Big Changes in Australia in Medical Devices

Arthur Brandwood, Brandwood Biomedical with the Medical Devices Group

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Joe Hage: Hello, this is Joe Hage and I have the privilege of leading your Medical Devices Group. As of this recording, we have 255,000 members worldwide. One of the reasons I think we've grown so large is we have members like Arthur Brandwood in the group who are available and willing to share their expertise with the group.

Arthur is phoning in from Australia this morning at 4:00AM, thank you Arthur. I think of him as my go-to for everything Australian. In fact you do more than Australian, isn't that right? 00:43

Arthur Brandwood: That's right, Australia and most of the Asia Pacific. We also support Australian companies coming to the US and to Europe. We've got a pretty global perspective from down here at the bottom of the planet.

Well, thanks Joe for the kind introduction. As he said I'm Arthur Brandwood. I am based down here in Sydney, Australia. I run a company, Brandwood Biomedical, which is a regulatory affairs and regulatory, quality and technical advisory firm based in Sydney and Wellington and in Beijing.

This is the obligatory opening side which tells you a little bit about us. As I said we do medical devices and IVDs. We have primarily a focus on the Asia Pacific. This little map here shows our main offices plus the locations of our regional partners so that we can support clients right across East and Southeast Asia and Australia and New Zealand.

We do have a pretty global perspective, and we as a firm believe that it's really important in this industry that you are highly networked and highly engaged. Both highly engaged with industry colleagues but engaged with regulators. I'm sure I don't need to convince Joe that he's one of the most networked people I know and it's certainly been a pleasure to be involved with Medical Devices Group and that to be able to support that enterprise in bringing us all together.

If you're interested in something broader we'll be talking about Australia today, but if you do have interests across the rest of the Asia Pacific I'd highly recommend that you take a look at this. We are putting together a meeting in the United States in March where we'll be bringing together a whole bunch of Asia Pacific experts all flying to the US from places like Taipei and Singapore and Jakarta and Australia. To bring a knowledge base of what happens and how regulatory affairs and market access works across the Asia Pacific. Have a look at the website and I'll remind you again at the end of webinar about this.

Let's just start with why Australia. Really there are a number of interesting things happening here at the moment which have really changed the environment in medical devices quite dramatically over the last year or so. I'm going to talk about some of them in this webinar.

They are that we have a new government which has got a very strong and aggressive deregulatory agenda. We have a clinical trial 03:33 Australia that is light touch in its regulation, is sophisticated and straightforward and results in lower costs to do clinical trials.

We have a series of tech concessions which support research and development both in tech support for companies and in generous taxation treatment for employee share options. Which allow startup companies to preserve capital by paying employees partially in equity.

I will touch briefly on Australia's rather unique position in Asia and it's increasing engagement with Asia in trade which again makes it an interesting place for the medical devices industry.

Let's start with that story. This is a graph that was published in the Australian Financial Review about six or eight months ago now. These are figures up to the end of 2013. What's really interesting is the change in Australia's trading partners. As you can see the traditional trading partners of Europe and the US and Japan have been gradually declining in the face of an increasing involvement with China which now, since this graph was published, we're now something like 40% of Australia's exports go to China.

Of course a lot of that is 05:02 production is iron ore and coal and all that sort of stuff. Australia is a very large 05:07 production exporter. The interesting part of this story is that manufactured exports are growing as a share of that pie and they're growing in interesting places. Because like in the US and in other parts of the world, 05:21 traditional industries like automotive are dying.

General Motors and Ford have both recently announced that they're going to quit Australia. Other new knowledge-based industries are taking over. This is the most interesting one is that now the single largest manufacturing sector exporting from Australia to China is actually the therapeutics sector; medical devices and pharmaceuticals. Based on recent data from the Australian Bureau of Statistics. The federal government has recognized this and one of the things they're doing is quite aggressively putting support in for this industry.

The Australian economy is doing well; there hasn't been a recession here for over 20 years. We're seeing, as you might expect, increasing expenditure on health which then flows on into a very robust market for medical devices. As you can see that the expenditure is growing right across the border both in government, private, private health insurance and direct spending by individuals and so we've got a very robust market here.

I just wanted to give that context of the economic situation in Australia as to why things are developing the way they are. I'm now going to change tact a little bit, and just talk a bit about the regulatory environment here. This is a view of the Therapeutic Goods Administration. This extraordinary building which sits in a field outside of the national capital of Canberra. Canberra is a bit like Washington, D.C. in that it exists in its own territory carved out of the state of New South Wales. It's an interesting place as well in that it was a result of a design competition. A design competition won by an American talent planner, Walter Burley Griffin who designed the whole city of Canberra complete with artificial lake and all sorts of interesting things. There it is, it's hidden in amongst the trees, and right on the edge of it is the TGA.

It's an interesting organization. It's a division of the Department of Health, very much the way the FDA is a division of the US Federal Health Department, but it's actually quite a small agency in medical devices. There are about 500 people who work in this building but less than 100 are in the devices sector. It was quite interesting when I did the numbers as part of a submission to a Senate inquiry here where I ...

The United States FDA has about more than 1,000 experts and technical people working in the devices programme. The 10 largest European notified bodies between them have approaching 10,000 experts. They have laboratories and auditors and experts all over the world. TGA has about 100 and in fact, I think they've probably got slightly less than that.

Trying to regulate an entire portfolio of medical devices because the Australian public expects to see the same devices as are available in the United States or in Europe. With only 100 people is kind of difficult for the agency.

The agency acts as both a competent authority and a Conformity Assessment Body in the European sense in that it does its own assessments but it also takes the primary responsibility for regulatory framework. It has a very strong scientific culture. This building was once a laboratory and has gradually become a regulatory agency in the last 20 years and the culture still pervades the whole organization. When you are dealing with them you do get some kind of scaly answers ... scaly questions from 08:58. They will get right to the sides.

Australia has taken the European regulatory system and adopted in this Australia law. I don't want to go through this in detail but just to point out this is the content page of the Therapeutic Goods Act, and right buried there in the box in the middle you will see the elements that are very familiar to anybody who understands the European regulatory framework and the medical device directives system based on essential principles, harmonized standards, conformity assessment procedures. Plus a register of

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medical devices, which is the key legal point of control. You cannot supply devices in Australia unless they're entered on the TGA's database, the Australian Register of Therapeutic Goods.

Here are the regulations that sit underneath. TGA has done what the Europeans are proposing to do. It's basically taken this European system into one set of regulations and included Active Implantable Medical Devices and In Vitro Diagnostic devices all in the same regs. Along with the rest of the medical devices.

It does that through a simple tweak of the classification rules where we have a rule which adds Active Implantable Medical Devices as a separate device class. We have four new rules for a Class 1 through four in vitro diagnostics. Then they're all dealt with under the same regulatory framework and assessment framework.

Again there in the regulations is the including ... the Part Five with is governed inclusion of medical devices in the Register.

I'm just going to try and map a little bit what ways you can supply medical devices in Australia. This is basically the whole landscape. We'll start with those circumstances where there is no TGA assessment of safety prior to supply.

The most obvious one of those that you'll be familiar with is clinical trials where we have two pathways. One is called the Clinical Trial Exemption pathway, CTX. It involves a direct TGA assessment of the protocol, it's expensive, it takes a lot of time, and it tends really to be used for high risk medicines really. It's really a bit of a mixture of an IND and a pre-submission. It allows the TGA to engage with the development process, and maximized the likelihood of subsequent approval based on clinical trial data.

The alternative pathway is Clinical Trial Notification. This is like a USID for a non-significant risk device. It's entirely managed by the ethics committee who do the conventional review of the protocol and oversight of the trial. TGA has the power to audit trials, and there is nominal fee for the notification. It's literally a couple of hundred dollars. To this stage all devices have gone down this pathway. In other words TGA does not get directly involved in the oversight of the trial although it does have the power to do so.

These are obviously for investigational use only and usually leading up to a subsequent regulatory submission. There are a number of different pathways for special access and I'm not going to get into those in detail in this webinar, but for humanitarian use both for individual patient cases and also for early access to new technologies through the authorized prescriber out which allows specified clinicians to prescribe specified devices to specified populations of patients pending a regulatory approval.

There is a personal import provision which allows any person to bring any therapeutic good with the obvious exception of Section Eight narcotics for their own personal use without requirement for

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regulatory approval. It is possible to import your own medicines or medical devices into Australia just for yourself.

Then we have devices which must meet safety and performance requirements. That includes custom-made devices made individually for a named patient through a clinical prescription. It includes exempt goods which are low risk worthy. Regulator specifically sends them by order. Things like hospital bedding and protective clothing and conventional toothpastes which strictly meet the definition of medical device but the regulator doesn't want to be involved in dealing with those. Are all exempted from entry onto the register. However, they still are required to meet the essential principles and are subject to post-market regulation.

Then finally, formal review and registration of medical devices of the classes that you see here. Australia uses the European classification system modified to add the Active Implantable Medical Devices and the In Vitro Diagnostics. Regulatory intervention is based on the level of risks, so the higher the risk the higher the review. Very much like happens in Europe. That's the landscape as it works in Australia. We'll be largely concentrating on that last bit of ARTG inclusion and how that works.

There is a requirement that there is a local authorized representative. We call the 'sponsors' in Australia. The sponsor must be an Australian company. You can use a third party. It's something that we do fairly regularly for overseas clients and hold the license on their behalf. The sponsor is responsible for providing manufacturing commission to TGA on demand. They manage the regulatory submissions and they respond and manage post-market activities such as adverse event reporting.

Luckily we've got a webinar; nobody is traveling to this election. Nobody is going to a conference, but if you're going to a conference as I did a couple of weeks ago in China you'll be familiar with this sort of scene. We 15:09 jam at the airport. You see all those guys with the special passes and the business class travelers who neat down the special fast track around the side and you're standing there in the long line and getting to be frustrated.

Well, TGA has a similar arrangement. TGA will accept your opinion certificates in lieu of the Australian certificate on most medical devices. We call that Fast Track. Basically you can present a CE certificate and get much more rapid regulatory approval rather than a direct TGA assessment.

Now to show you how this works. Really there are three parties. There is the manufacturer who could be anywhere in the world. There is the sponsor who has to be an Australian company, and there is the TGA located in Canberra. The manufacturer is responsible for gaining the CE certificate for holding the technical file and for doing things like determining the specific Australian classification of the device. There are a few small differences, and for preparation of an Australian Declaration of Conformity. TGA has its own particular template for doing that.

The sponsor then takes the CE certificate and submits that to TGA. This little e here is the e-business portal for TGA. It's simply an online HTML form and you provide the CE certificate as a PDF attachment.

That's provided to TGA who do a very quick assessment and they then place that on their database. Now there is an Accepted Manufacturer Evidence for the main manufacturer associated with that sponsor. That process is very quick, it takes at most a couple of days.

Then the sponsor can now make registration applications for medical devices within the scope of that certificate. Again those applications are made to TGA via a web form or web interface. TGA assesses them and that results in a ARTG entry. Once that happens you can then supply the device. Really it's all done online.

There is however, at this stage of assessment, for some devices something called an application audit. What that means is that TGA before completing their ARTG entry will request to see some of the high level technical file data. For particular high risk devices this is done every time. That's known as a mandatory application audit and it attracts an application fee. TGA can request an application audit for any medical device. Although if it's not one of those where there's a standard mandatory audit there is no fee applied for the lower risk devices.

Typically they'll ask to see things like the risk assessment report, the essential principles checklist, and the clinical evaluation report. This process of assessment can take anything between as long as several months if it's a high risk device which requires a decent amount of review of the application audit documents. It can be very quick, and recent experience we've seen some devices going through in a 18:22 seven days so you can ... and those including Class 2B devices. You can have quite a rapid entry to the market by presenting a CE certificate.

There are a couple of exclusions. Any device with an integral medicine or any device with an integral biological component that includes recombinant products and blood products, does require direct assessment by TGA. That's done using the conventional conformity assessment models that are found in Europe by audit to the regulations in the same way that an MDD audit is done plus an ISO 13485 audit. So that we review the technical file plus an onside ISO 14385 audit for these types of medical devices.

Until recently, the other group that was required to undergo direct TGA assessment irrespective of the risk class of the device except for Class 1 non-measuring and non-sterile were Australian-manufactured devices. Australian manufacturers did not have the option of using the CE certificate. This has been a contentious issue for many years, and big news was that this was changed recently as part of the current government's deregulatory agenda. This rather cute website now the Australian Government Cutting Red Tape website. They have had two repeal days, the spring and the autumn repeal days. What they're doing is getting rid of a lot of old regulation and looking to see what regulation can be removed if it's unnecessary.

One thing that caught us all by surprise really is that a few weeks ago towards the end of October, this appeared as part of this Cutting Red Tape platform. The idea of using International Standards and Risk Assessment in lieu of direct local regulation. One thing that was said was that if we want to see greater opportunity and greater acceptance of International Standards and Risk Assessments.

The Prime Minister put out a press release and lo and behold right there in the middle of it the very first step the Government was taking as part of this new initiative was to enable local Australian manufacturers to use CE certificates in place of TGA certification in the same way that it's been available for overseas companies for some time.

So there was the first step, and that caused quite a scare as you can imagine amongst the domestic medical devices community. But having said that this Fast Track pathway has been available to international companies for some years now.

Again there are some, as I said there are some exclusions but now the Australian manufacturers are no longer in there. However, there is a counterweight to this. Of course the PIP breast implant scandal amongst other well-known post-market failures of high risk medical devices including 21:31 metal and metal orthopedic implants, has attracted public and political attention in Australia as it has in most countries.

There has therefore been a push particularly from some independent politicians who often hold balance of power in the upper house in the Australian Senate. There has been a push for increase in regulation. So there is attention between public pressure for most scrutiny of medical devices particularly high risk medical devices and the deregulatory agenda from the government. How has that resolved?

Well, we've seen all of these reviews. The public pressure has resulted in three senate inquiries, an Auditor General review, and a Health Technology Assessment review all within the last few years. TGA is being reviewed almost continuously.

And really my view is that it's all about confidence. We talk at the moment about confidence building and TGA is undertaking an active programme right now of confidence building with the European Notified Bodies. What that is meant to do is to establish documented evidence for confidence in the assessments carried out in Europe so that TGA can say to the Australian public that it's reasonable and safe to rely upon audits and reviews which are conducted in Europe and result in CE certifications. And that those are relied upon for the purpose of Australian regulatory approval.

So TGA is quite actively doing shared audits, shared document reviews, and exchanging information. And it's about TGA building its confidence in the European Notified Bodies. It's also about TGA building the confidence of the Australian public in the regulatory framework that relies upon International Regulatory Assessments.

It's likely that the confidence building process as it develops will result in reduced application audits for those notified bodies in which TGA formally establishes confidence. There are a large number of notified bodies. As you're aware there's something like 80 in Europe. They are of variable quality, and TGA is actively looking to see which one it can establish confidence in so that it can reduce the level of document review or application audit based for applications that come certified by those notified bodies.

I just want to talk briefly about the clinical trials environment. You remember this slide earlier and the Clinical Trial Notification process. Remember that it's simply a matter of conventional Ethics Committee review the institutional review board. Once that Ethics Committee review is done, the only thing that then is required to satisfy TGA is that a one-page form is signed off by the Chairman of the Ethics Committee, posted off toe TGA with a nominal notification fee, and then the clinical trial can commence.

The clinical trials environment in Australia is quite well streamlined. There is a standardized National Ethics Committee Application system with a standardized electronic form. You can see all of this at the website that's listed on the slide there. The Ethics Committees have been revamped and there have been a review of the way Ethics Committees operate to create a group of, if you like, super-Ethics Committees that are 25:18 system. Certain Ethics Committees are considered to be ones which can be recognized by others.

So if a clinical trial which is multisite is reviewed by one of these first-year Ethics Committees, then all of the other Ethics Committees are required to recognize that institutional review. So there is no requirement to have multiple Ethics Committee reviews for multiple sites. That then very much streamlines the Ethics Committee process for multisite trials.

That has big effect on costs, and don't take my word for it. Here's a couple of quotes, one from Richard Haiduck at Burrill & Co "Clinical trials can be done in Australia far cheaper than they can be done in the rest of the western world." And he says that, "clinical trials in Australia is the best bargain there is."

Alex Safarian of Novotech tries to put a number on that the order of 35 to 40 per cent cheaper than the US. So quite a streamlined clinical trial environment. Of course a very sophisticated health system in Australia and much lower cost of doing trial here and much quicker.

And then coming back to Medical Devices Group, those of you who follow the group will probably have seen this discussion from Joe a little while ago on the tax incentives going on here. I just quote a couple of things from him. There is a tax incentive paid for research and development here results in cash payments paid quarterly to startup companies. The mathematics of this mean that the tax incentive effectively ends up as a subsidy. And the difference between the rebate and the corporate tax rate, the rebate is at 45 per cent, corporate tax rate is 30 per cent so you're actually getting a subsidy for the activity.

How does that work?

It works a bit like this, and there's a website you can go and look at there. But firstly there's a 45% Refundable Offset. For firms less than $20 million aggregate turnover, that 45% is refunded as if you were paying tax. For firms which are in profit or over $20 million, it's not refundable.

But the way it works then is that there is a 45% tax break on your tax bill for eligible research and development activities. But if you are a startup, you're not yet making money, the taxman effectively assumes that you are and that you're paying the tax and then refunds that tax. Even though it's not being paid. With it being a 45% Refundable Offset, that's a very large contribution towards the cost of the research and development activity.

This available to any Australian company doing eligible research and development activity. It's also available to foreign companies in countries which have a double taxation agreement with Australia, and which have their own local permanent office here in Australia. Most of the large western countries have got double taxation agreements with Australia.

It's also possible to do some of the R&D work outside of Australia and still get this offset. For example, multicenter clinical trials where it's necessary because of the nature of the R&D to do some of the work offshore then the cost of the offshore component can be included and attract the tax refund.

I'll just give an example of this. Some of you will be familiar with this particular medical device, the PillCam. This is a capsular endoscopy. It's a device that comes from an Israeli company, Given Imaging, who are also very well established here in Australia.

Given when they set up PillCam here, this is an alternative to standard endoscopy, so instead of using an endoscope which can also reach so far into the gut, the way this works is you swallow this pill. This is a marvel of microelectronics. It's got a couple of strobe lights and a video camera all miniaturized into the pill. It can take a high definition movie of the complete length of the gut as it passes through, so you end up with these sorts of images and which are used for diagnosis.

When Given set up, they needed to do a couple of things. Particularly the preparation, the bio preparation protocols that were in existence in Australia were not particularly effective. There needed to be a different protocol just because of the nature of the device. They required to demonstrate that this different protocol was effective in order to move forward to get reimbursement.

Now that required a significant investment to develop the data that needed a clinical trial with fairly large sample size. The clinical trial had to be the conventional multicenter, randomized, audited trial, 300 patients. It was about $1 million budget. Simply the Australia & New Zealand operations of Given didn't have the budget to support that kind of trial.

What did they do? Well it was interesting. Because they had an Australian subsidy, they were able to seek an R&D tax refund. They actually went forward and got a ruling in advance. 31:00 this is really valuable to actually consult with the relevant government departments. They got a ruling that the trial was going to be eligible. That provided them with the opportunity to proceed with the trial. And because they were able to supply the devices from offshore and manage the transfer pricing, the way this worked out was that it actually became a cash flow positive activity. The whole thing was essentially funded by the R&D tax incentive.

So here's a real example of a company with an international headquarters, a very substantial local presence who were able to do a large clinical trial and get the whole thing essentially funded by means of the R&D tax incentive.

Just a quick one, there has been recent changes well in the area of employee share options. Of course it's very important for startup companies to be able to preserve their capital. And usually startup companies their largest cost is people, and it helps to be able to pay those partially in salary and partially in equity. There has been a recent adjustment to the law here on employee share options. This will commence in July next year. And a number of things will happen. The tax will now be deferred until the date of exercise for options. Previously tax was accrued at the time the options were granted. There's a very generous maximum deferral time of up to 15 years. And there will be a standardized documentation scheme to simplify the administration of employee share schemes.

There is a particular concession within the Employee Share Scheme legislation for startup companies. That defined as any unlisted company with an aggregate turnover of less than $50 million and which has been incorporated less than 10 years.

One thing is that a small tax exemption for the $1,000 of shares or options granted for employees under a salary of under $180,000. Companies are allowed to provide shares at a discount of up to 15% with no tax liability for the employee. That discounted portion is exempt from Capital Gains Tax at the time of sale.

Shares must be held at least three years to attract the benefit here. But we can see that now we've got a favorable treatment for both options and share grants which allow far more flexibility to use equity incentives for attracting staff.

So just to wind up, coming back to the original agenda slide. I just want to come back, we've talked about deregulation, we've talked about clinical trials, and we've talked about taxation. I just want to come back to this point about trade with Asia. Australia as you there on that little globe sits right in the same time zones as the larger Asian economies of Japan and Asia, and very close to Southeast Asia.

There are some interesting things happening here demographically as well. Of course Australia was originally founded as a British Colony 200+years ago but the demographics of the country are changing quite rapidly. This is a graph of the number of Australians born in different countries. You can see that Asian-born Australians are becoming much more part of the mix, and the Brit particularly are declining. So the demographics of this country are changing quite dramatically as the country becomes very much more involved with its Asian neighbors.

That makes it interesting in terms of the trade from here. I talked about the trade with China but there's a lot of trade with the rest of the region as well. Australia really is quite a good place to do business if you're interested in expanding more broadly into the Asia Pacific. However, there are a lot of different

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things going on there and a lot of different regulatory agencies and a lot of regulatory change. Here's a list of just some of them. We have major change going on in China.

We have the Southeast Asian Nations, ASEAN, Medical Device Directive coming into effect beginning of next year. We have substantial change in Japan happening just this month, and a lot of other things going on. It's a very fluid environment with a lot of opportunity.

I just remind you that if you really want to learn more broadly about Asia and Asian regulatory affairs 35:47, market access, please do consider coming along to the Asia Pacific Device Summit to be held in San Diego in March. There's the website link there, we'll send the details in the follow-up email from this webinar, but please do take a look. I'm sure it's going to be a fascinating show. We're bringing a lot of experts from the region into the US, so you don't have to fly all over the South Pacific and Asia to meet them yourself. You can go to one place and see them all in San Diego.

And with that I'll say-

Joe Hage: I can tell you that there is interest because I've had my chat window open and a couple of folks have been visiting the site while you've been speaking so.

Arthur Brandwood: Good.

Joe Hage: Perhaps they'll be joining us.

Arthur Brandwood: I do hope so.

Joe Hage: I think you were wrapping up and that's good because the questions are coming in and I'd like to ask them now unless you have something more you'd like to add.

Arthur Brandwood: No no, I'm absolutely ready to, as I said, let's talk let's have a few questions.

Joe Hage: Okay, so first question cameth from Christopher and he asks, how much of the export shift is due to currency exchange?

Arthur Brandwood: That's a good question, I'm not sure I'm the expert to answer that. The Australian dollar has been on an interesting ride in that the Australian dollar has appreciated strongly in the last few years, but then its reversed course in the last couple of years. That doesn't appear to have had much of an impact on the exports. There are other things happening particularly with the largest trading partner of China which I think are more powerful drivers rather than the straight currency exchange. But really it's not my area of expertise and so that's my lay interpretation of what's going on.

Joe Hage: Okay. Chad asks, if you have multiple distributors of a product in Australia, does it have to be registered by all sponsors or by just one sponsor?

Arthur Brandwood: You can do it either way. Some folks have multiple distributors each of which holds their own license. Some use one distributor to hold the licenses, and some use a third party such as ourselves. I would point out that it's generally a good idea to separate out the relationships with the distributor which deal with the commercial arrangements for distribution and supply. With the relationships with the regulatory representative.

For a number of reasons. Frequently distributors just don't have the expertise that's present in an expert regulatory firm. Some do but many don't. Separately if you do find that things are not going to plan with your distributor or you want to make some changes, the distributor can make life very difficult for you if they don't cooperate in terms of releasing the license. In some parts of the world you actually have to start again if the distributor will not release the license.

The distributor is actually in a powerful position if you allow them to hold your license for you. But in Australia you can do it any way you choose. You can have multiple sponsorships; you can have one held by a distributor or one held by a third party.

Joe Hage: If I remember correctly, there's a whole topic on distributors, distributor power and managing them in the summit. Is that right?

Arthur Brandwood: That's correct. Yes, we'll be looking at that issue in some depth because it works differently in different markets although there are some common themes particularly around whether it's wise to use a distributor for holding regulatory licenses.

Joe Hage: Do you recall who that speaker is or where that person's from?

Arthur Brandwood: We'll have several different speakers talking to that but one will be Davey Han from our Beijing office who talks specifically about experiences in China. I've seen some horror stories especially in China where surprisingly well-known large multinational names have built relationships with Chinese distributors who have magnanimously offered to handle the regulatory free of charge as a sweetener to get the contract.

They then outsource it to a very low-cost local supplier who either makes a mess of it or even worse gets into some improper conduct. In markets like China where you have renew the registration every few years, what usually happens is the initial regulatory provider had disappeared and then all of the faults come to light and a lot of hard work has to be done. We've certainly been involved in trying to negotiate with the CFDA to keep a product in the market when it's been discovered that a regulatory submission was actually falsified and it's possible to do that-

Joe Hage: Let's table that for San Diego because 41:13 questions are kind of pouring in right now.

Arthur Brandwood: Sure.

Joe Hage: Peter asks, how does the new allowance for Australian manufacturers to bypass TGA approval in lieu of a CE mark impact these companies?

Arthur Brandwood: Well, it means as a regulatory advisor I'm no longer telling Australian companies to go and move offshore. That's a simple as that. The problem was previously that the requirement to have a direct TGA assessment meant that companies in Australia would effectively require to double up on their conformity assessment.

Because the TGA process is very closely modeled on that of Europe, and TGA was generally slower and sometimes more expensive than having a CE from a notified body. But if you have an Australian manufacturer, typically you'd want to get the CE mark as well. So basically Australian manufacturers were being asked to pay twice and to take longer. That will no longer be the case; they will now be in exactly the same footing as everybody else.

Joe Hage: Got it. And his follow up is, how do you think it impacts the medical device market overall in Australia?

Arthur Brandwood: I think we'll see more local innovation. That will be one of the main impacts. Whether it will ... I don't think it will change the total size of the market or anything like that. It just means that competition is more equal now between domestic and international manufacturers.

Joe Hage: Okay. 42:55 from Bangalore asks, what is the timeline for registration of our Class 3 device?

Arthur Brandwood: Again it depends if ... I'm assuming that we're not talking about Class 3 devices with a medicine or a biologic. If we're talking about any other Class 3 medical device, then typically it's been between three and six months to pass through an application audit for an assessment based on a CE certificate for that medical device.

If you're going through a direct TGA conformity assessment for one of those devices with a medicine or a biologic, or if you choose to go for a direct TGA conformity assessment because you don't have a CE certificate, then that can take a lot longer. That can take six months to a year or even longer. But typically six months for a high risk medical device to be assessed in Australia.

But when the Confidence Building programme gains ground, we're expecting to see those times come down very rapidly.

Joe Hage: He also asks, if a clinical trial a must for a Class 3 device if it is an established device with another regulated market?

Arthur Brandwood: TGA expects to see clinical evidence, and in Class 3 devices that usually means direct clinical trials on the device. It doesn't mean that you can't get away with no clinical trial if it's an established technology. But in most cases you will have to have some direct clinical trial evidence.

TGA is particularly strict on clinical evidence. They I think rightly consider that they've been ahead of the game compared to the Europeans. And we're certainly seeing in the latest changes in Europe for example, a considerable tightening on the requirements for clinical evidence. Where in Europe as the new regulations come in, they will be the default position that all Class 3 devices require direct clinical trial evidence, unless there's a strong justification otherwise. That has been the position in Australia for some years.

Joe Hage: Okay. 45:11 asks, compared to the US, if I wanted to move my startup to Australia, how easy is it to access raw materials in Australia? And he notes that distributors in Europe are mainly from Germany and in Canada ... Oh, distributors in Europe are mainly from Germany, and in Canada they're probably US. So how easily can you access raw materials in Australia?

Arthur Brandwood: I'm assuming we're talking about biomaterials and components for medical devices. In these days of-

Speaker: 45:51 is that right?

Joe Hage: Go ahead I'll let you know what he 45:54.

Arthur Brandwood: In these days of internet commerce and availability of information about supply, it's relatively straight-forward. There's a fair bit of distance of course, you've got to ship things but, you know, internet trade is pretty popular here as it is in the rest of the world so it's ... It was more difficult 10 or 15 years ago; it's really not that much now.

Joe Hage: Okay. Capy 46:19 asks, how are true diagnostic products regulated by the TGA? Often these are self-certified for CE mark registration.

Arthur Brandwood: Yeah, and I haven't touched on IVDs much in the presentation today, so I'll try and summarize. But Australia has adopted the Global Harmonization Taskforce Classification System for IVDs. And as the questioner has pointed out, that's very different to what goes on in Europe. Here we have a four-tier classification and most IVDs are in Class 2 or Class 3 which means that they require a conformity assessment.

Most of those IVDs would be self-declared in Europe, and so it's not possible to produce a CE certificate that will be acceptable to TGA. There are therefore two pathways. One is to produce your ISO 13485 certificate to demonstrate there is quality management ... certified quality management system in place. And then to add on to that an application audit of the technical file. So it's basically a desk audit of the technical file plus a review of the third party certification of the quality system.

So that's one way through. The other is based on the Canadian certification because the Canadian regulatory system is very similar to the Australian for IVDs. Canadians use a very similar classification system that's similar to Conformity Assessment System. So for Class 3 IVDs particularly and you can enter the Australian market but if you have a Canadian certificate.

One difference that happens here that's not in Canada or in Europe is that there is a requirement for Class Four IVDs, the highest risk categories, for a type-test at a national reference laboratory. One of two laboratories here. And so that's for diagnostics for things like HIV and Hepatitis. Things used to screening the blood supply where there in additional layer of type-testing.

That's still working at Australian very much on the bleeding edge for IVD regulation. It's interesting that the Europeans are proposing to change the IVD Directives, the In Vitro Diagnostic Directive, and pick up pretty much the same classification system. We're expecting the Europeans to actually catch up with the Australian regulatory framework over the next couple of years.

Joe Hage: Great. By the way, I encourage you to keep asking your questions even if we can't get to all of them because there's quite a queue. But Arthur will receive the full list of all your questions and be able to respond to you after he gets his sleep I suspect.

Next is 49:09 who asks, are EU notified bodies accepting the clinical data collected in Australia for the purposes of CE certification?

Arthur Brandwood: To my knowledge the answer to that is yes. Certainly I've been involved in a number of product developments taking place here in Australia which have proceeded to CE mark based on clinical trials conducted here in Australia. Anecdotally I'm aware of quite a number of cases where that has been the case, so I'm assuming that generally Australian clinical data are acceptable in Europe.

With the caveat that all international clinical data has to be suitable in terms of the demographics of the patient population and the local clinical practice. There will be occasions where clinical data don't translate across borders. But the Australian medical system is pretty similar to the sophisticated medical systems in Europe so I'd be surprised if clinical data was not acceptable.

Joe Hage: Okay, thank you. Candice asks, can you renew your registration using a CE recertification certificate if this was not your initial certification path?

Arthur Brandwood: Okay. I'm not quite sure what the underlying question is there, but let me try and answer the question. If you're talking about somebody who's currently got a direct TGA assessment and then wants to use a CE certificate, then that's going to pretty straightforward.

Firstly, registrations don't need renewing. Once they're on the register they remain on the register providing you pay the annual fee. So there's no review of a registration in Australia once it's done. A registration that's been entered, for example, under an Australian TGA Conformity Assessment certificate, could stay on the register if the manufacturer in the future shifted to a CE certificate. They could choose to simply update the manufacturer evidence by filing the certificate with TGA for putting on a manufacturer database. But there would be no need to renew the ARTG entry.

Joe Hage: Thank you. Francesc asks, how long does it take to register molecular diagnostic cartridges for respiratory disease? Can you register it before having a distributor with a CE mark?

Arthur Brandwood: Again if we're talking about diagno ... I'm assuming that's referring to when we say molecular diagnostics that's an IVD. Again it will depend. If it's a Class 3 IVD as some molecular diagnostic may be, then a CE mark may not help you unless you've got a CE mark which is for a List A or List B diagnostic in Europe where there's been a notified body conformity assessment.

Again you may need to undergo a TGA desk audit of your technical file in conjunction with an ISO 13485 certificate to achieve a local registration here in Australia for those kinds of devices.

Joe Hage: Speaking of here in Australia, your friend Peter is on the line.

Arthur Brandwood: Uh-huh.

Joe Hage: And Peter has two questions. Do you have any further information regarding the TGA undertaking Confidence Building with other EC notified bodies?

Arthur Brandwood: What can I say? TGA is currently in dialog with a number of notified bodies. I think that's still going on and that's not all public information and I'm not privy to at all. There is intent to move that along fairly quickly, and I think complete the initial round of Confidence Building by early in 2015. I think that's what they're aiming to do but that will of course depend on how things work with notified bodies.

The industry has been working very hard to support TGA in that process through things like particular companies offering to host join audits between TGA and the notified bodies. And provide all three parties access to all the documentation to facilitate a transparent comparison. So there's a lot of hard work being done by both the regulatory agencies in Europe and in Australia and by the industries to make this process go forward.

Joe Hage: And I can answer Peter's second question, and the answer is yes. We are sending a replay of this recording, the transcript and the slides to everyone once we happen. The transcript typically takes up to a week.

54:27 is on the line. What would be the process for non-CE marked medical devices manufactured outside Australia? For example, gut sutures were banned in Europe so there is no CE mark on them.

Arthur Brandwood: Okay. If there is no CE mark, then the other alternative is to submit to direct TGA Conformity Assessment. And that doesn't matter wherever the device is manufactured. If there is no CE mark then you need to be directly assessed by TGA in a conventional conformity assesment process which will involve an onsite audit of both the quality system and the technical file.

And if it's something like a gut suture that's got a biologic in there, then there will be close attention paid to the biologic component in the same way that in Europe there is close attention paid to biologic components for medical devices. And with a separate review done there by the medicines agency in

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Europe. TGA will do a separate review and look at the biologic component particularly with regard to things like sourcing and viral and activation, and all the well-known risks for biologic source materials.

Joe Hage: Arul 55:47 has a barrel of questions I suspect you cannot answer. If a clinical trial is a must, what will be the timeline for a clinical trial for a Class 3 device? And I'm think that's hugely variable.

Arthur Brandwood: It is indeed. It could be anything from weeks to several years; it really depends on the device. If you've got a heart pump, you could take many months to a couple of years. If you've got an In Vitro Diagnostic, you can do it in a couple of weeks. And I hasten to add that that was not my phone.

Joe Hage: No no it was mine, and 56:27 and you'll all be pleased to know that it was some random solicitation 56:32 I suspect.

56:36 asks, what is the estimated cost savings for a Australian manufacturer to use a notified body?

Arthur Brandwood: Okay. Costs for conformity assessment by a notified body are broadly comparable to costs for conformity assessment by TGA. To give some idea of that, the basic cost for conformity assessment is around $50,000 whichever agency you go through. The problem was that previously domestic manufacturers had to do it twice so those costs were doubled. Now the costs are reduced to the cost of getting the CE mark, plus the cost of the ARTG application in Australia. And that can vary from as low as just over $1,000 for a lower risk device a Class 2A, to of the order of $10,000 for a high risk device with an add-on application audit. So the costs have come down dramatically.

Joe Hage: Okay, thank you. We spent our whole hour and while there's another question or two, I just wanted to let everyone know in case you're watching the clock. But Arthur if you can stay on the line-

Arthur Brandwood: I can for as long as-

Joe Hage: If folks do have to hang up, remember we're recording this and we'll make his answers available.

And Ned 58:10 asks, how is the route to register medical device Class 1 in Australia that have CE registration in Europe?

Arthur Brandwood: Okay. Class 1 medical devices don't require a CE certificate. They don't require a certificate in Europe either. Class 1 medical ... When I'm saying Class 1 I'm saying Class 1 medical devices with no measuring function and non-sterile. Those devices are self-declared in Europe that are CE marked but simply by the manufacturer. There is notified body review, and no CE certificate issue.

The same arrangement applies in Australia; there is a self-declaration process. They do however have to be entered onto the Australian Register for Therapeutic Goods. That's done through the online interface. There's no certificate got to be lodged, and there is no application fee. So it's a free

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registration and it's automatic. So you file the registration and the registration is granted overnight. The database refreshes overnight, so it's a 24-hour process.

There are a number of smarts 59:19 built in to the TGA database, so if you attempt to register something which the intelligence built into the database concludes it should not be a Class 1 medical device, then the system will not accept it directly and it is subject to review. But for genuine Class 1 medical devices it's simply filling the form online and the thing is approved overnight. TGA can then do a post-market audit and call for technical file data.

So it is unwise in the extreme to enter something onto the register if you don't actually hold the technical file including the clinical evidence. You need to have the full technical file for your Class 1 device. It is a criminal offense to make an entry onto the register when you don't hold the technical file evidence.

Joe Hage: And I'm going to ask a question. When we talked about it in the group about the Fast Track process and the campaign that you were among the champions of, TGA agreed to give domestic manufacturers the same access as importers.

Arthur Brandwood: Mm-hmm (affirmative).

Joe Hage: Is there an implication or anything changing for importers?

Arthur Brandwood: No, I think this has been to correct an imbalance, a different treatment. Australia I think was the only market in the world that I knew of that actually treated its domestic companies more harshly than its importers. Normally there are incentives the other way around. So that incongruence has been removed, but I don't see from here on in that the two groups of applicants being treated any differently.

Joe Hage: Arthur do you have some closing comments?

Arthur Brandwood: Yes, I'd just like to again say thank you for listening everybody. It's an interesting time in Australia. There's a lot of things going on here which are making the market very much more favorable for medical device development. And we're certainly seeing a lot of interest in that already. We're seeing companies looking to come and establish here, and we're seeing a greater willingness to take risk and to establish startups locally.

But also it is a fascinating time to be in Australia because of the engagement with the surrounding Asian nations. And particularly with China but not just with China. If you want to learn more about that I will remind you again, come along to the Asia Pacific Summit in San Diego next March, and which should be a great show. I'm really looking forward to coming over to the US and to meeting with many colleagues there and participating in that event.

Go deeper on this and related topics.
Join Arthur at The Asia-Pacific Summit for Medical Devices, March 5-6, San Diego, USA

Joe Hage: I will be there too. And on behalf of Arthur and the Medical Devices Group I thank you all for listening. Look in your emails for a link to this replay, the slides and the transcript. Thank you.

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