the device is regulated accordingly.

To address the barrier of the lack of insurers' endorsement in 3DP medical devices, three root-causes were identified. Solutions to the root-cause of 'lack of evidence' will be discussed in section 4.1. For the root-cause of 'custom-made exemptions', the recommended solutions was collaboration with the TGA's consultation papers. And finally, for the root-cause of 'disruptive devices not being suitable for established categories', the recommended solution of planning for reimbursement during product development was proposed. This is depicted in figure 4 below.

Figure 4. Root-Cause Diagram for Lack of Insurers' endorsement in 3DP Medical Devices with recommended solutions



3.3 Liability Issues With Decentralised Manufacturing

As noted in Section 1, decentralised manufacturing involves outsourcing parts of the manufacturing process to an external party, such as a supplier. In such situation, the liability issues regarding 3DP medical devices that were designed, manufactured, and sterilised by different stakeholders stem from the uncertainty of who is liable for an unfortunate case of a medical device failure. Device failure is generally placed on the seller of the device via strict liability in tort law. An example of this was given by an SME,

> "Only 20% of Boeing's parts are made by Boeing but if something happens, the liability is fully on Boeing"

Tort law is also decided by discussion through case law. Therefore, if the seller of the device could identify what made the product fail and which member of the supply chain is responsible, then that would be decided in a court.

By further digging into the reason of concerns with liability for decentralised manufactured devices, three root-causes have been identified:

1. The lack of enforced requirements to have a valid QMS employed for medical devices that were regulated through the 'custom-made' exemptions
2. Problems with the potentially inefficient quality testing of medical devices, especially for low-volume devices
3. Concerns with patient data confidentiality

3.3.1 Root causes

Lack of QMS for custom-made medical devices

The ISO 13485:2016 QMS section 4.2.1 states, "The organisation shall apply a risk-based approach to the control of the appropriate processes needed for the quality management system." Currently, under the TGA's custom-made medical device regulations, manufacturers are exempt from having a certified QMS employed. This greatly increases the risk of medical device failure and causes strain between the stakeholders responsible for decentralised manufacturing, namely the medical device designer, manufacturer, and sterilisation bureau.

Having a valid QMS for the manufacture of medical devices, according to ISO 13485, would effectively apply monitorisation of medical device design, manufacture, sterilisation, and worker training to reduce the risk of device failure which is the source of all liability concerns.

Insufficient testing of custom-made medical devices

Isufficient testing is a high concern for devices that are produced in low volume. Typically, for mass manufactured devices, the liability concern is fairly low due to the intensive fatigue and statistical testing for process validation before premarket approval. Unfortunately, the typical manufacturing n=100 functional medical devices for mechanical testing for producing one patient specific device, is not practical. Therefore, some alternative methods of verification are being explored, as discussed in part one of the report in section 4.3.4 [1]. In response to the new ways of process validating to overcome liability as a manufacturer, an insurer states

> "What you would be doing is creating a precedent for manufacturers to be able to create devices and avoid liability because they thought they were doing the right thing. Intent does not count."

They follow, stating,

> "As soon as you can prove that it is a good device, then liability becomes much less of a problem"

The enhanced liability concerns could also affect surgeons, hospitals, and insurer adoptions. A 3D printer manufacturer states,

> "We need certification that the part is good, it is not damaging to health and we give the confidence to surgeons, insurers and hospitals. That certification is not there yet."

Patient data confidentiality

Liability issues can also be related to concerns about patient-data confidentiality. The concern regarding patient data confidentiality was originally raised in response to the implementation of General Data Protection Regulation within the European Union. Keeping patient data confidential is important for all the stakeholders involved because a breach could violate the important trust between patients and clinicians. In decentralised manufacturing, when there are multiple stakeholders involved in producing an implant for a specific patient, the risk of patient data being breached is inevitably increased. In further interviews with stakeholders, they note that it is important to maintain patient-data confidentiality There are current methods being employed to anonymise and encrypt confidential patient data, such as removing all personal information and assigning the patient a number as soon as an order is received.

3.3.2 Recommended Solutions

Solution 1: Device designer holds all liability

The first recommendation is about the proactiveness of device designers, who are often the Intellectual Property holder as well. They can typically perform Quality Assurance on every stage of production (performed by an external service bureau) before the final product release. Such solution has already been adopted by many Australian SMEs that use a decentralised business model, which is however, relatively unknown to the rest of the industry. A general manager of an Australian medical device manufacturing SME specified,

> "For our business, to manage the end product, we would assume we are the manufacturer; we own all the designs, specifications, final QA based around these products release. We assess the reports of every stage of the device during manufacturing. e.g. porosity of its texture, polish, etc. In addition, the main criteria in being a part of our supply chain is whether you have ISO13485 certification, skill and qualification to manufacture a 3DP medical device, a robust QMS and cyber security"

Although this solution of being a proactive designer in taking the responsibilities of the entire product works domestically in Australia, this could prove to be difficult if the manufacturing were to be done overseas for international patients.

Solution 2: Implementation of a unique device identification (UDI) system

The second solution was recently proposed by the TGA in a consultation paper titled 'Proposal to introduce a Unique Device Identification (UDI) system for medical devices in Australia'. The UDI system proposed by the TGA would provide improved traceability of medical devices in the supply chain. This will result in faster and more accurate identification of problems, better quality evidence-based data associated with the manufacturing specification and patient clinical information, and a reduction in medical and surgical procedural error. Thus, the healthcare professionals can trace a device and its characteristics quickly.

In the TGA's proposal, custom-made devices are exempted from the UDI system. However, it was not clarified whether this exemption is only for devices made under the 'custom-made' provisions, or for all customised 'patient-specific' devices, including devices that are listed on the ARTG. If it is the former, ARTG enlisted custom-made devices could theoretically benefit from the improved traceability, especially those made by decentralised manufacturing.

This could clarify liability, create harmonisation between other regulatory systems such as the FDA and the EU regulations, and provide enhanced effectiveness of post-market safety-related activities. The means of implementation of the UDI system, in case of being approved, is the key factor on whether it will be beneficial to the industry. An insurer states,

> "What you are saying sounds like a registry and if they make it easy enough to have a sort of registry, then that can only be a good thing. What they might do [instead] is make it so hard that it is actually impossible for anyone to comply in a cost-effective manner. Is it a good thing? It depends how much it is going to cost"

However, we would like to maintain that if all customised 'patient-specific' devices are exempt from the UDI system, including devices that are already listed on the ARTG exception, the implementation of the UDI system will have no effect on the barrier of decentralised manufacturing liability.

Solution 3: Anonymisation of patient's data

Patient data confidentiality has been raised as a cause of liability concerns. This is because it can enable multiple stakeholders to have access to patients' data which happens via a cloud system for practicalities. Generally, using a digital platform increases the risk of vulnerability to hacking and leaks. However, interviewed SME members and surgeons have proposed a solution to ensure maintaining patient data confidentiality. An SME founder whose company uses patient data and outsources manufacturing stated,

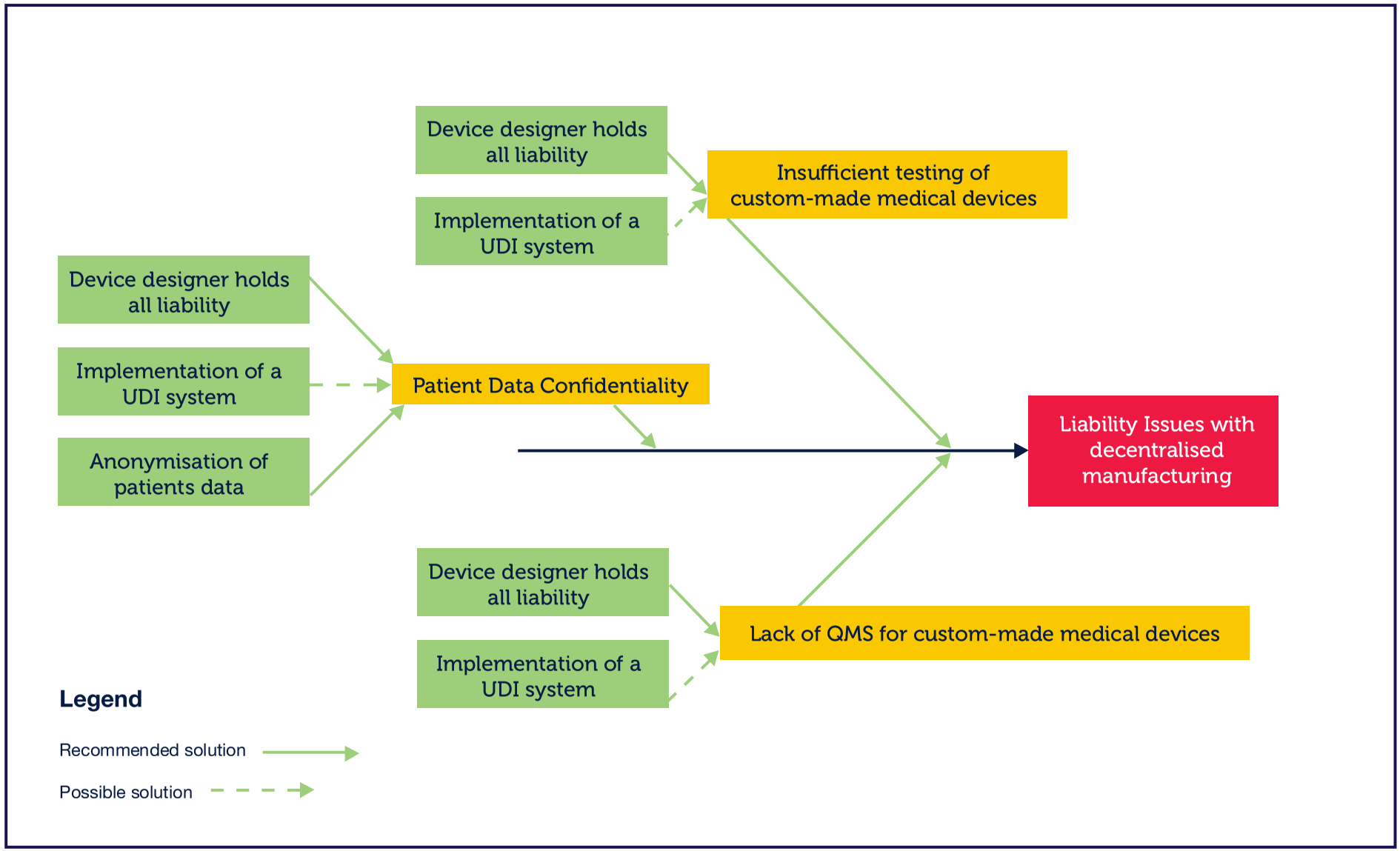
> "You have to be smart about it and you can codify it. When you get a file, you don't have to label it 'Grace Jones', just give it a number. Anonymise it. That way the company [manufacturer] doesn't have to know who the patient is. That is easily fixed. Just send us the hospital number; we have no access to hospital bases"

Another SME representative states,

> "At least for our device, as soon as the order is received, they get allocated a number. If you look at patient records, all the parts in the production process from receiving an order to then despatch, the patient is a number, not a name. That includes the entire design process. If someone hacked into our cloud computer, they will only see a number for the dental record. They will then have to hack into another system which has a whole lot of secure to try match a number with a name. That is how we treat that. The other thing is that, for a while, we had some records around other aspects of the patient, e.g. their sleep quality, and we attached a name. When we were doing that, we implemented a HIPAA compliancy system which was in retrospect not the direction we wanted to go so we have gone away from that. Now, the only patient records we have is nothing around their sleep problems, it is purely around the dental records and we separate the name and just have a number"

The recommended solutions to address liability issues are depicted in figure 5. This figure identifies ‘Device designer holds all liability’ as a solution that addresses all liability root-causes and would ultimately eliminate liability issues as a barrier. The implementation of a UDI system is noted as a possible solution because it is dependent on whether the TGA enlists the custom-made devices in the proposed system. To address patient data confidentiality concerns, the anonymisation of patient data is being used and it is recommended to be used by all stakeholders other than the hospitals and surgeons.

Figure 5. Root-Cause Diagram for Liability Issues with Decentralised Manufacturing with recommended solutions



3.4 Quality And Economic Feasibility Issues With Hospital-Based Manufacturing

All interviewees had a consensus that the in-hospital manufacturing of class IIb and III custom implants is unfeasible for the foreseeable future. The root causes of their concerns can be broken down into the aforementioned

1. Quality concerns
2. Economic feasibility

3.4.1 Root causes

Quality concerns

Surgeons, manufacturers (both SME and large ones) and researchers who have investigated the case of in-hospital manufacture were dismissive that implantable medical devices would be manufactured in hospitals. The primary reasons are the quality concerns and the lack of QMS certification. As a researcher in the field note

> "The purpose of the hospital is to cure you, not to manufacture."

An SME owner who manufactures 3DP implants states,

> "The TGA would never allow independent printers in hospitals that haven't been certified. Our certification process, which is ISO13485, has taken us 3 years and has cost us hundreds of thousands of dollars to get certified as a medical device company."

Another stakeholder from a large manufacturing company further iterates,

> "Manufacturing plants have clean rooms, people dressed in the right way, etc. Hospitals pose the concern of people going back and forth (out of the manufacturing site), being at the mercy of funding and creating a hard to control specific area for manufacture."

Originally, the idea of Just-In-Time-Implants manufacturing had the perspective of manufacturing a custom-made medical device while a patient was in the theatre. However, in reality, there are far more steps involved to manufacture a medical device including post-processing, polishing, and sterilisation, all of which involve equipment to be kept in certified manufacturing cleanrooms for which hospitals do not have capabilities yet. The updated aim of the Just-In-Time-Implants project is to reduce the waiting time for bone cancer patients after diagnosis.

Currently, the waiting time from diagnosis to operation is eight to nine weeks. The Just-In-Time-Implants project aims to reduce that to one week. If it is going to take approximately one week in time, the advantage of having the manufacturing equipment in the hospital is void. Manufacturing next to a hospital (rather than inside the hospital) would be a more feasible option instead. As a large manufacturer of medical devices states,

> "Personally, I would be surprised if hospital manufacturing happened. It would make more sense for us to manufacture nearby."

Quality concerns

The economic concerns with hospital-based 3DP implant manufacture depend greatly on the level of adoption of 3DP medical devices and its associated economies of scale. The expenses for the reassignment of hospital resources, manufacturing clean-room setup, manufacturing and sterilisation equipment, raw material storage, trained staff, and the certification and licensing will have extremely large costs, well into tens of millions of dollars. For that investment to pay itself off, most of the implantation surgeries conducted in that hospital and possibly nearby hospitals, would require the use of that manufacturing precinct and it must be cost-competitive to off-the-shelf implants. The problem is that currently, most 3DP medical devices are custom-made patient specific devices that are for extreme or rare cases, as opposed to every-person cases, where off-the-shelf devices are suitable. A health insurer, who has no preference where the device is manufactured, states,

> "If making it hospital based will increase the cost substantially, then that is simply not a good thing. Every time you increase the cost of a service, it forces you to deny funding other services"

3.4.2 Recommended Solutions

From discussions with all categories of stakeholders in the 3DP medical device industry, there is a widespread acknowledgement that manufacturing implantable medical device in-hospital is not currently viable, nor might be viable in short-term future using the current technologies available. This is particularly the case for high-risk medical devices (as opposed to low risk surgical models). This does not mean that it will never happen, because a future trend could be manufacturing tissue engineered implants using a patients' own stem cells which will need to be sourced from a hospital visit and likely cultured nearby. For the immediate future, however, two recommendations have been highlighted to stimulate the in-hospital manufacturing that eventually leads to the expansion of the 3DP medical device industry. The first is having hospital-based manufacturing for patient specific 3D printed anatomical (surgical) models, using FDM plastic printers for advanced surgery planning. The second recommendation is to have ISO 13485 certified manufacturing sites near or partnered with hospitals, acting as a connector of SME manufacturers to potential patients.

Solution 1: Hospital and manufacturer collaboration

Partnership and collaboration between hospitals and 3DP medical device manufacturers (including designers) could be a key step in stimulating the possible in-hospital manufacturing, which provides more custom-made medical devices to patients. This solution includes having custom-made medical device designers on-site in the hospital, enabling collaboration between the surgeon, radiographer, and custom-made medical device designer to potentially provide superior clinical outcomes and patient satisfaction. This initial step could eventually lead to in-hospital manufacturing under the condition that the clinical results are positive and it is cost-effective to invest in 3DP manufacturing technologies to provide a shorter lead-time of production.
This solution could also be beneficial to SMEs who are currently hindered by the convoluted referral pathway before they are connected to the patient they can help. An example provided by an oral maxillofacial surgeon was

> "For patients to reach us, they would go through a general practitioner doctor, to a dentist, to a radiographer, back to the dentist then to an oral maxillofacial surgeon, each time leading to a loss of possible patients coming to us"

Having a hospital and manufacturer partnership could help educate medical professionals on the capabilities of 3DP devices and rapidly connect SMEs to patients who could benefit from custom devices.

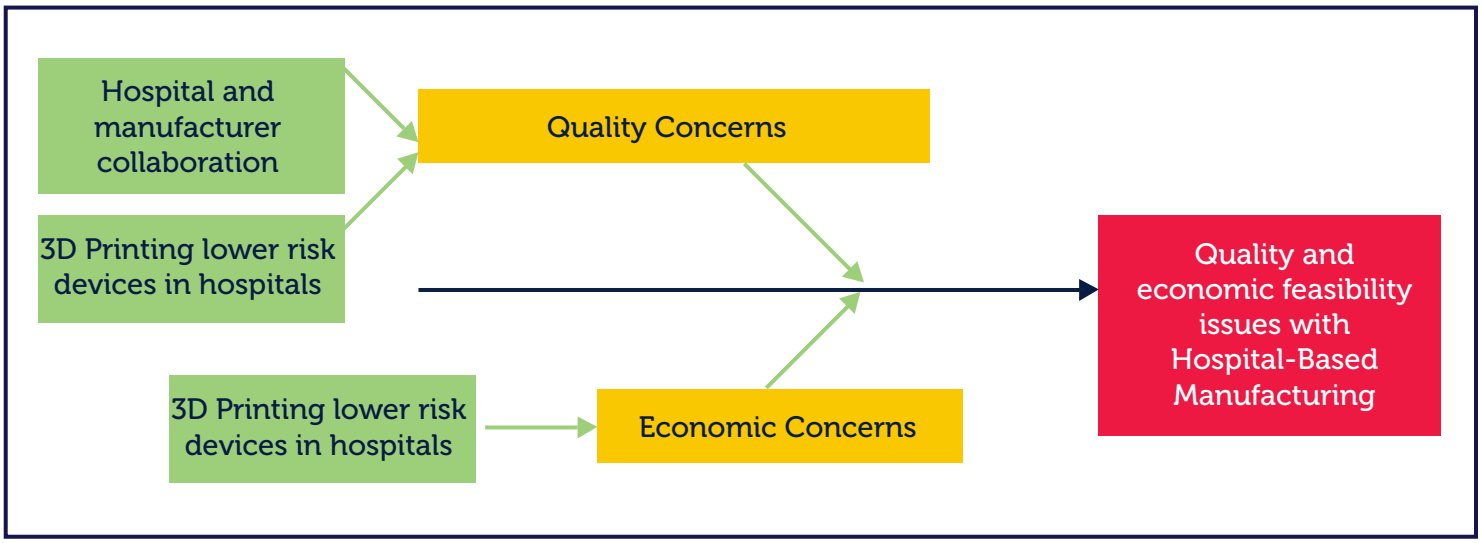
Solution 2: 3D Printing lower risk devices in hospitals

The second solution is simply to change the focus and ambition from 3D Printing of high-risk devices (e.g., implants) to low risk devices (e.g., surgical models). This way, the current concerns about the quality and economic feasibility of the In-Hospital manufacturing of 3DP devices would be alleviated. For certain applications, where operations are not straight forward, 3D printed surgical models have resulted in reduced operation times, improved anatomic understanding, and also improved patient understanding of their procedure [10]. This also leads to decreased risk since it lowers time spent under anaesthesia. It needs to be noted that, however, anatomical models could also potentially add risk if the model does not accurately represent the patients' anatomy. In the TGA consultation paper "Proposed regulatory scheme for personalised medical devices, including 3D-printed devices" published in February 2019, anatomical models with the purpose of patient diagnosis and surgical planning were proposed to be regulated as class IIa medical devices, the same as CT scans.

TGA further clarifies that if the device is for training or education purposes, it would not require to be regulated. Also, if hospitals or healthcare practitioners used a medical device production system to produce the anatomical models, and this production system was included in the ARTG, the requirement for conformity assessment evidence would not apply to them. Adopting this technology immediately links additive manufacturing to healthcare and enables benefits. It would require training for the radiography staff, which also most likely implies for new job creations. But more importantly, it could lead to more efficient surgeries and better patient outcomes.

The effect of each solution is visualised in figure 6. Hospital and manufacturer collaboration and the increase in adoption of 3D printing surgical models in hospitals leads to addressing some quality concerns with in-hospital manufacture. 3D printing surgical models in hospital will also lead to a more robust economic analysis to identify whether increased surgical planning methods definitively provide more cost-effective treatments for the healthcare system. That could eventually lead to hospitals being more open to adopt higher risk implantable 3DP medical devices for patient specific applications and if the volume is high, a hospital could either have on-site manufacturing or it can partner with a local manufacturer who can rapidly supply 3DP medical devices to the hospital.

Figure 6. Root-Cause Diagram for concerns with Hospital-Based Manufacturing with recommended solutions



3.5 Lack Of Global Harmonisation Of Regulatory Requirements

The lack of global harmonisation of regulatory requirements significantly affects Australian SMEs in the 3DP medical device space who are looking to go global with their products. Most Australian SMEs look to go global relatively soon because it is difficult to be profitable only by supplying products with a niche market in a relatively low-populated country. The root causes of this barrier have been identified by interviewees as

1. Lack of 3DP manufacturing standards
2. Inefficient regulation systems

3.5.1 Root causes

Lack of 3DP standards

For most methods of manufacturing and processing, standards are adopted to ensure the products are safe, reliable, and of good quality. There are several standards in place for medical device manufacture, the most popular of which is ISO 13485 – quality management systems for medical devices, which details the requirements for a valid QMS for regulatory purposes. There are also device-specific standards and standards that address good clinical practices for the designing, conducting, recording, and reporting of clinical investigations. However, standards for the 3DP manufacturing of medical devices are lacking. This is not merely about the lack of standards for 3DP medical devices, but rather, it is about the lack of 3DP manufacturing technologies in general. This is due to the existence of the variety of parameters that are involved in producing a functional and replicable product.

For a metal medical device, some important parameters to consider are: the material to be printed, the consistency of the metal power (the size of powder granules and non-contamination of different powders or molecules), the method of deposition (SLS or EBM), and whether there are multiple lasers or different electron-beam firing modes. The complexity of these parameters are further amplified by the printer settings, whether it is the print speed, the orientation that the device is printed at, or where and how much support material there should be. On top of all these parameters, there is also the consideration that the devices' dimensions need to be within a certain tolerance. These parameters are just for metal 3DP and the standards will also need to account for other materials such as plastic or ceramic printing. It is extremely difficult to establish developing new manufacturing standards, as it involves rigorous testing and often international collaboration. Harmonising the standards for 3DP and the medical device requirements is also difficult since adoption often happens at a global level through the International Organization for Standardization (ISO). An insurer stated that

> "Global harmonisation might be an obstacle, not because it does not exist but because it does. The only obstacle that exists is if there is one regulatory body that has not created regulations, then all groups have not created regulations."

This means that to create standardisation, an standards body must actively coordinate and sanction the collation of data from the volunteering material scientists and engineers around the world, organise task groups and committees, write, propose and vote on the adoption of the standards. This requires both time and resources and if there is not a global market to buy the standards, it decreases the standards body's motivation.

Inefficient regulation systems

As stated in section 3.2, there are several inefficient regulatory procedures that are currently in place which make it difficult to harmonise the Australian regulatory framework with the international regulatory bodies. One of the inefficiencies, which is a global problem itself, is the existing 'custom-made' medical exemptions.

Many regulatory authorities are looking to modify them to reduce risk to the patients. If these regulation systems are not harmonised, it could prove difficult for Australian SMEs to venture offshore because they will need to go through further expensive regulatory procedures before they can supply their devices internationally. Since the medical application of the 3DP technology is relatively young and most regulations authorities are looking to adjust their regulation process, it will prove advantageous for all stakeholders if there is a global adoption of regulatory pathways for custom-made devices. In this regard, a regulations expert for a large medical device manufacturer stated,

> "The TGA is part of an international consortium, IMDRF, and they meet twice a year and the topic of discussion last time was how to set up a system; one of them being a change of definition and Australia led this discussion. So from a harmonisation point of view, I don't think we will have too many obstacles."

3.5.2. Recommended solutions

Solution 1: Establishing 3DP standards through Standards Australia

Developing standards for 3DP or AM has been a work-in-progress by ASTM International since 2013, with certain design, material testing, and product testing methodologies already being advised. As there are hundreds of variables and parameters to be assessed, several 3D printer manufacturers are unsure about the time that the standards will be in place. For example, they stated,

> "I think you will find that they do not have a mechanism for standardising the printing process. The specification mechanism at the moment for 3D printing is going to have to include so much that I don't think (standardisation) is going to happen any time soon."

While manufacturers are not exactly certain when the standards for 3DP manufacture will be developed, researchers are confident that it will surely be developed. For example an Australian researcher active in 3DP design and manufacturing noted that Standards Australia are setting up a committee for additive manufacture, of which

> "The committee will look at all the data from EU and US standards and come up with an Australian version depending on those". They further state that establishing standards "will make the industry more confident, whether it is for medical, defence or aerospace applications. Seeing that the devices are met with certain standards will provide more confidence. It will also be easier and faster for the TGA to certify devices"

Solution 2: Collaboration with the TGA

This solution is about tackling the inefficient regulation systems root-cause. Stemming from section 3.2.2, the best approach to achieve an ideal regulation system is that all stakeholders need to actively contribute to the consultation papers from the TGA and the IMDRF. After the consultation from the TGA, regarding the definitions of the custom-made medical devices, has concluded, the regulatory pathways for each definition will be further clarified. A 3DP machine manufacturer was in support of the changes, primarily for the 'patient-matched' category. He stated,

> "I am hoping that the TGA will start to approve companies that have templated specific medical devices so the company can receive the CT scan,tailor the template to match what is required and conduct their structural analysis, before printing and supplying the medical device to the surgeon."

That will likely be the business model employed by the Australian SMEs who outsource manufacture. Besides, that will be even more advantageous if international regulatory authorities also adopt the same definitions and regulatory criteria.

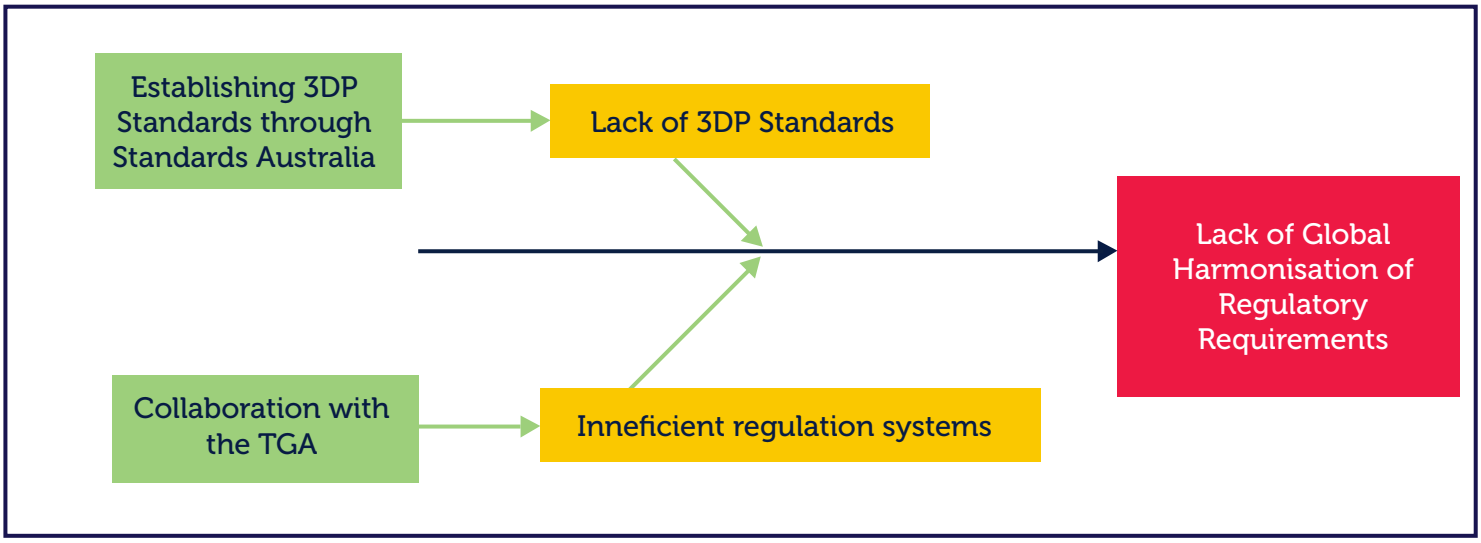
Another potential solution was raised by a stakeholder in the 3DP machine manufacturing sector. The solution was to have an accrediting body that independently assesses the safety and performance of a medical device and assigns a 'star rating', similar to the Australasian New Car Assessment Program (ANCAP) that rates for the car safety assessment. The stakeholder states,

> "If you were to buy a vehicle tomorrow, you are likely to look for an ANCAP rating. Most of the general public won't buy a car unless it has been ANCAP tested. That ANCAP equivalent in the medical industry is not there. It might not needs to be the TGA. If there is a company that the TGA trusts that can do the equivalent 'ANCAP testing' for a knee joint, then that could be a great opportunity for a commercial entity to step in."

This potential solution would theoretically reduce some of the workload of the TGA. However, having such solution in practice can be challenging, too. The TGA will likely need strict oversight on all conducted evaluations. It will also be extremely difficult to implement, because the organisation responsible to assess the medical device will likely require a guaranteed contract with the TGA before investing large sums of money in the machinery, staff and the required workplace to assess the medical devices. The TGA, on the other hand, will not consider this unless the organisation has consistently provided positive results.

These two solutions and their effects on the root-causes of the lack of 3DP standards and the inefficient regulation systems are visualised in figure 7 below.

Figure 7. Root-Cause Diagram for Lack of Global Harmonisation of Regulatory Requirements with recommended solutions



3.6 Difficulties In Protection Of Intellectual Property

Protection of Intellectual Property (IP), such as patents, is essential for innovative medical device companies, as it is the case for all innovations in any industry. Such IP protection is typically through patents that protect the inventor's product or technology in the jurisdiction the patent is granted. There can also be other forms of protection, such as copyrights. Although it might be part of a business strategy not to pursue a significant IP protection in order to avoid exposing the invention to competitors, the IP protection is typical for an innovative company. However, applying for IP, particularly filing for patent, is very expensive, which poses difficulties particularly for SMEs. Such difficulties in turns can significantly reduce SMEs' incentive for innovation.

The IP protection, apart from being a natural incentive for innovation, is particularly important for SMEs because without it, they have severe difficulties to attract external funding opportunities from funding bodies. This is because it is also difficult for funding bodies to justify the investment in companies without I.P. protection, since another company might develop a similar technology or a device and patent that before the company without IP protection. This makes it more difficult for a return on investment.

3.6.1 Root causes

The root causes of this barrier have been identified as:

1. The lack of governmental support for SMEs
2. The lack of private funding support, stemming from a catch-22 scenario.

Lack of governmental support for SMEs

The first root cause of this barrier is identified to be the lack of support and the lack of funding for IP applications at the government level (which can be a state or federal level). As stated by an SME representative,

> "What is available for an SME right now for patent protection assistance? There are probably some free services you can tap into but none of it is, in my view, not all that useful to be honest"

Lack of private funding support: A catch-22 scenario

As noted earlier, without IP, SMEs have severe difficulties to attract external funding opportunities, especially from private funding bodies. This is because funding bodies cannot justify the investment in an SME without I.P. protection. That is because another company might develop a similar technology or device and patent it before the company without IP protection, making it more difficult for a return on investment. On the other hand, without external funding, SMEs have difficulties to innovate and go for filing patents in the first place. This poses a complex root cause that will be discussed in section 4.2.

3.6.2. Recommended solutions

Solution 1 to Lack of governmental support for SMEs: Benchmarking the state-of the-art governmental support programs from innovative countries

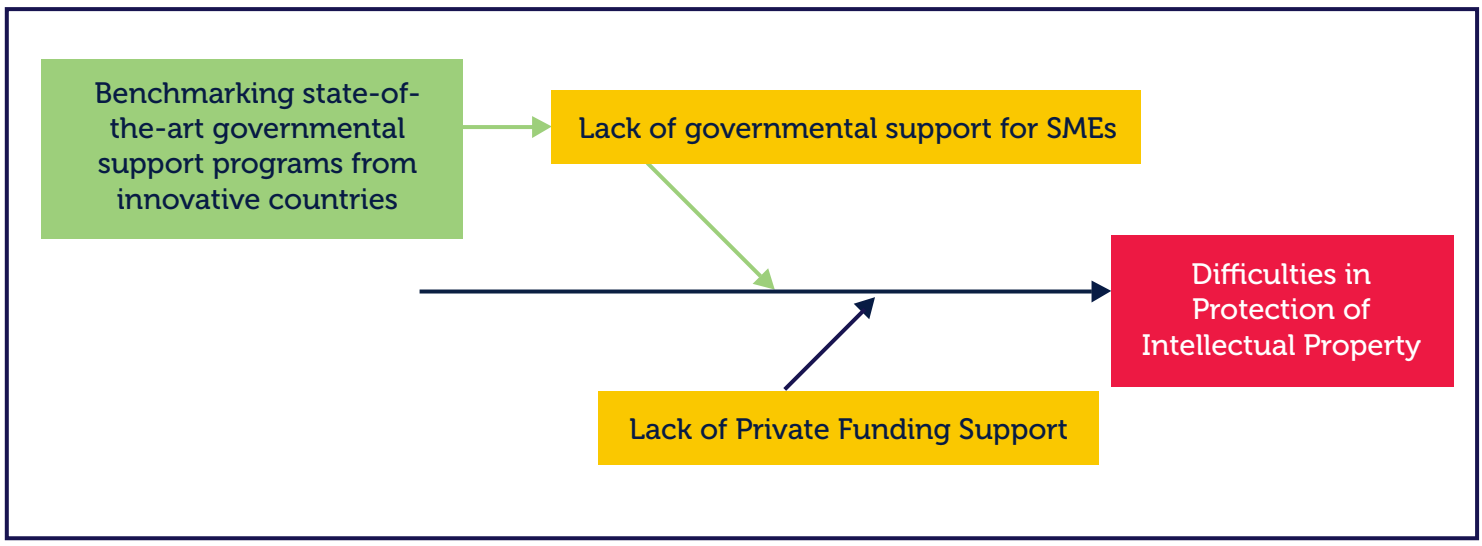
Stakeholders have stated that other countries have assistance programs at a governmental level. Australian government may bench mark and adopt certain existing and successful programs from innovative countries.

Example of such countries include Israel and the U.K. As an interviewed SME stated,

> "We need to find a way to significantly assist SME's with patenting a device. In the U.K, they have the patent box which has great merit. Israel backs SME IP so that innovation isn't halted by the cost burden. Australia has none of that. We also have trouble extrapolating our patents into other jurisdictions. Whatever they are doing in Israel at the government level to support innovation and innovative companies with the development of the products, IP protection globally and supporting companies that take their products offshore is something that the world, and particularly Australia can learn from."

This solution could provide Australian government examples for support mechanisms that can be modified and instituted to benefit Australian SMEs. Its impact is reflected in figure 8 below. Regarding the root cause of the lack of private funding support, discussion and recommended solutions are provided in section 4.2.

Figure 8. Root-Cause Diagram for Difficulties in Protection of Intellectual Property with recommended solution



3.7 Sterilisation

The advanced manufacturing industry roadmap from CSIRO identifies high-value customised solutions in low-volume as an opportunity area on which Australia can capitalise [7]. This opportunity area is halted for products that require sterilisation, because it is a volume-based business. An Australian SME in medical device space states,

> "Whether you have 1 or 10 (devices), it does not matter. You have rented the chamber, and the chamber is at a fixed cost, depending on its size. And then on top of that, you have to pay for all of the validation processes and checks and certificates related to your product, because that is your responsibility. So it is a significant cost of burden on a low-volume-driven business"

The fact that the business is operated on a volume-base is not going to change because whether the machine is full or at 1% capacity, the costs for running a sterilisation cycle will remain constant. On top of that, there are very limited numbers of sterilisation service providers, which leads to little competition between them. This makes the sterilisation service almost a monopoly in Australia. From our interviews, we have identified that the lack of affordable sterilisation and other post-processing methods, such as hot isostatic pressing (HIP), are a barrier for SMEs who, unlike large firms), typically have to outsources the sterilisation of their products to those limited number of sterilisation service providers.

3.7.1 Root causes

We have identified one root cause for this barrier that is about the almost monopolistic nature of the sterilisation market in Australia.

Sterilisation in Australia is almost a monopoly

It is difficult to find sterilisation offered as a service in Australia. In total, 3 companies that provide service to medical device manufacturers were identified: Steritech, Merit Medical (formerly ITL Healthcare), and Sabre Medical. Sabre Medical does not advertise sterilisation as a service because they have a small capacity, but they use Ethylene Oxide (EtO) sterilisation adjunctively to their core business (which is packaging). The other two sterilisation bureaus have larger volume sterilisation chambers for EtO sterilisation, however, what makes their service almost a monopoly is the capability for gamma ray irradiation, for which only Steritech has the equipment Australia-wide.

An Australian SME representative states,

> "Steritech have facilities in Sydney, Brisbane and Melbourne, with their main facility in Melbourne. They have facilities for Gamma Ray irradiation. They are the only gamma provider in the whole country. If you require that type of sterilisation, they are huge and basically the monopoly runner."

They proceed, saying:

> "If I decide to have it gamma sterilised, well, if I cannot get it done in a timely or cost-efficient manner through Steritech, then you are automatically going to have to look offshore for at least your sterilisation processes, and possibly your packaging processes. If this country is serious about manufacturing medical goods and devices, it needs to start to assess the sterilisation services."

As one would imagine, the volume of the sterilisation chamber scales with cost, which makes smaller chambers more cost effective for implant applications since they do not require much space. Unfortunately, only Sabre Medical has small EtO sterilisation chambers.

> "It is dependent on the size of the chamber. Steritech has very large chambers, as would Merit, I imagine. It will be more. Sabre have a small chamber as it's a small part of their service offering, so that happens to suit companies like ours and probably many others. It is still a large cost burden given the small size of our medical devices."

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> "If I am just doing one implant in the chamber then I am running at a loss, more than likely. Because I won't recoup those costs if I am spending 5000+ on sterilisation per run."

This is not ideal for the patients, as it drastically extends the wait-time for a custom implant. The SME representative further elaborates,

> "So I can get an implant done in a week if everything worked well. But in essence, I am never delivering in a week because I am waiting for other things to fill the chamber to do a run, and then release. And so my timeframe has become from one week to four weeks or six weeks."

3.7.2. Recommended solutions

There are four recommended solutions that could help remedy the barrier of sterilisation for SMEs and one potential solution that needs to be further discussed with sterilisation bureaus. The first is to explore sterilisation via autoclave, which is routinely done in hospitals for surgical equipment. The second is to approach large manufacturers who have sterilisation equipment, similar to Merit Medical, to see if they would consider providing the service. The third recommendation, particularly if the other two are unviable, is a government intervention. Finally, the fourth potential solution is to develop and maintain a booking system for SMEs to share the volume of the chamber. Below is the explanation and associated challenges concerning each of the above mentioned solutions.

Solution 1: Hospitals servicing SMEs for sterilisation

If the medical device could be sterilised inside the hospital via conventional autoclave sterilisation, it could be ideal for the manufacturer and patients. To have this as a possibility, two issues need to be addressed. The first issue is to assess whether it is viable to sterilise that particular device via autoclave. This would involve investigating ISO 17665 and substantiating the instructions for operation and validation of the sterilisation process. One consideration to be made is whether the device needs to be packaged. If the sterilisation of the medical device happens in the same hospital in which the surgery will occur, the packaging could possibly be avoided. If the device needs to be transported, however, this will probably not be a viable solution. The second issue to be addressed is hospital adoption. One researcher, who is affiliated with a hospital, is unsure if hospitals will be willing to sterilise the device since there is a large increase of risk due to the deviation from their current established QMS.

> "Hospitals have always sterilised surgical instruments, but for an implanted device there is a large increase of risk."

It is possible that if a manufacturer has substantiated to follow the sterilisation operation and validation protocol, then a hospital might be able to sterilise the device (in case of their capability).

Solution 2: Large manufacturers servicing SMEs for sterilisation

Large manufacturers of implants typically deliver their medical devices sterile with the method of sterilisation labelled and a sterility expiration date. Having additional actors who provide sterilisation services could help reduce the monopoly of the industry, providing a competitive market for SMEs to choose from. Ultimately, it depends on whether it makes sense economically. A researcher states,

> "It depends on the volume of implants that would come through the facility. If a large manufacturer feels like they can only do 80% of the capacity, they may as well sell the other 20% of the capacity."

Solution 3: Government intervention

A recommendation from an SME was for the government to provide some incentives for a private enterprise to set up a sterilisation bureau or to make government owned sterilisation facilities, which are currently in place for research, available to public for a cost-effective fee-for-service rate that supports innovation. Before this is done, a business case must be brought for CSIRO, for instance. A state government representative said,

> "Ask how you could develop an opportunity to work with the CSIRO to establish a place for SME's to sterilise and develop a commercial opportunity. Or look into the A.M precincts where a precinct could be established for A.M and have a sterilisation unit there. Maybe if the CSIRO has a spare area for it and pay for half of it and the other half by everyone else, then perhaps a deal can be made. It's a matter of putting an initial business case for CSIRO."

Solution 4: Sterilisation booking system

Another potential solution is to create a booking system where SMEs can share the volume of the sterilisation chamber, thereby sharing the costs as well. Although easier to imagine in theory, there might be practical challenges associated with this recommended solution. The reason why this might not be a possibility is because different devices from different SMEs would probably not be validated via the same method. An SME, when approached with this idea stated,

> "I would see challenges at the actual delivery of sterilisation services, not the booking system to fill the chamber. That would not be much of an issue. That would be quite helpful, however, I think the practicality of different goods being mixed up from different manufacturers using potentially different materials and different validation processes and different families, that would be potentially a challenge."

They also go on to say

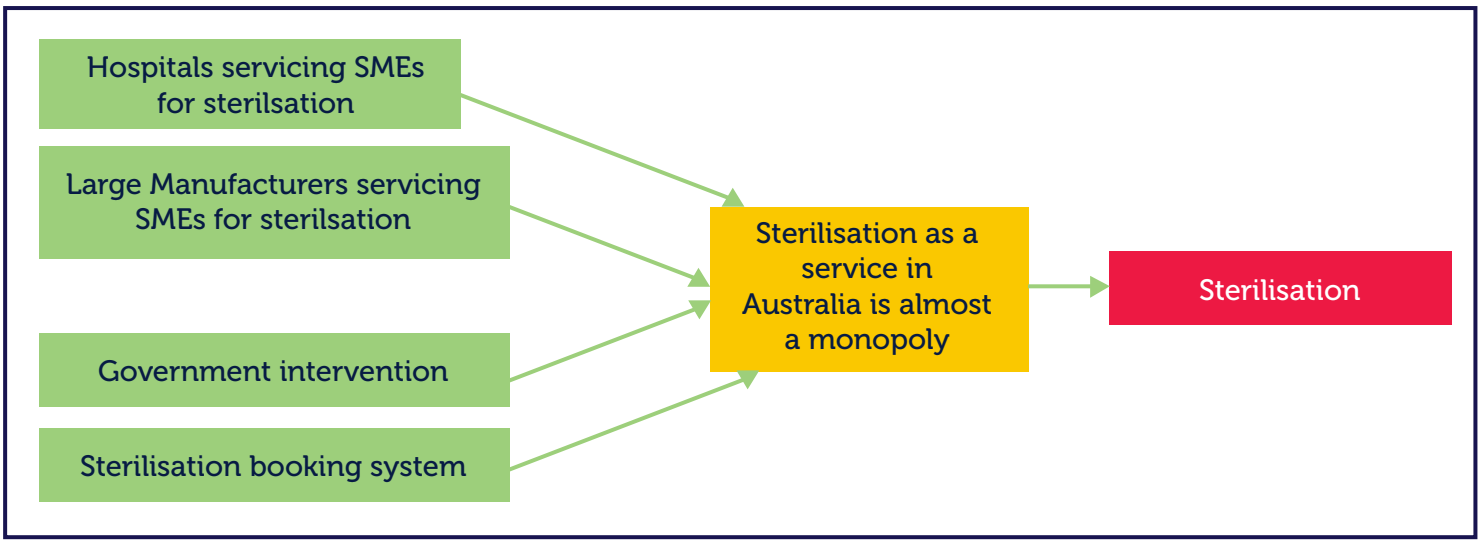
> "That would be a conversation to have with sterilisation providers. Just ask if you have different suppliers with different products coming in, could we run a system where people can book chambers. It has not been flagged with me as a potential option in any of the discussions I've had with the sterilisation providers."

Therefore, although appealing at first sight, an effective implementation of this recommended solution requires further discussion with SMEs and sterilisation bureaus.

Each of these four solutions address the same root cause as shown in figure 9, however, they can do so in different ways. The recommended solution of hospitals and large manufacturers providing sterilisation services for SMEs addresses the root cause since it creates multiple actors in the sterilisation industry instead of behaving almost like a monopoly.

Government intervention could either involve co-funding a sterilisation bureau or provide sterilisation services, which are currently being used for research, for SMEs with a fee-for-service. The fourth solution does not remove the root cause of the industry being almost a monopoly, but it could address a major problem with monopolistic companies, and that is the cost of the service. Creating a system to share the sterilisation chamber and its associated costs, could provide a more affordable service for SMEs if their devices are validified via the same method.

Figure 9. Root Cause Diagram for Sterilisation with recommended solutions



3.8 Funding

Funding for Australian SMEs was identified as a barrier both by the SMEs and also the intermediate investors active in the 3DP industry. One investor, who actively gathers funds for 3DP MedTech SMEs, stated,

> "The biggest problem we have in all of this is finding the funding. In Europe you can get a 3DPrinter at 5 % interest rate and the bank will give you the money right away but here, you won't get approved for a loan. We had to raise equity and it was really tough to raise equity in a market people aren't familiar with."

Two root causes were identified from our interviews. First, the lack of 3DP awareness, its processes, and its benefits in Australia, and second, the requirement of I.P. protection for SME device designers.

1. The lack of 3DP awareness, its processes, and its benefits in Australia
2. The requirement of I.P. protection for SME device designers

Courtesy of RMIT AMP

3.8.1 Root causes

Lack of 3DP awareness by investors

There is an expressed concern for stakeholders that larger investors are hesitant to invest in 3DP medical devices due to the lack of understanding and awareness of what 3DP offers in MedTech. Furthermore, a venture capitalist has stated,

> "If you want a lot more funding, you need the Industry Super Fund investments. Say that the Industry Super Funds invest 1% their funds into 3DP and the industry would boom. They lack the awareness of 3DP."

Given that 3DP is an emerging manufacturing method, often simplified in common media, it is understandable that investment firms are unfamiliar with the technology including all the post-processing involved in making a production part. Investment firms are also looking for a strategic position to invest in a company that is at a significant growth acceleration stage. Thus, they can deliver maximum return for their stakeholders on the shortest possible investment strategy. This was once again raised by an SME,

> "They are looking for companies that can deliver a significant growth quotient in the shortest possible time, on the shortest possible investment strategy up-front. I think part of the problem for 3DP MedTech companies is because of the niche nature of what they are doing, and/or the customised nature of what they're presenting as a patient outcome, doesn't necessarily extrapolate to a significant growth opportunity. So, for example, we might say a total hip that is customised and printed for specific types of pathology, might represent a very small total percentage of the total hip market. An investor looking for maximum return and maximum growth opportunities are not going to be interested in a small, niche growth opportunity globally, as opposed to a mass opportunity that presents a significant return on their investment"

When it comes to government funding, SMEs have stated,

> "There are phenomenal opportunities including tax incentives, business and research grants. The problem is finding them and applying for them."

Nevertheless, this issue faces SMEs that spin-off from governmental research institutes or collaborate with CSIRO less severely. This is because they maintain connections with the department of trade and industry and are alerted to available grants. So they did not consider identifying funding opportunities as a barrier.

Requirement for IP protection for SMEs

As reflected in section 3.6, IP protection and funding are closely interlinked, especially for medical device designers and manufacturers. IP protection is often a requirement for funding and funding is a requirement for the expensive patent application process, creating a catch-22 scenario depicted. This will be further discussed in section 4.2.

3.8.2. Recommended solutions

Solution 1: Public education

The stakeholders, who voiced 'lack of investor awareness' as a root cause of the funding barrier, also proposed a recommended solution. Education about the capabilities of 3DP, for both investors and public, should be facilitated by the education system, government, and the actors in 3DP industry. An interviewed investor stated,

> "Well it's up to us to educate initial investors but to further spread the word of 3DP printing for commercialisation, I think the labour party is developing a precinct for 3DP and make people more aware of it. If there was a mechanism for funding, it would have been very helpful for us. I think as the market matures, the need for 3D Printers would increase and a second-hand market too. We just bought a second-hand printer. So that proves the market is there. Funding for scanners would also help, since it's so expensive. The high-tech stuff is there (i.e. our factory) but with minimal assistance, so a widespread understanding and appreciation that this industry is potentially massive would go a long way."

Furthermore, addressing the perception to what goes into 3D printing a medical device, would give due credit to SMEs on how complex and novel their devices are. As stated by an SME,

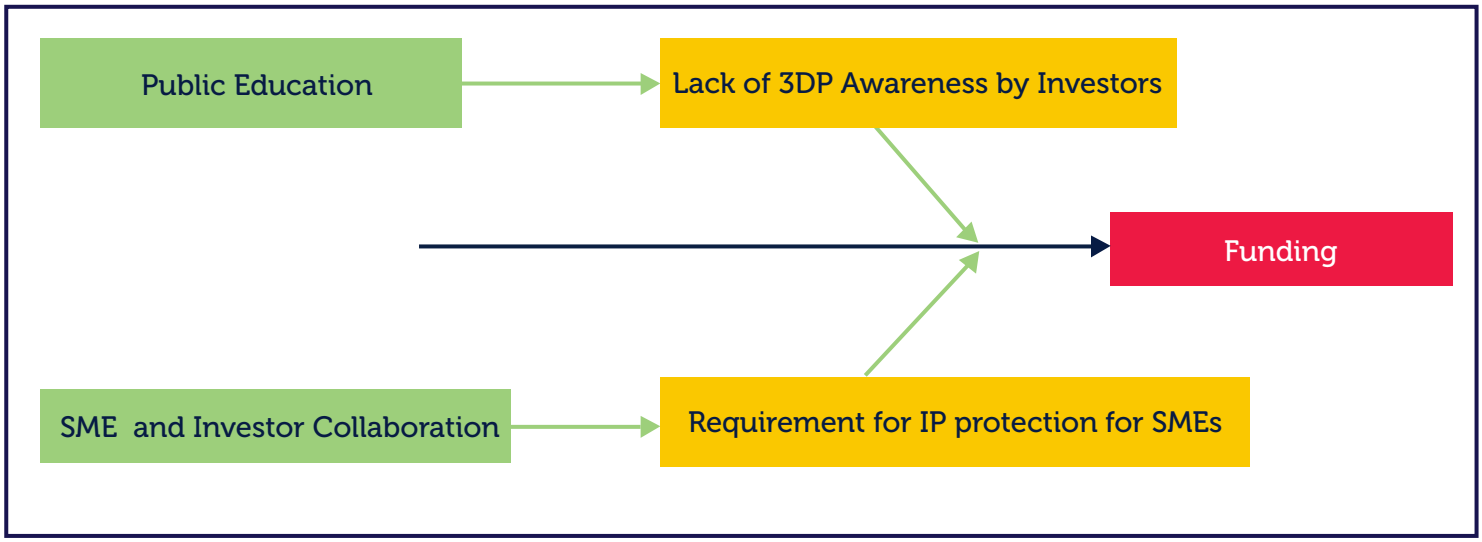
> "I don't think there is a great understanding of the requirements around implants. I think there is a perception that if I am talking to someone who is not quite across this business sector and suggested that we are doing 3D printed titanium oral maxillofacial implants, that we would be performing the manufacturing here in-house in the middle of the CBD. That is potentially possible, but the machine that is required for a finished product is beyond just the 3D printer. And I think there is a poor understanding if we go back to the investors. I think there is a very poor understanding of the complex nature of what is required to actually produce a finished good. So, yes, anyone can send cad files to a 3D printer, but to actually create something that is specific to a patient that actually fits and meets some quality governance requirements as well as regulatory requirements, is quite a bit more complicated as a task. And not strictly speaking an option for the lay-person."

Solution 2: SME and investor collaboration

This solution, which is detailed in section 3.6.2., proposes SMEs to collaborate with investors, where possible, to provide IP and patent application support, in terms of for instance, co-patenting. This proposed solution is an alternative for a conventional way in which SMEs approach investors in hope of solely getting funding as a one-off contract and then, in a second and separate step, they contact patent attorneys for a fee-for-service. This solution will only be viable if SMEs are willing to part up with investors in co-patenting. The investors must also have the knowledge and capability to prepare patent applications to the jurisdictions of interest and whether they see value in the technology.

The relationship that each solution has with each root cause is presented below in figure 10. Additional discussion regarding the root cause of 'requirement for IP protection for SMEs' along with the recommended solutions are provided in section 4.2.

Figure 10. Root Cause Diagram for Funding for Australian SMEs with recommended solutions



Section 4: Catch 22 Scenarios

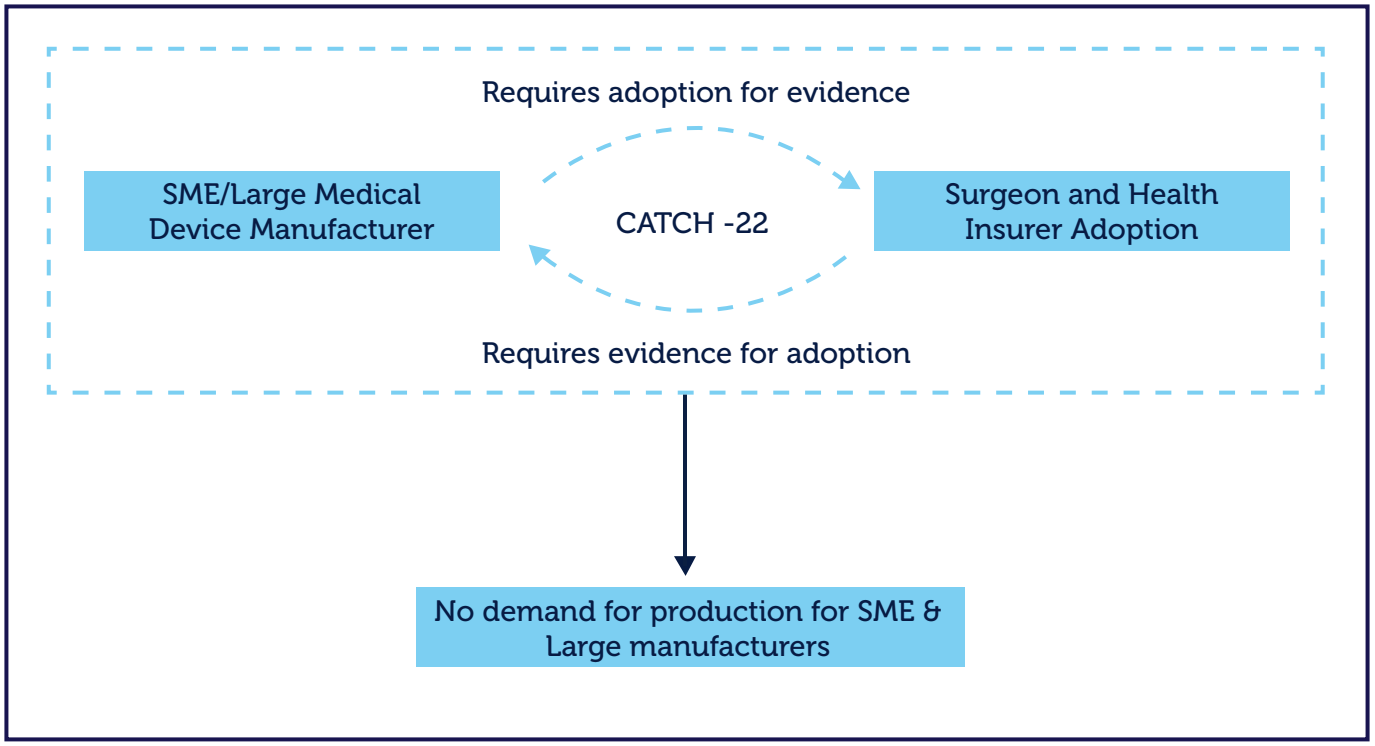
Courtesy of RMIT AMP

SECTION 4 - CATCH 22 SCENARIOS

In conducting the Root Cause Analysis of the identified barriers in Section 3, we have noticed two catch-22 scenarios, which complicate the root cause analysis of barriers and consequently proposed possible solutions to overcome these barriers. In this section, we will provide details on those catch-22 scenarios and how to overcome them. The first identified catch-22 is the lack of sufficient clinical and economical evidence (concerning barriers 1 and 2) requested by both surgeons and insurers, as the two most influential stakeholders in the industry.

Finding a remedy for this root cause and eventually for the barrier 1 and 2, has a clear benefit for the widespread adoption of 3DP medical devices. This is because it can drastically affect surgeon and insurer adoption, and it certainly affects funding bodies who are looking to invest in an otherwise highly innovative space. However, finding a remedy for the lack of evidence is not straightforward. This is because, on one hand, surgeons and health insurers require evidence in order to endorse the technology. The primary evidence providers are the SMEs and/or large manufacturers. On the other hand, the SMEs and/or large manufacturers require endorsement from surgeons and insurers before they commit themselves to produce 3DP medical devices, so that they can be confident there will be demand for their product. This interlinked catch-22 scenario is shown in Figure 11.

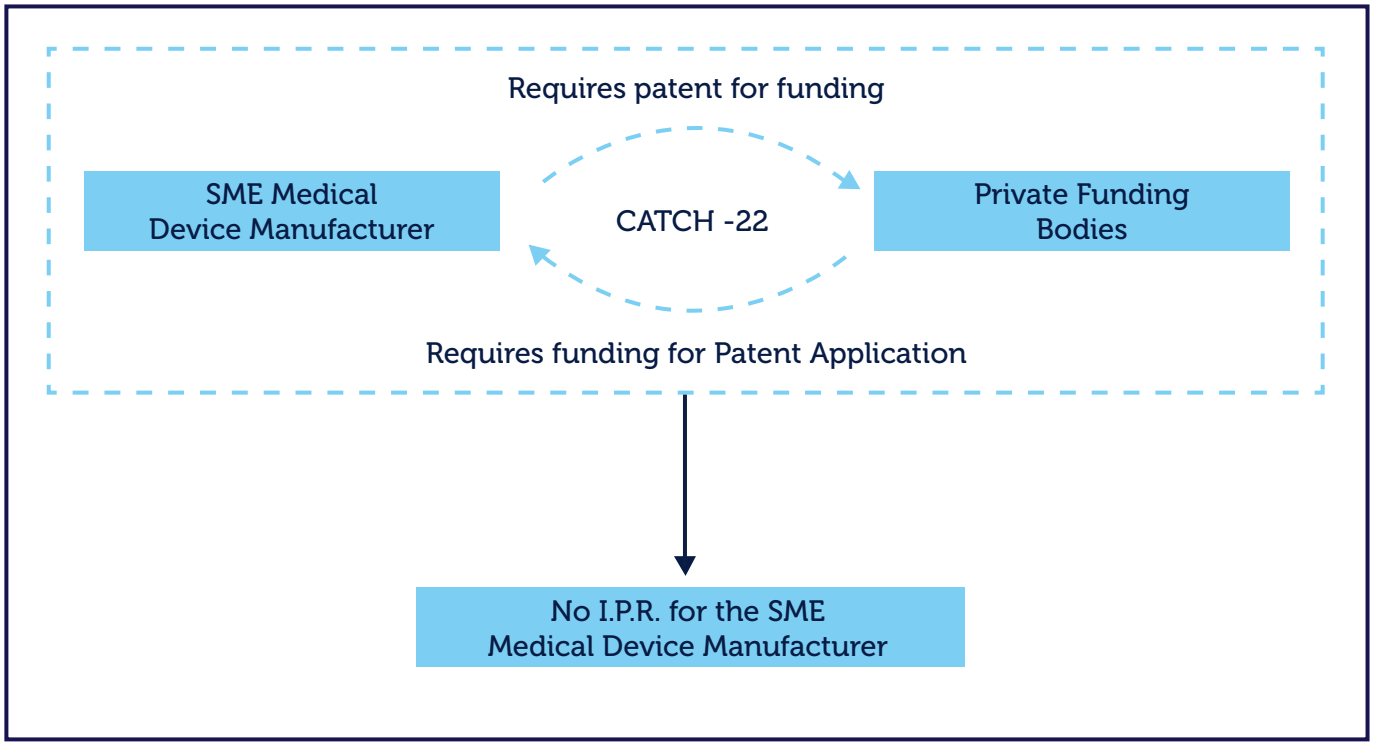
Figure 11. The Lack of Evidence Catch-22



The second catch-22 scenario is a root cause of barriers 6 and 8; namely the protection of IP and funding for SMEs. These two barriers are highly related, especially when it comes to acquiring investment from private funding bodies. IP protection, predominantly in the form of patents, is essential for most innovative medical device companies, however, applying for patents is very expensive which poses difficulties for SMEs.

Although it is expensive, private funding bodies require a patent for being considered as a viable candidate for investment. This is because it is difficult for funding bodies to justify investment in companies without IP protection, since another company might develop a similar technology or device and patent it before the company without IP protection and that makes it more difficult for a return on investment. The catch-22 scenario for the lack of funding for IP protection is depicted in figure 12.

Figure 12. Lack of Funding for IP Protection Catch 22



4.1. Catch-22 Scenario 1: Lack Of Evidence

4.1.1 Explanation

To describe the first catch-22, which is about the generation of evidence, it is important to note that there are two types of evidence that are currently lacking. The first type is the 'clinical' evidence which could show better patient outcome, since we cannot assume that patient-specific devices always provide better results for the patients.

The second type of evidence is the 'economical' evidence, showing that the technology is cost-effective for patients and the healthcare system as a whole. The lack of both types of evidence creates an environment where surgeons, health insurers, and funding bodies are hesitant to invest, whether with the required time to learn about adopting the new technology, insuring the cost of 3DP devices, or funding the business ventures using this new technology.

The most important aspect of any novel medical device is demonstrating that it works as intended and it is beneficial to patients. If the device provides better results for patients, then it is more likely that surgeons, insurers, and other stakeholders will adopt it at a higher rate.

The limited volume of the empirical clinical evidence in support of 3DP medical devices, will result in the low amount of surgeon adoption [11]. Nevertheless, for extreme and unconventional medical cases, the freedom of design enabled by 3DP is certainly advantageous and it is currently the area where 3DP devices are the most successful.

Although there have been strides in the development of 3DP medical devices due to more advanced and reliable 3D printers, scanners, software tools, and design engineering skills, it is important to acknowledge that the introduction of certain 3DP medical devices was not successful in the past, which is making the insurers sceptical. An insurer states,

> "You talk about the technology as though it is new, and how we need to overcome the obstacles to entry. It is not entry that is the obstacle, it's actually overcoming the history (of non-effective devices)."

3DP medical devices have been manufactured since the early 2000's, primarily for dental implants and custom prosthetics, some of which have not been as effective as off-the-shelf devices [12]. The insurer continues,

> "The paradigm (of obvious benefits) stated by the manufacturer are not 'real', taking into account peoples' experience, taking into account history and what we know to have been the case for a long time. If you are going to state benefits, we need to know what is different now? Has the difference overcome some of the obstacles? How would an insurer justify spending money on something that nobody can determine whether it can do the same job as an existing, alternative technology that is proven?"

Looking at a systematic review that identifies the clinical efficacy and effectiveness of 3DP medical devices, it is shown that these devices have been indeed clinically effective in the fields of musculoskeletal surgery, oral and maxillofacial surgery, and anatomical model fabrication. However, out of the 350 studies reviewed, only 21 were randomised control trials and the article concluded that the efficacy and effectiveness of 3D-printed devices remain undetermined for the majority of medical fields [13].

In another review article with data taken from 2017, authors note that 92 clinical trials were being conducted with over 6000 patients worldwide [11]. Most of the clinical trials are projected to finish from 2017 to 2019, therefore, there should be an influx of longer term data available from clinical trials registries soon which also provides the ability to compare 3DP devices to conventional ones.

SME manufacturers, who are seeking to provide more evidence for their 3D printed devices, have hit a major roadblock, especially in the implant industry. A representative of an SME, who is a surgeon and also develops patient-specific implants, states,

> "The feedback we get when we go to conferences and we have a table to present our stuff, they (surgeons) say "where's the evidence? This paper is only 3 years old, I want 10 years." To which I say, "in 10 years this device won't exist anymore because we will have a better device." Testing a device that's 10 years old makes no commercial sense. No one is going to pay the researcher to look at a 10-year-old device that's not on the market because it's useless to publish…it's not there anymore. No one sells it anymore. I say that to surgeons and they still don't get it."

Although it might be financially impractical to provide reports on 10-year-old devices that have stopped being manufactured, it is extremely important from the surgeons' and health insurers' perspective. As a result of an aging population, implants are staying in patients for longer, and thus, providing data on long-term clinical trials which is increasingly more important. A regulations expert from a large manufacturer states,

> "Clinical evidence is not just for safety and effectiveness of the device but also proves it's worth (financial)."

An insurer who is optimistic about using the technology in certain circumstances also contributes saying that the method of creating evidence needs to change.

> "I actually do perceive there to be room for the technology, and I am disappointed that people are not selling it in a way that makes sense. I have not seen any pilot programs. I have not seen any offers for pilot programs. The only thing that they try to do is justify exorbitant payments for trial and error treatment. Their approach has been a problem. It's better to say that insurers would not be supportive if the approach to try use and sell this technology does not change."

If a 3DP medical device proves beneficial to the patient, the next stage is to provide economical evidence that the device is cost-effective. An SME representative says,

> "You need evidence showing that it is beneficial for the patient, the clinician and the healthcare system. That is more than just safety and efficacy, but what it does for the hospital and the health economics (system). That is the way it is in the medical device industry."

Currently, the most effective way to prove cost-effectiveness is to compare the cost and performance of the novel medical device to a treatment with the same function that is already on the market, as an example, comparing a 3DP personalised implant for bone defects to the conventional autologous bone grafts. To compare the cost of the choices, it is important not to look solely at the cost of the devices and the associated surgery costs, but to see the figures that go routinely unnoticed as well. These figures are, for instance, costs associated with the length of the hospital stay, or if the device creates a lower risk of revisional surgeries and rehabilitation costs. This economical evidence contributes to incentivise private health insurers to enlist the device on the prosthesis list, providing a higher incentive for patients to use 3DP medical devices, which then results in more evidence.

4.1.2 Recommended solutions

There are four recommended solutions with the aim of providing more evidence to increase the endorsement and hence adoption of surgeons, health insurers, and potential industry partners. These solutions can 'break' the catch-22 cycle, which was explained above.

The first solution is the creation of a procedure that can initiate, support, maintain, and organise the 'generation of evidence'. This involves the inclusion of more detailed post-surgery follow ups, and the data needs to be explicitly categorised as a 3DP medical device stating whether it is patient-specific or not. This can facilitate a comparison of 3DP medical devices with conventionally manufactured devices.

The second recommended solution is a component of the evidence generation procedure and it details the implementation of the patient-specific device registry which is necessary to collate and compare the data from post-surgery follow ups. The third and fourth recommendations are both related to how to tackle the lack of funding mechanisms for clinical trials.

The third recommendation advises the use of research grant referral systems and suggests applying for cooperative research centres' (CRCs) projects grants that have the aim of supporting the industry-led collaborations to develop new technologies, products, and services.

The fourth recommendation is for large manufacturers to continue to spearhead pre-clinical trials, laying the groundwork for the case of 3DP medical devices via animal trials.

Solution 1: Developing evidence generation procedure

In discussion with multiple SMEs, large manufacturers, insurers, and surgeons, a disconnection was found in their understanding of what evidence is required, especially when the device is made to be patient-specific. From the manufacturers' perspective,

> "Just by changing a screw hole, it's no longer the same device."

Meaning, results from the same "type" of device, for example a 3D printed patient-specific sternum implant, are not comparable to each other. This is also in line with the Australian Regulatory Guidelines for Medical Devices (ARGMD). An insurer replies to this perspective, saying

> "There has been plenty of time and a lot of evidence has not been reached because people [medical device manufacturers] have taken a purist approach to what evidence means. What they say is "Because everything is customised, everything is different and so you cannot get a statistically significant outcome on n=1 studies. Really, that is incorrect because if you create a set of criteria for people who are getting customised devices of this nature and you follow up with those people, and of 100 people 100 get good outcomes, that is all the evidence that anyone needs."

This is an interesting approach, although against how medical devices are routinely assessed, whereby a singular device is tested in a homogenous consort of patients to see whether there are consistent positive outcomes or not. With customised devices, there will be devices that are largely the same, although not identical, and they will be tested in a heterogeneous consort of patients. As the results will not be standardised, the best way to assess the results is to establish an acceptable set of clinical outcomes that cover safety and include long-term assessment through a medical device registry.

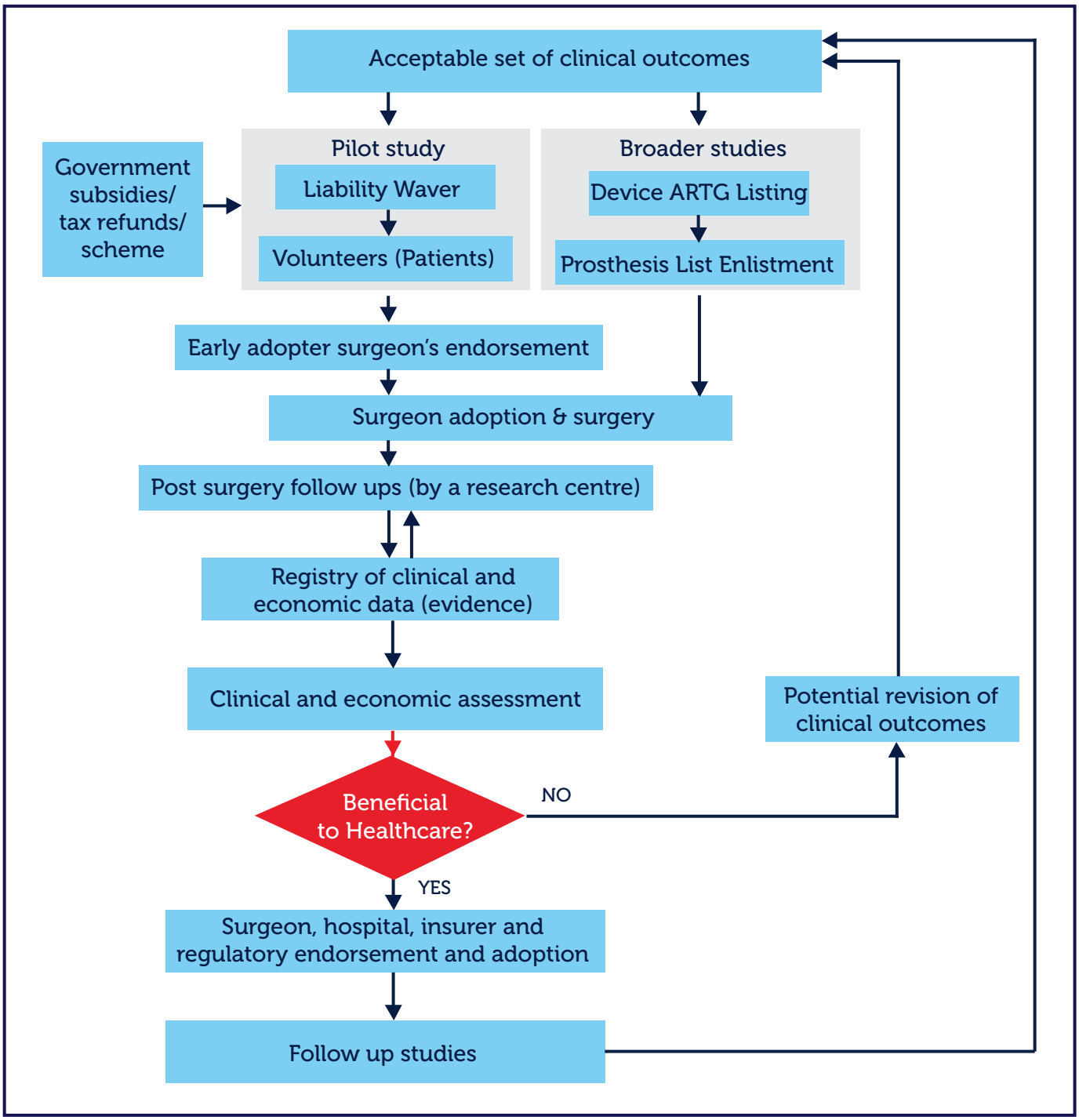
This is in line with insurers' perspective, as noted above.To illustrate this, we have developed an 'evidence generation procedure', which is depicted in Figure 13. It begins with establishing an acceptable set of clinical outcomes for each implantable device category (i.e., knee, hip, shoulder, and spinal devices) based on revision-rate data derived from the Australian Orthopaedic Association's National Joint Replacement Registry (AOANJRR), the Australian Spine Registry (ASR), and the Victorian Orthopaedic Trauma Outcomes Registry (VOTOR).

The acceptable set of clinical outcomes will be superior device success-rates compared to the industry standard. The pilot study needs patients to sign a liability waiver as the device will likely not be registered on the ARTG. The pilot study will only be able to attract early-adopting surgeons, some of whom might be affiliated with the manufacturer of the device. After surgery, follow-ups will be conducted by research institutes.

From there, data can be entered into the registry and can be categorised as either a patient-specific device or a standard device. Comparing the data between the types of devices provide some immediate economical evidence for the average length of hospital-stay and rehabilitation costs. Over time, long term studies can be conducted using information from the registry, showing if it makes a difference in revisional surgery rates. After that, that set of acceptable clinical outcomes might require updates as technology improves.

This creates a feedback loop into other pilot studies on other devices or possibly into broader studies using the already assessed devices with supporting evidence being prepared for market entry. This feedback loop will continue until a threshold is met and there is a conclusive evidence with health insurers and surgeons, indicating that the device is beneficial, both clinically (in terms of health outcomes for the patient) and economically (in terms of reducing the total cost for healthcare system). If the data does not clinically and economically confirm that the device is superior, this would allow the device manufacturers to modify their device or leave the market.

Figure 13. Framework to providing clinical and economical evidence: Evidence Generation Procedure



Solution 2: Developing registry for patient-specific devices

One component of the evidence generation procedure (Figure 13) is the registry of clinical and economic data. In this respect, it is worthy to note that currently, there exists several application-specific registries in place, such as the AOANJRR, and also an assortment from Monash University including the ASR and the VOTOR. A large manufacturer representative highlights the benefits of using registries to gather data. They say,

> "Registries are great and better than randomised clinical trials. Because if you have a new technology, what's your comparator? But you can have a joint registry as a comparator. You can benchmark through a registry. You would have to agree on parameters to measure; patient related outcome measures. It could then build validation for reimbursement."

However, the existing registries neither categorise the devices as whether they are custom-made or mass-manufactured, nor do they specify whether a device was 3D printed or not. Having a new registry data available would provide evidence showing whether the custom-made devices, particularly 3DP devices, result in superior patient results. Moreover, the development of new registries do not need to be from scratch. It can be built upon the existing related registries. Accordingly, a large manufacturer representative explains the method of implementing the registry by referring to the existing registries, saying

> "If there are no current registries that will accept custom made devices, you would have to establish your own registry, like Monash University did and the South Australian Health and Medical Research Institute (SAHMRI) centre. They have the statisticians, at a cost, but it's there and has the capacity ."

Registry is the most practical method of data gathering for low-volume custom-made devices, however, the type of data gathered by existing registries are not rich, i.e. as noted earlier, there is no specification in the registries showing whether a device is 3D printed or not. Another shortcoming for current registries is that there is no follow up procedure to investigate whether a medical device performs well in short-, medium-, and long-run. The only indication of the performance of a medical device is observing if the device required revisional surgeries. This is fairly extreme.

> "The registries do not have a follow up system. They only track revisions and the reason for revision. The registries have revisions as an endpoint."

Therefore, in combination with the registries that categorise custom-made and standard devices, there could also be another method of data gathering via patient surveys, automating the process of gathering 'follow-up' data. This could significantly expand the volume of available data for each medical device and can be implemented via My Health Record or a secure online framework hosted by the research centre. This is not a simple solution as there would be additional barriers to implementing a health record that is hosted online.

A stakeholder says,

> "There is a lot of unutilised data that could be put together to determine what does and doesn't work. What is best practise and what isn't? The one thing that could have done that, 'My Health Record', is in disarray due to cyber security concerns."

Increasing the publics' knowledge about My Health Record and addressing their cyber security concerns would be a barrier, however, it would provide an enormous amount of data that could be used to determine the best medical devices and operational procedures.

Solution 3: Finding external funding schemes for SMEs for clinical trials

Clinical trials are essential to the development of new medical devices since they provide the platform to evaluate device performance in human patients. However, for SMEs to run clinical trials, certain external and matched funding mechanisms will be needed because the clinical trials are expensive and SMEs do not have the capital required to self-fund researches. That is also the major reason for their rapidly entering the market in the first place as they need to recoup costs spent on getting the device appropriately regulated. For large manufacturers, the lack of funding for clinical trials is not a major barrier and they could be required to kick-start the compilation of evidence from clinical trials. This scenario will be talked about in section 4.2.4.

Currently, there are research funding mechanisms available to SME manufacturers, including the R&D tax incentive, grants from the National Health and Medical Research Council (NHMRC), Biomedical Translation Fund (BTF), the Medical Research Future Fund (MRFF), the Medical Research Commercialisation Fund (MRCF), various sorts of R&D grants through the Australian Research Council (ARC), and projects with Cooperative Research Centres (CRC).

It is important for SME manufacturers to utilise these incentives and research grants in order to be involved in human clinical trials and generate evidence. If the results of the clinical studies indicate better patient outcomes with using 3DP devices, this could lead more manufacturers into using the technology and leveraging the results from clinical trials to indicate why their product could also be successful, and such is created a 'snowball effect' in the creation of clinical evidence.

During our interviews, two particular funding mechanisms were highlighted by SME representatives as being practical and fruitful. The first one is the R&D tax incentive. An SME representative pointed out,

> "The real government support that we got was from the R&D tax credit, which is lucrative and is a great scheme. That applies to clinical trials as well. That is a 43.5% roughly, benefit. Cash back."

This scheme is beneficial for any company that is a registered R&D entity and has incurred notional deductions of at least $20,000 on eligible R&D activities. The second funding mechanism that helped the interviewed SMEs was participating in CRC-projects (CRC-P), which include grants that require the prerequisite of at least one SME and one Australian research organisation in collaboration to develop new technologies, products, or services. The CRC-Ps are matched funding schemes, so they require an amount of capital from both the research organisation and the SME manufacturer.

It is important to note that it is not always easy to access the existing funding mechanisms, particularly for SMEs. A government representative that works in the department of jobs, precincts and regions noted that,

> "Although these funding mechanisms exist, it is a challenge for SMEs to know what schemes are available, when they are and how to access their funds. What you will find is that schemes are temporarily available. If you don't know that they are there, it's like a ship in the night. You won't know it left."

In order to aid SMEs overcome the barrier of identifying the research grants and applying for them, CSIRO created SME Connect. The SME Connect has several matched funding schemes that offers researcher placements to fast-track SME R&D projects and aids SMEs apply for commonwealth research grants. A state government representative says,

> "When you are running an SME at 60 hours a week, the last thing you want to do is get hurdled by a form or seeking for opportunities. If you can match the opportunity with the receptor, you can make some major advances."

This program has been beneficial for more than 400 Australian SMEs since it began in 2008, however, the program has conditions regarding SME eligibility. Two other grant referral systems also actively benefit Australian SMEs. GrantConnect is the Australian Government's grant information system which provides current and forecasted grant opportunities that can be sorted by keywords. Grantguru is another grant referral service which is free to search, with 3,931 grants available that can be sorted via industry, location, and activity; i.e. R&D, Manufacturing, marketing, etc. They also offer a paid subscription service which enables email alerts if a grant is available in the users' industry. These tools are recommended to SMEs to overcome some of the challenges with keeping up to date with the available grants and funding mechanisms.

Solution 4: Large manufacturers spearheading clinical trials

As stated in the previous solution, large medical device manufacturers are not typically encumbered by the cost of clinical trials. Therefore they may be required to 'kick-start' the generation of evidence for 3DP medical devices. A researcher states,

> "It is a completely different subject if we were talking about Stryker funding clinical trials (compared to SMEs). They would have no problem paying for the clinical trials." Another researcher, who is a part of an industry project with Stryker, says, "Evidence will come out of current projects from large manufacturers who have the capital to conduct animal and clinical trials"

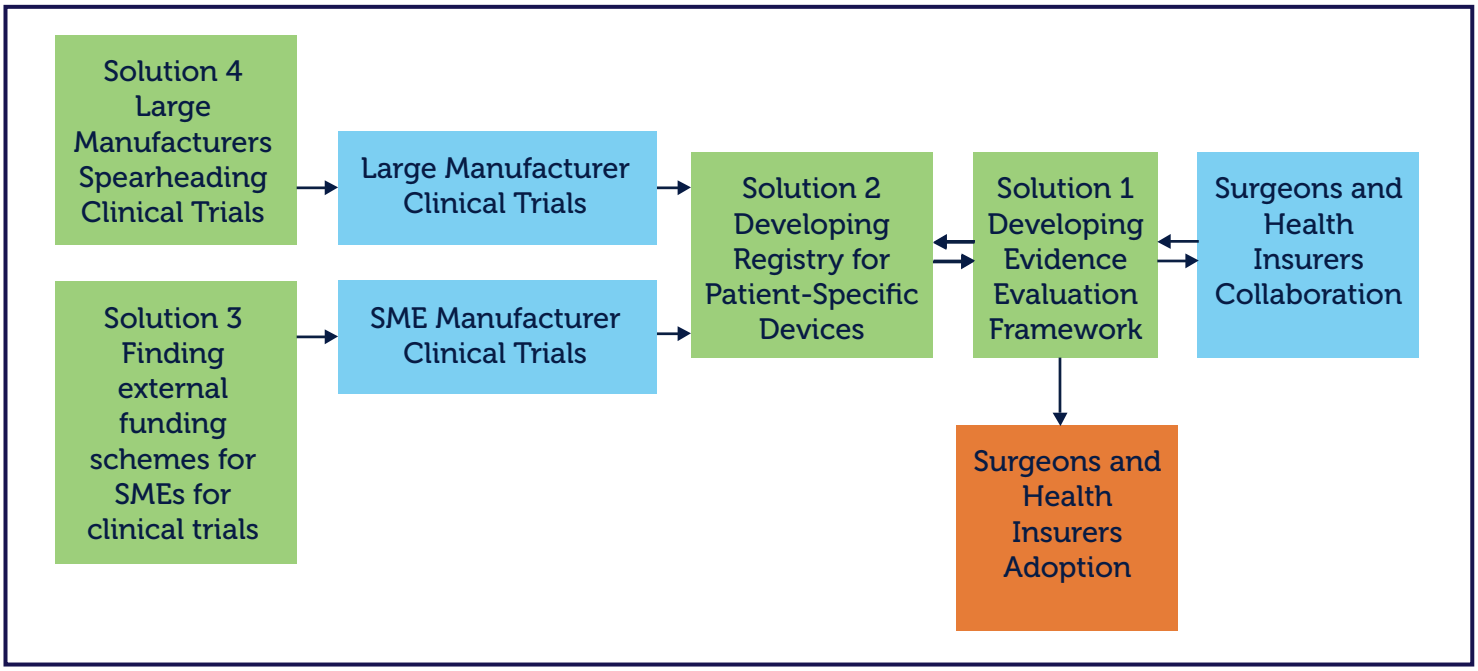
Animal trials will be conducted for highly innovative devices or materials that require proof-of-concept, however, for already established devices, such as titanium 3DP orthopaedic implants, animal trials will not be necessary and human clinical trials can be more productive. In this regard, a researcher stated,

> "We know that lattice-implants will stimulate bone integration and growth. We are not testing for that with animal trials. We are not sacrificing animals trying to produce what we already know."

If the results of the clinical trials conducted by large manufacturers are positive, they can possibly be leveraged by SMEs to acquire more funding to conduct their own clinical trials, whether it is for a novel device or biomaterial.

A summary of the four proposed recommended solutions (and their relationship with relevant stakeholders) to resolve the 'lack of evidence catch-22 scenario' is depicted in Figure 14.

Figure 14. Summary of Recommended Solutions for resolving the Lack of Evidence Catch-22



4.2. Catch-22 Scenario 2: Lack Of Funding For SME's IP Protection

4.2.1 Explanation

As discussed in the beginning of Section 4, SMEs require external funding for the expensive patent application process, however, external private funding bodies are looking to invest in innovative, high-value companies who 'already' have their IP protected by patents. This creates another Catch-22 scenario in which two stakeholders in the industry are waiting for one another to proceed. With inputs from variety of stakeholders, two recommended solutions are proposed in order to break this catch-22 scenario's circle:

1. SME and Investor Collaboration
2. Applying for governmental financial support

4.2.2 Recommended solutions

Solution 1: SME and investor collaboration

SMEs and investors can collaborate in various forms of partnership in the process of IP application. As stated by an interviewed SME representative,

> "Part of what could be useful to small businesses, like ours, is where there is that service. Where it is not just a fee paid service offering, but an investment partnership offering where you get good advice and they are going to come with you for the ride. The cost burden (of hiring an IP attorney) can be reduced significantly or eliminated and you end up with global protection which then becomes very appealing for investors."

This solution is dependent on whether the investor has the knowledge and capability to prepare patent applications to the jurisdictions of interest and also if they see value in the technology.

Solution 2: Applying for governmental financial support

Acquiring funds for IP protection from private funding bodies is especially difficult for Australian companies, however, there are certain governmental grants that provide assistance for SMEs with funds for legal, IP, and patenting advice. Both federal and state governments offer grants for innovation and R&D and some grants are targeted towards the medical device industry, increasing the chance for SMEs who are active in the innovative 3DP medical device space. This solution is dependent on the SMEs' ability to identify and apply for the grant.

A state government representative states,

> "Although these funding mechanisms exist, it is a challenge for SMEs to know what schemes are available, when they are and how to access their funds. What you will find is that schemes are temporarily available. If you don't know that they are there, it's like a ship in the night. You won't know it left."

To aid SMEs in identifying grants, it is advised to use a grant referral system such as GrantConnect and GrantGuru (as elaborated in the section **'Finding external funding schemes for SMEs for clinical trials'**). However, both of these grant referral system are fairly general and they are not industry-specific. We will come back to this point in Section 5 with a proposal for the development of an industry-specific grant referral system.

Section 5: The Future Avenues

Courtesy of RMIT AMP

SECTION 5 - THE FUTURE AVENUES

In this section, we highlight potential four practical endeavours which may facilitate the adoption and diffusions of 3DP medical devices. These four future avenues are derived based on existing gaps in the industry, which we identified based on our two White Papers (the second one being this report).

I. Leading the Collection of Post-Surgery Follow ups Data

Multiple stakeholders, including expert regulatory consultants, suggested that clinical data registry was the most suitable method of collecting clinical data to determine whether the custom-made devices (3DP or not) provide superior patient outcomes compared to conventional devices. This was due to the difficulty of implementing randomised control trials for patient-specific devices but not for pre-set sizes, such as conventionally manufactured devices. As stated in section 4.1.2, the existing registries in Australia have two major shortcomings, including the lack of follow up registries and also the lack of specifying custom-made and/or 3DP devices.

Nevertheless, the already existing registries can be certainly helpful as a starting point to generate a more comprehensive registry. The registries we could contact to propose the collection of data for patient specific devices are the AOANJRR, ASR, and VOTOR registries. The AOANJRR is the largest joint replacement registry in Australia and it collects data on knee, hip, shoulder, elbow, wrist, ankle, and spinal disc replacement surgeries. Joint reconstruction devices, followed by spinal devices, have the largest share in the orthopaedic device market [14] and the data from both categories of devices are reflected in the AOANJRR. It is therefore important to collaborate with the South Australian Health and Medical Research Institute (SAHMRI) who actively collects data for registry.

SAHMRI's method of data collection includes forms that specify patient characteristics, the prosthesis type and features, method of prosthesis fixation, and the surgical techniques used. Two more checkboxes could be added to this criterion, tracking whether the device was conventional or custom-made for the patient and 3D printed. Using that data, a novel automated system of data generation could be created, tracking patient recovery, rehabilitation rates, and overall satisfaction with the surgical procedure and medical device. The assessment criterion can be developed under consultation with the Australian Digital Health Agency, health insurers, other research centres, and surgeons.

This follow-up system will be largely beneficial since currently there is no system in place to track device performance in vivo. Registries only track revisions and their reasons. Having an assessment of device performance over time, will lead to an influx of clinical evidence, identifying the best performing medical devices. This project can begin with the scope of comparing patient-specific orthopaedic devices to conventional ones, however, it could be extrapolated to all medical devices.

II. IP Protection for SMEs

Medical device manufacturing SMEs have identified IP protection as a major barrier that inhibits their innovation. For example, an SME representative stated,

> "If you want to work on something, find a way to significantly assist SME's with patenting a device. In the U.K, they have the patent box which has great merit. Israel and South Korea backs SME IP so that innovation isn't halted by the cost burden. Australia has none of that. We have trouble extrapolating our patents into other jurisdictions. However, and whatever they are doing in Israel at the government level to support innovation and innovative companies with the development of the products, IP protection globally and supporting companies that take their products offshore is something that the world, and particularly Australia can learn from. We have trouble here because of the costs."

This raises the potential research question, **"What programs do highly innovative countries utilize to develop and protect their I.P.?"** Further sub-questions can be asked, such as **'how do the highly innovative countries protect their I.P. nationally and globally?'** And 'for SMEs, **'what services are available?'**. The project can use Australia as a benchmark and compare current strategies implemented by government and their resulting impact on innovation rates. Countries with exceptional innovation rates and IP protection services that can be investigated are Switzerland, South Korea, Japan, United Kingdom, and Israel. This project could lead to programs that benefit SMEs across all industries and provide insight on a global scale.

III. Developing Decision Making Tool for Manufacturers

A decision-making tool for medical device manufacturers, who are either looking to adopt or have already adopted 3DP technologies, could provide streamlined cost effectiveness analysis, leading to more efficient manufacturing and logistical processes. The efficient mechanisms for device manufacture and delivery will hopefully translate into improved outcomes for the patients, providing quicker and more affordable treatments. A large manufacturer representative, who has a project in manufacturing time-sensitive patient-specific implants for osteosarcoma patients, states,

> "Speed is important for their survival and because the geometry changes over time as the tumour grows, so quickly acting on a scan is paramount before a growing cancer makes the device dimensions redundant. Time is of the essence. Transportability is important since implants are exposed to different temperatures, pressures, etc. So minimising transport would be of great value and having an efficient logistical system that would minimise risk of implant damage during transport"

The proposed decision-making tool will ask the manufacturers a series of questions. These question could range from determining whether 3DP is the most suitable method of manufacture, to some inquiries about the applicable materials, the cost of the manufacture and the logistical process, and also the regulatory costs. It can aid with determining the value of the device and could state the saved costs compared to devices made via conventional manufacturing.

The proposed decision-making tool has had mixed feedbacks from medical device manufacturers. The positive feedback came from large manufacturers or the SMEs who manufacture their devices in-house. An SME that provides custom dental implants says,

> "That would be a great tool in the toolbox. It would be helpful".

This was primarily because the tool was useful when estimating manufacturing and post-processing costs. For SMEs who design medical devices and outsource the manufacturing process, certain functions of the tool will not be applicable and that was reflected in their feedback, saying, "I do not think the tool is necessary."

IV. Online Booking Tool for Sterilisation Bureaus

As discussed in section 3.7, SMEs have difficulty in making medical devices that are produced in low-volume, cost-competitive due to the large sterilisation service fee which is at a set cost depending on the size of the sterilisation chamber. The only way to make this service more affordable for manufacturers and patients is to utilise batch processing, however, that extends the device delivery process from what should be 1 week to 4-6 weeks. One potential solution that could be explored is that the SMEs, who develop similar products, share the sterilisation chamber volume, split the service fee, and make the procedure more affordable. This could easily be instituted via an online-booking tool that could be made available to SMEs, however, there is a major challenge to address.

Sterilisation, as a service, is more advanced than inserting a medical device into a chamber and running the machine. An SME representative states

> "I would see challenges at the actual delivery of sterilisation services, not the booking system to fill the chamber"

The sterilisation service involves a strict validation protocol for each device to determine that it has been appropriately sterilised. If multiple manufacturers' devices were to be sterilised together, they would most likely use different validation protocols. The current method of batch processing, that individual SMEs employ, includes grouping the different medical devices under a family banner. An SME representative explains,

> "For example if we have 6 different product lines that we are looking to sterilise, we have to lump them under a family of the most difficult to clean, sterilise and validate. If we can group them under a family banner, then our process is good." From an SME representatives' perspective, this would be difficult to implement and will require a lot of coordination between different SMEs. "I think the practicality of different goods being mixed up from different manufacturers using potentially different materials and different validation processes and different families, that would be potentially a challenge."

Section 6: Concluding Remarks

Courtesy of RMIT AMP

SECTION 6 - CONCLUDING REMARKS

3DP as a technology is considered an opportunity area for growth in Australia's evolving manufacturing industry. Utilising 3DP in the medical sector shows potential benefits for patients, health care system, and industry growth, however, widespread adoption and diffusion of the technology is currently slow. The aim of this White Paper was to investigate the state-of-the-art application of 3D Printing (3DP) in medical device industry in Australia from a Business Model perspective. In order to do so, we have identified non-technical and business-model-related barriers to adoption and diffusion of 3DP medical devices.

This is the second White Paper in a series of studies of a funded project by RMIT University running from 2017-2020. The first White Paper was published in November 2018, which outlined a broader perspective on adoption and diffusion of 3DP in medical device industry. The first White paper also included technology, material science, and regulatory aspects.

The empirical material in this White Paper comes from an extensive qualitative data collection obtained from various stakeholders in the industry during a two-year period, 2017-2019. The stakeholders involved are manufacturer (large firms and SMEs), surgeons, patients, hospitals, research centres, regulatory bodies (TGA), insurers, and industry associations. The multi-stakeholder perspectives reflected in the White paper are praised by stakeholders themselves as a unique endeavour. For example an SME's representative noted

> "It's good that you brought so many different people [stakeholders] together in one room. Because a lot of industries tend to dislike their competitors or related stakeholders, but they should be working together to mutually benefit."

Such rich collected data from various categories of stakeholders has guided us in investigation of the followings in this White Paper:

- Identifying various Business Model types in the industry, both currently practiced and potentially future ones
- Identifying non-technical and business-model-related barriers hindering a wider adoption of 3DP in medical device industry
- Mapping identified barriers against Business Model types and weighting their severities
- Conducting the Root Cause Analysis of each barrier in order to identify where each barrier comes from
- Identifying complex Catch-22 scenarios in conducting Root Cause Analysis
- Offering recommended solutions to overcome the barriers and associated Catch-22 scenarios
- And finally, proposing future avenues for developing practical tools that enhance the engagement of various stakeholders in the industry and hence a wider adoption of 3DP

This White paper was the first ever effort to dig deep into non-technical barriers associated with blockage of adoption of 3DP technologies in medical device industry, particularly in Australia.

This White Paper report will be beneficial for industry actors (SMEs, large manufacturers, and service bureaus) in order to get a holistic and multi-stakeholder perspective of the prospect of the current and future business models, associated barriers to the business, and potential solutions. It is also beneficial for governmental research agencies, such as IMCRC and CSIRO to design targeted grants for areas where there are market failure blockages that require third party interventions. It can be helpful for regulatory bodies to get insight on a wide range of opportunity areas in the industry that can be explored through smoother, faster, and more transparent regulatory pathways, particularly for SMEs. Last but not least, the findings in this White Paper is beneficial for health insurers to facilitate their informed decision making about coverage of certain high-risk 3DP medical devices.

References

[1] Tavassoli S, Elghitany A, Pope L, Brandt M, Mention, AL, Cole I. Adoption and Diffusion of Disruptive Technologies: The Case of 3D Printing in the Medical Device Industry, 2018

[2] Shuang F, Hu W, Shao Y, Li H, Zou H. Treatment of Intercondylar Humeral Fractures With 3D-Printed Osteosynthesis Plates. Medicine (Baltimore). 2016;95(3):e2461.

[3] Baj A, Bolzoni AR, Giannì AB. Virtual planning and patient-specific implants in mandibular reconstruction surgery: A micro-costing analysis. Value in Health. 2016;19(7):A723.

[4] Resnick CM, Inverso G, Wrzosek M, Padwa BL, Kaban LB, Peacock ZS. Is There a Difference in Cost Between Standard and Virtual Surgical Planning for Orthognathic Surgery? Journal of Oral and Maxillofacial Surgery. 2016;74(9):1827-33.

[5] D. Shidid, M. Leary, P. Choong and M. Brandt, "Just-in-time Design and Additive Manufacture of Patient-specific Medical Implants", Physics Procedia, vol. 83, pp. 4-14, 2016. Available: 10.1016/j.phpro.2016.08.002.

[6] CSIRO, Medical Technologies and Pharmaceuticals Roadmap - A Roadmap for unlocking future growth opportunities for Australia, 2017

[7] CSIRO, Advanced Manufacturing Roadmap - A Roadmap for unlocking future growth opportunities for Australia, 2016

[8] TGA, Consultation: Proposed regulatory changes related to personalised and 3D printed medical devices, 2018

[9] TGA, Consultation: Proposed regulatory scheme for personalised medical devices, including 3D-printed devices, 2019

[10] Matsumoto, J., Morris, J., Foley, T., Williamson, E., Leng, S., McGee, K., Kuhlmann, J., Nesberg, L. and Vrtiska, T. (2015). Three-dimensional Physical Modeling: Applications and Experience at Mayo Clinic. RadioGraphics, 35(7), pp.1989-2006.

[11] J. Witowski et al., "From ideas to long-term studies: 3D printing clinical trials review", International Journal of Computer Assisted Radiology and Surgery, vol. 13, no. 9, pp. 1473-1478, 2018. Available: 10.1007/s11548-018-1793-8.

[12] B. Gross, J. Erkal, S. Lockwood, C. Chen and D. Spence, "Evaluation of 3D Printing and Its Potential Impact on Biotechnology and the Chemical Sciences", Analytical Chemistry, vol. 86, no. 7, pp. 3240-3253, 2014. Available: 10.1021/ac403397r.

[13] L. Diment, M. Thompson and J. Bergmann, "Clinical efficacy and effectiveness of 3D printing: a systematic review", BMJ Open, vol. 7, no. 12, p. e016891, 2017. Available: 10.1136/bmjopen-2017-016891.

[14] S. Ugalmugale, "Orthopedic Devices Market Size By Product, Industry Analysis Report, Regional Outlook, Application Potential, Price Trends, Competitive Market Share & Forecast, 2019 – 2025", Global Market Insights, 2017.

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